PATENT APPLICATION

We, being the persons identified below as the Applicant, request the grant of a patent to the person identified below as the Nominated Person, for an invention described in the accompanying standard complete specification.

Full application details follow.

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[54] Invention Title: PHARMACEUTICAL COMBINATION PREPARATION OF AN INHIBITOR OF THE SODIUM/HYDROGEN EXCHANGER AND A MEDICAMENT FOR THE TREATMENT OF CARDIOVASCULAR DISEASES

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By our Patent Attorneys,
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DATED this 26th day of August 1998.

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Pharmaceutical combination preparation of an inhibitor of the sodium/hydrogen exchanger and a medicament for the treatment of cardiovascular diseases

These combinations of an NHE inhibitor can comprise one or more therapeutically active compounds having cardiovascular activity. The combination of the cardioprotective properties with known therapies of cardiovascular diseases leads on the one hand to an improvement of the quality of the treatment and on the other hand in a large number of combinations to an additive or potentiated increase of the cardiovascular effects of the individual active compounds alone.
Application Number:  
Lodged:

Invention Title: PHARMACEUTICAL COMBINATION PREPARATION OF AN INHIBITOR OF THE SODIUM/HYDROGEN EXCHANGER AND A MEDICAMENT FOR THE TREATMENT OF CARDIOVASCULAR DISEASES

The following statement is a full description of this invention, including the best method of performing it known to us :-
Description

5 Pharmaceutical combination preparation of an inhibitor of the sodium/hydrogen exchanger and a medicament for the treatment of cardiovascular diseases

The invention relates to the combination of inhibitors of the sodium/hydrogen exchanger with other substances having cardiovascular activity for treating cardiovascular diseases.

Over the last years, inhibitors of the sodium/hydrogen exchanger (NHE) have been characterized in numerous preclinical studies as substances which, in cases of heart hypoperfusion, are suitable in a superior manner for preventing the destruction of the heart tissue at risk. The protection of the heart tissue by NHE inhibitors includes all manifestations of the damage caused by hypoperfusion, from arrhythmia, hypercontraction of the heart muscle and temporary loss of function up to necrosis of heart tissue and associated permanent damage.

The mechanism of action of the NHE inhibitors consists in a reduction of the increased sodium ion influx which is caused in hypoperfused tissues due to intracellular acidification and subsequent activation of the NHE. This results in a delay of the sodium overload of the tissue. Since sodium and calcium ion transport are coupled in heart tissue, this also prevents the life-threatening calcium overload of the heart cells. This unique mechanism of action of the NHE inhibitors makes it possible to combine them in an advantageous manner with active compounds which are used for treating various cardiovascular diseases and whose cardiovascular action is based on a variety of mechanisms of action.

These combinations of an NHE inhibitor may comprise one or more active
components having therapeutic vascular action. The combination of the heart-protecting properties with known therapies of cardiovascular diseases leads on the one hand to an improvement in the quality of the treatment and on the other hand in a large number of combinations to an additive or potentiated increase of the cardiovascular effects of the individual active components. In this context, the mechanistical prevention of sodium overload of the heart cells by the NHE inhibitors is particularly advantageous for the success of the treatment with the combination partner having cardiovascular activity.

The active compounds which are known and identified as NHE inhibitors are guanidine derivatives, preferably acylguanidines, inter alia such as described in the following publications and patent disclosures: Edward J. Cragoe, Jr., “DIURETICS, Chemistry, Pharmacology and Medicine”, J. WILEY & Sons (1983), 303 - 341, additionally compounds of the following formulae:

I. (HOE 89/F 288 - US 5 292 755)

a) benzoylguanidines of the formula I

\[
\begin{array}{c}
\text{R(1)} \\
\text{R(2)} \\
\text{N} \\
\text{HN} \\
\text{R(3)} \\
\text{R(4)} \\
\text{R(5)}
\end{array}
\]

in which:

\( R(1) \) or \( R(2) \)

is \( R(6)-S(O)_n^- \) or \( R(7)R(8)N-O_2S^- \);

and the other substituent \( R(1) \) or \( R(2) \) in each case

is \( H, \ F, \ Cl, \ Br, \ (C_1-C_4)-alkyl, \ (C_1-C_4)-alkoxy \) or \( \text{phenoxy} \), which is unsubstituted or substituted by 1 - 3 substituents

selected from the group consisting of fluorine, chorine, methyl and methoxy;

or the other substituent \( R(1) \) or \( R(2) \) in each case
is \( R(6) \)-S(O)\(_n\) or \( R(7)R(8)N^- \); 
\( n \) is zero, 1 or 2; 
\( R(6) \) is \((C_1-C_6)\)-alkyl, \((C_5-C_7)\)-cycloalkyl, cyclopentylmethyl, cyclohexylmethyl or phenyl, 
which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of fluorine, chlorine, methyl and methoxy; 
\( R(7) \) and \( R(8) \) identically or differently are H or \((C_1-C_6)\)-alkyl; 
or 
\( R(7) \) is phenyl-\((CH_2)_m\); 
\( m \) is 1 - 4; 
or 
\( R(7) \) is phenyl, 
which is unsubstituted or substituted by 1 - 2 substituents selected from the group consisting of fluorine, chlorine, methyl and methoxy; 
or 
\( R(7) \) and \( R(8) \) together are a straight-chain or branched \((C_4-C_7)\)-chain, 
where the chain can additionally be interrupted by O, S or \( NR(9) \); 
\( R(9) \) is H or methyl; 
or 
\( R(7) \) and \( R(8) \) together with the nitrogen atom to which they are bonded, are a dihydroindole, tetrahydroquinoline or tetrahydroisoquinoline system; 
\( R(3), R(4) \) and \( R(5) \) independently of one another are H or \((C_1-C_2)\)-alkyl, 
or
R(3) and R(4) together are a (C₂-C₄)-alkylene chain;

or

R(4) and R(5) together are a (C₄-C₇)-alkylene chain;

and their pharmaceutically tolerable salts;

(HOE 92/F 034 - US 5 373 924)

b) benzyloxyguanidines of the formula I

\[
\begin{align*}
\text{R(1)} & \quad \text{N} & \quad \text{NH₂} \\
\text{R(2)} & \quad \text{R(3)} & \quad \text{N} & \quad \text{NH₂} \\
\end{align*}
\]

in which:

R(1) is R(4)-SO\text{m} or R(5)R(6)N-SO₂⁻;

m is zero, 1 or 2;

R(4) and R(5) are Cl-C₆-alkyl, C₃-C₆-alkenyl or -C₆H₂₇-R(7);

n is zero, 1, 2, 3 or 4;

R(7) is C₅-C₇-cycloalkyl or phenyl, which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(8)R(9);

R(8) and R(9) are H or C₁-C₄-alkyl;

or

R(5) is H;

R(6) is H or C₁-C₄-alkyl,

or

R(5) and R(6) together are 4 or 5 methylene groups, of which one CH₂.
group can be replaced by an O, S, NH, N-CH₃ or N-benzyl;
R(2) is hydrogen, F, Cl, Br, (C₁-C₄)-alkyl, O-(CH₂)ₘₚₚₚₚₚₚₚₚ₋₁, or -X-R(10);
  m is zero or 1;
  p is 1, 2 or 3;
X is O, S or NR(11);
R(10) is H, C₁-C₅-alkyl, C₆-C₇-cycloalkyl, cyclohexylmethyl,
cyclopentylmethyl or -CₙH₂ₙ₋₁-R(12);
n is zero, 1, 2, 3 or 4;
R(12) is phenyl,
which is unsubstituted or substituted by 1 - 3
substituents selected from the group consisting
of F, Cl, CF₃, methyl, methoxy und NR(8)R(9);
R(8) and R(9)
are H or C₁-C₄-alkyl;
R(11) is hydrogen or C₁-C₅-alkyl;
or
R(10) and R(11)
together are 4 or 5 methylene groups, of which one
CH₂ group can be replaced by O, S, NH, N-CH₃ or
N-benzyl;
R(3) is defined as R(1), or is C₁-C₆-alkyl, nitro, cyano, trifluoromethyl, F,
Cl, Br, I or -X-R(10);
X is O, S or NR(11);
R(10) is H, C₁-C₅-alkyl, C₆-C₇-cycloalkyl, cyclohexylmethyl,
cyclopentylmethyl or -CₙH₂ₙ₋₁-R(12);
n is zero to 4;
R(12) is phenyl,
which is unsubstituted or substituted by 1 - 3
substituents selected from the group consisting of F,
Cl, CF₃, methyl, methoxy und NR(8)R(9);
R(8) and R(9)
are H or C₁-C₄-alkyl;
R(11) is C₁-C₃-alkyl,

or

R(10) and R(11)
together are 4 or 5 methylene groups, of which one
CH₂ group can be replaced by O, S, NH, N-CH₃ or
N-benzyl;

and their pharmaceutically tolerable salts;

(HOE 92/F 035 EP- Offenlegungsschrift 556 673)
c) ortho-substituted benzoylguanidines of the formula I

\[
\text{I}
\]

in which:

R(1) is F, Cl, Br, I, C₁-C₆-alkyl or \(-X\)-R(6);

X is O, S, NR(7) or Y-ZO;

Y is O or NR(7);

Z is C or SO;

R(6) is H, C₁-C₆-alkyl, C₅-C₇-cycloalkyl, cyclohexylmethyl,
cyclopentylmethyl, \(-(\text{CH}_2)_m\text{C}_p\text{F}_{2p+1}\) or \(-\text{C}_n\text{H}_{2n}\)-R(8);

m is zero or 1;

p is 1 - 3;

n is zero to 4;

R(8) is phenyl,

which is unsubstituted or substituted by 1 - 3
substituents selected from the group consisting
of F, Cl, CF₃, methyl, methoxy and NR(9)R(10);

R(9) and R(10)
are H or C₁-C₄-alkyl;

R(7) is H or C₁-C₃-alkyl;
or

R(6) and R(7)

together are 4 or 5 methylene groups, of which one CH₂

group can be replaced by O, S, NH, N-CH₃ or N-benzyl;

5 R(3) is H or -X-R(6);

X is O, S, NR(7) or Y-ZO;

R(7) is H or C₁₋C₃-alkyl;

Y is O or NR(7);

where Y is bonded to the phenyl radical of the

10 formula I,

Z is C or SO;

R(6) is H, C₁₋C₆-alkyl, C₅₋C₇-cycloalkyl, cyclohexylmethyl,

cyclopentylmethyl, -(CH₂)ₘC₆F₂ₙ₋₁ or -CₘH₂₋ₙ-R(8);

m is zero or 1;

15 p is 1 - 3;

n is zero to 4;

R(8) is phenyl,

which is unsubstituted or substituted by 1 - 3

substituents selected from the group consisting

20 of F, Cl, CF₃, methyl, methoxy and NR(9)R(10);

R(9) and R(10)

are H or C₁₋C₄-alkyl;

or

R(6) and R(7)

together are 4 or 5 methylene groups, of which one CH₂

group can be replaced by O, S, NH, N-CH₃ or N-benzyl;

25 R(2) and R(4)

identically or differently are R(11)-SO₃⁻ or R(12)R(13)N-SO₂⁻;

q is zero - 2;

30 R(11) is C₁₋C₄-alkyl,

which is unsubstituted or carries phenyl as a substituent,

where phenyl is unsubstituted or substituted by 1 - 3
substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(9)R(10);
R(9) and R(10)
are H or C₁-C₄-alkyl;

R(12) and R(13)
are defined as R(6) and R(7);
or one of the two radicals R(2) or R(4)
is hydrogen or is defined as R(1);
R(5) is H, methyl, F, Cl or methoxy,
and their pharmaceutically tolerable salts;
(HOE 92/F 036 - US 5 364 868)
d) benzoylguanidines of the formula I

\[
\text{I) } \begin{array}{c}
\text{R(1)} \\
\text{R(2)} \\
\text{0} \\
\text{NH₂} \\
\text{N} \\
\text{NH₂} \\
\end{array}
\]

in which:

R(1) or R(2)
is an amino group -NR(3)R(4);
R(3) and R(4)
identically or differently are H, C₁-C₆-alkyl or C₃-C₇-cycloalkyl;
or
R(3) is phenyl-(CH₂)ₚ-
p is 0, 1, 2, 3 or 4;
or
R(3) is phenyl,
where the phenyl in each case is unsubstituted or carries one to two
substituents selected from the group consisting of fluorine, chlorine,
methyl and methoxy;
or
R(3) and R(4)
together can be a straight-chain or branched C<sub>4</sub>-C<sub>7</sub>-methylene chain, where one -CH<sub>2</sub>- member of the methylene chain can be replaced by oxygen, S or NR(5);

R(5) is H or lower alkyl;

the other substituent R(1) or R(2) in each case is H, F, Cl, C<sub>1</sub>-C<sub>4</sub>-alkyl, C<sub>1</sub>-C<sub>4</sub>-alkoxy, CF<sub>3</sub>, C<sub>m</sub>F<sub>2m+1</sub>-CH<sub>2</sub>-, benzyl or phenoxy, where the respective phenyl radical is unsubstituted or carries one to two substituents selected from the group consisting of methyl, methoxy, fluorine and chlorine;

and their pharmaceutically tolerable salts;

(92/F 197 K - NZ 248 013)

e) benzoylguanidines of the formula I

\[
\begin{align*}
\text{R(1)} & \quad \text{R(2)} \\
\text{R(3)} & \\
& \quad \text{R(1)} \quad \text{R(2)} \quad \text{R(3)} \\
& & \quad \text{R(3)} \\
& & \quad \text{R(1)} \quad \text{R(2)} \\
& \quad \text{R(3)} \\
& \quad \text{R(1)} \quad \text{R(2)} \\
\end{align*}
\]

in which:

R(1) is R(4)-SO<sub>m</sub> or R(5)R(6)N-SO<sub>2</sub>-;

m is zero, 1 or 2;

R(4) and R(5)

are C<sub>1</sub>-C<sub>9</sub>-alkyl, C<sub>3</sub>-C<sub>8</sub>-alkenyl or -C<sub>n</sub>H<sub>2n</sub>-R(7);

n is zero, 1, 2, 3 or 4;

R(7) is C<sub>5</sub>-C<sub>7</sub>-cycloalkyl or phenyl, which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF<sub>3</sub>, methyl, methoxy and NR(8)R(9);

R(8) and R(9)

are H or C<sub>1</sub>-C<sub>4</sub>-alkyl;
or

R(5) is H;

R(6) is H or C<sub>1</sub>-C<sub>4</sub>-alkyl;

or

R(5) and R(6)
together are 4 or 5 methylene groups, of which one CH<sub>2</sub> group can be replaced by an O, S, NH, N-CH<sub>3</sub> or N-benzyl;

R(2) is hydrogen, straight-chain or branched (C<sub>5</sub>-C<sub>8</sub>)-alkyl,
-CR(13)=CHR(12) or -C=CR(12);

R(12) is phenyl,
which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF<sub>3</sub>, methyl, methoxy and NR(14)R(15);

R(14) and R(15)
are H or (C<sub>1</sub>-C<sub>4</sub>)-alkyl;

R(12) is (C<sub>1</sub>-C<sub>9</sub>)-heteroaryl,
which is unsubstituted or substituted as phenyl,

R(12) is (C<sub>1</sub>-C<sub>6</sub>)-alkyl,
which is unsubstituted or substituted by 1 - 3 OH,

R(12) is (C<sub>3</sub>-C<sub>8</sub>)-cycloalkyl;

R(13) is hydrogen or methyl,
or

R(12) is (C<sub>3</sub>-C<sub>9</sub>)-cycloalkyl, (C<sub>3</sub>-C<sub>8</sub>)-cycloalkyl-(C<sub>1</sub>-C<sub>4</sub>)-alkyl, phenyl,
C<sub>6</sub>H<sub>5</sub>-(C<sub>1</sub>-C<sub>4</sub>)-alkyl, naphthyl, biphenyl, 1,1-diphenyl-(C<sub>1</sub>-C<sub>4</sub>)-alkyl, cyclopentadienyl, pyridyl, pyrrolyl, furanyl, thiienyl,
thiazoly, oxazoly, indenyl, quinoly, indoly, benzofurany, benzothieny, benzothiazoly, benzoazoly, imidazoly, pyrazoly, triazoly, tetrazoly, isoxazoly, isothiazoly,
pyrazinyl, pyrimidinyl, pyridazinyl, indazolyl, isoquinolyl, 
phthalazinyl, quinoxaliny, quinazolinyl or cinnolinyl;

\( R(3) \) is defined as \( R(2) \);
and where the aromatic substituents \( R(2) \) and \( R(3) \) are unsubstituted or
substituted by 1 - 3 substituents from the groups F, Cl, CF\(_3\), (C\(_1\)-C\(_4\))-alkyl or
-alkoxy, or NR(10)R(11) with R(10) and R(11) being H or (C\(_1\)-C\(_4\))-alkyl;
and their pharmaceutically tolerable salts;

(HOE 92/F 303 K - EP- Offenlegungsschrift 589 336, NZ 248 703)
f) benzoylguanidines of the formula I

\[
R(1) \quad \begin{array}{c}
\text{C} = \text{C} \\
\text{C} = \text{C} \\
\text{C} \\
\text{N} = \text{C} \\
\text{NH}_2
\end{array} \\
\begin{array}{c}
\text{N} \\
\text{NH}_2
\end{array}
\]

in which:
R(1) or R(2)
is \( R(3)\)-S(O)(n)- or

\[
\text{R(4)} \quad \begin{array}{c}
\text{N} - \text{O}_2 \text{S} \\
\text{N}
\end{array}
\]

the other substituent R(1) or R(2) in each case
is H, OH, F, Cl, Br, I, C\(_1\)-C\(_4\)-alkyl, C\(_1\)-C\(_4\)-alkoxy, benzylxy or
phenoxy,
which is unsubstituted or carries one to three substituents
selected from the group consisting of fluorine, chlorine,
methyl, methoxy, hydroxyl and benzylxy,
R(3)-S(O)(n)-, -NR(4)R(5) or 3,4-dehydr-piperidine
R(3) is C\(_1\)-C\(_6\)-alkyl, C\(_5\)-C\(_7\)-cycloalkyl, cyclopentylmethyl,
cyclohexylmethyl or phenyl, 
which is unsubstituted or substituted by one to three
substituents selected from the group consisting of
fluorine, chlorine, methyl and methoxy;

R(4) and R(5)
identically or differently, are H or C₁-C₆-alkyl;
or

R(4) is phenyl-(CH₂)ₘ⁻;
m is 1, 2, 3 or 4;
or

R(4) is phenyl,
which is unsubstituted or carries one to two
substituents selected from the group consisting of
fluorine, chlorine, methyl and methoxy;
or

R(4) and R(5)
together are a straight-chain or branched C₄-C₇-chain, where the
chain can additionally be interrupted by O, S or NR(6),
R(6) is H or methyl;
or

R(4) and R(5)
together with the nitrogen atom to which they are bonded, are
a dihydroindole, tetrahydroquinoline or tetrahydroisoquinoline
system;
n is zero, 1 or 2;

and their pharmaceutically tolerable salts;

(92/F 304 - US 5 416 094)
g) isoquinolines of the formula I

\[
\begin{align*}
X(4) & \quad X(1) \\
X(3) & \quad X(2) \\
R(1) & \quad R(2) \\
\text{COG} & \\
\end{align*}
\]

in which:
R(1) is hydrogen, alkyl, cycloalkyl, arylalkyl, alkenyl, substituted
aminoalkyl or an aryl or heteroaryl ring;

where the rings are unsubstituted or substituted by 1 - 3 groups selected from the group consisting of halogen, nitro, amino, mono(lower alkyl)amino, di(lower alkyl)amino, lower alkyl, lower alkoxy, benzyloxy, phenoxy, hydroxyl, trifluoromethyl,

\( R(2) \) is hydrogen, halogen, alkyl or aryl;

which is unsubstituted or substituted by 1 - 3 groups selected from the group consisting of halogen, nitro, amino, mono(lower alkyl)amino, di(lower alkyl)amino, lower alkyl, lower alkoxy, benzyloxy, phenoxy, hydroxyl,

\( G \) is

\[
\begin{align*}
\text{N} & \quad \text{N} \\
\text{R(3)} & \quad \text{R(4)} \\
\text{R(5)} & \quad \text{R(6)}
\end{align*}
\]

\( X(2), X(3) \) and \( X(4) \)

independently of one another are hydrogen, halogen, nitro, amino, alkyl, sulfonamide, mono(lower alkyl)amino, di(lower alkyl)amino, lower alkyl, benzyloxy, hydroxyl;

\( X(1) \) is hydrogen, oxygen, sulfur or \( NR(7) \);

\( R(7) \) is hydrogen, alkyl, cycloalkyl, arylalkyl, alkenyl, substituted aminoalkyl or an aryl or a heteroaryl ring;

which rings are unsubstituted or substituted by 1 - 3 groups selected from the group consisting of halogen, nitro, amino, mono(lower alkyl)amino, di(lower alkyl)amino, lower alkyl, lower alkoxy, benzyloxy, phenoxy, hydroxyl and trifluoromethyl;

in which substituents each alkyl chain or alkenyl chain can be interrupted by oxygen, sulfur or \( NR(8) \);

\( R(8) \) is hydrogen, alkyl, cycloalkyl, arylalkyl, alkenyl, substituted aminoalkyl or an aryl or heteroaryl ring,
which rings are unsubstituted or substituted by 1 - 3 groups selected from the group consisting of halogen, nitro, amino, mono(lower alkyl)amino, di(lower alkyl)amino, lower alkyl, lower alkoxy, benzyloxy, phenoxy, hydroxyl and trifluoromethyl;

and their pharmaceutically acceptable salts;

(92/F 404 - EP 602 522, NZ 250 438)

h) compounds of the formula

\[
\begin{align*}
\text{R(1)} & \quad \text{is hydrogen, F, Cl, Br, I, } -\text{NO}_2, -\text{C} = \text{N}, -\text{CF}_3, \text{R(4)}-\text{SO}_m \text{ or } \\
\text{R(5)} & \quad \text{is zero, 1 or 2;} \\
\text{R(4)} & \quad \text{are } (\text{C}_1-\text{C}_9)-\text{alkyl}, (\text{C}_3-\text{C}_9)-\text{alkenyl}, -\text{C}_n\text{H}_{2n}-\text{R(7)} \text{ or } \text{CF}_3; \\
\text{n} & \quad \text{is zero, 1, 2, 3 or 4;} \\
\text{R(7)} & \quad \text{is } (\text{C}_3-\text{C}_7)-\text{cycloalkyl} \text{ or phenyl,} \\
\text{which is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF}_3, \text{methyl, methoxy and NR(8)R(9);} \\
\text{R(8) and R(9)} & \quad \text{are H or C}_1-\text{C}_4-\text{alkyl;} \\
or & \quad \text{R(5)} \quad \text{is H;}
\end{align*}
\]
R(6) is H or \((C_1-C_4)\)-alkyl;

or

R(5) and R(6)

together are 4 or 5 methylene groups, of which one \(\text{CH}_2\) group can be replaced by oxygen, S, NH, N-CH\(_3\) or N-benzyl;

R(2) is -SR(10), -OR(10), -NHR(10), -NR(10)R(11), -CHR(10)R(12),

-\([\text{CR}(12)\text{R}(13)\text{OR}(13')]\), -\([\text{C-}[\text{CH}_2-\text{OR}(13')]\)R(12) R(13) or

-\([\text{CR}(18)\text{R}(17)]_p-\text{(CO)}-\text{[CR}(19)\text{R}(20)]_q-\text{R}(14)\);

R(10), R(11)

identically or differently

are -\([\text{CHR}(16)]_s-(\text{CH}_2)_p-(\text{CHOH})_q-(\text{CH}_2)_r-(\text{CHOH})_t-\text{R}(21)\) or

-\((\text{CH}_2)_p-O-(\text{CH}_2-\text{CH}_2\text{O})_q-\text{R}(21)\),

R(21) is hydrogen, methyl,

p, q, r identically or differently

are zero, 1, 2, 3 or 4;

s is zero or 1;

t is 1, 2, 3 or 4;

R(12) and R(13)

identically or differently are hydrogen, \((C_1-C_6)\)-alkyl or,

together with the carbon atom carrying them, are a

\((C_3-C_8)\)-cycloalkyl,

R(13') is hydrogen or \((C_1-C_4)\)-alkyl;

R(14) is H, \((C_1-C_6)\)-alkyl, \((C_3-C_8)\)-cycloalkyl or \(-C_8\text{H}_{2a}-\text{R}(15)\);

a is zero, 1, 2, 3 or 4;

R(15) is phenyl,

which is unsubstituted or substituted by 1 - 3
substituents selected from the group consisting of F, Cl, CF\(_3\), methyl, methoxy and NR(8)R(9);

R(8) and R(9)

are H or \((C_1-C_4)\)-alkyl;

or
R(15) is (C₁-C₉)-heteroaryl,
    which is unsubstituted or substituted as phenyl,
    or
R(15) is (C₁-C₆)-alkyl,
    which is unsubstituted or substituted by 1 - 3
    OH;
R(16), R(17), R(18), R(19) and R(20)
    are hydrogen or (C₁-C₃)-alkyl;
R(3) is defined as R(1),
    or
R(3) is (C₁-C₆)-alkyl or -X-R(22);
    X is oxygen, S or NR(16);
R(16) is H or (C₁-C₃)-alkyl;
    or
R(22) and R(16)
    together are 4 or 5 methylene groups, of which one
    CH₂ group can be replaced by oxygen, S, NH, N-CH₃
    or N-benzyl;
R(22) is defined as R(14);
and their pharmaceutically tolerable salts;
(HOE 92/F 405 - EP 602 523, NZ 250 437)
i) benzoylguanidines of the formula I

\[
\begin{align*}
  &\text{R(1)} \quad \text{R(2)} \\
  &\text{R(3)} \\
\end{align*}
\]

in which:
R(1) is hydrogen, F, Cl, Br, I, -NO₂, -C≡N, R(16)-C₆H₄-p-O₂, R(4)-SO₃⁻ or
R(5)R(6)N-SO₂⁻;
    m is zero, 1 or 2;
p is zero or 1;
q is zero, 1, 2 or 3;
R(16) is C_rF_{2r+1};
   r is 1, 2 or 3;
R(4) and R(5)
   are (C_1-C_6)-alkyl, (C_6-C_9)-alkenyl, -C_nH_{2n}-R(7) or CF_3;
n is zero, 1, 2, 3 or 4;
R(7) is (C_3-C_7)-cycloalkyl or phenyl,
   which is not substituted or is substituted by 1-3
substituents selected from the group consisting
of F, Cl, CF_3, methyl, methoxy and NR(8)R(9);
R(8) and R(9)
   are H or C_1-C_4-alkyl;
or
R(5) is H;
R(6) is H or (C_1-C_4)-alkyl;
or
R(5) and R(6)
   together are 4 or 5 methylene groups, of which one CH_2
   group can be replaced by oxygen, S, NH, N-CH_3 or N-benzyl,
R(2) is (C_1-C_6)-heteroaryl,
   which is linked via C or N and which is unsubstituted or
   substituted by 1-3 substituents selected from the group
   consisting of F, Cl, CF_3, CH_3, methoxy, hydroxyl, amino,
methylamino and dimethylamino;
or
R(2) is -SR(10), -OR(10), -NR(10)R(11), -CR(10)R(11)R(12);
R(10) is -C_9H_{2a}(C_1-C_6)-heteroaryl,
   which is unsubstituted or substituted by 1-3
substituents selected from the group consisting of F,
   Cl, CF_3, CH_3, methoxy, hydroxyl, amino, methylamino
   and dimethylamino;
a is zero, 1 or 2;

R(11) and R(12)

independently of one another are defined as R(10) or are
hydrogen or (C₁-C₄)-alkyl;

5 R(3) is defined as R(1), or is (C₁-C₆)-alkyl or -X-R(13);

X is oxygen, S, or NR(14);

R(14) is H or (C₁-C₃)-alkyl;

R(13) is H, (C₁-C₆)-alkyl, (C₃-C₈)-cycloalkyl or -C₆H₂₅-R(15);

b is zero, 1, 2, 3 or 4;

10 or

R(13) and R(14)

together are 4 or 5 methylene groups, of which one CH₂

group can be replaced by oxygen, S, NH, N-CH₃ or N-benzyl;

R(15) is phenyl,

15 which is unsubstituted or substituted by 1 - 3

substituents selected from the group consisting of F,

Cl, CF₃, methyl, methoxy and NR(8)R(9);

R(8) and R(9)

are H or (C₁-C₄)-alkyl;

20 and their pharmaceutically tolerable salts;

(HOE 92/F 411 - NZ 250 450, EP 603 650)

k) benzoylguanidines of the formula I

\[
\begin{align*}
\text{R(1)} & \\
\text{R(2)} & \\
\text{R(3)} & \\
\text{R(4)} & \\
\text{N} & \\
\text{NH₂} & \\
\text{NH₂} & \\
\end{align*}
\]  

(1)  

30 in which:

one of the substituents R(1), R(2), R(3) or R(4)
19

\[
\begin{array}{c}
\text{is an amino group} \quad \overset{\text{R(5)}}{\text{N}} \quad \overset{\text{R(6)}}{\text{C}_n\text{H}_2n}
\end{array}
\]

\[R(5)\text{ is hydrogen or } C_{(1-8)}\text{-alkyl;}
\]
\[n\text{ is zero, 1, 2, 3 or 4;}
\]
\[R(6)\text{ is } H\text{ or } C_{(1-4)}\text{-alkyl;}
\]
\[5\text{ in which one CH}_2\text{ group can be replaced by 1 sulfur atom or a group}
\]
\[\text{NR(7);}
\]
\[R(7)\text{ is hydrogen, methyl or ethyl;}
\]
or
\[R(6)\text{ is } C_{(3-8)}\text{-cycloalkyl or phenyl,}
\]
\[10\text{ which is unsubstituted or carries 1, 2 or 3 substituents}
\]
\[\text{selected from the group consisting of } F, \text{ Cl, Br, methyl, methoxy, } -NR(8)R(9);
\]
\[R(8) \text{ and } R(9)
\]
\[\text{are } H, \text{ methyl or ethyl;}
\]
or
\[R(5) \text{ and } R(6)
\]
\[\text{together with the nitrogen atom are a 5-, 6- or 7-membered}
\]
\[\text{ring, in which 1 carbon atom can be replaced by oxygen, } S \text{ or}
\]
\[\text{NR(10);}
\]
\[20\text{ R(10) is } H, \text{ } C_{(1-3)}\text{-alkyl or benzyl;}
\]
and the other substituents R(1), R(2), R(3), R(4) in each case are:

\[\text{hydrogen, } F, \text{ Cl, Br, I, CN, CF}_3, \text{ NO}_2, \text{ CF}_3\text{-O-, } C_{mF_{2m+1}}\text{-CH}_2\text{-O- or}
\]
\[R(11)-C_qH_{2q}X_p-;
\]
\[m\text{ is } 1, 2 \text{ or } 3;
\]
\[25\text{ q is zero, 1, 2, 3 or 4;}
\]
\[p\text{ is zero or 1;}
\]
\[X\text{ is oxygen or } NR(12);
\]
\[R(12)\text{ is } H \text{ or } C_{(1-3)}\text{-alkyl;}
\]
\[R(11)\text{ is hydrogen, } C_{(1-6)}\text{-alkyl, } C_{(3-8)}\text{-cycloalkyl or phenyl,}
\]
which is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, CH₃, CH₂-O- and NR(13)R(14); R(13), R(14) are H, methyl or ethyl;
and their pharmaceutically tolerable salts;
(HOE 92/F 422 - EP 604 852)
l) benzoylguanidines of the formula I

\[
\begin{align*}
R(1) & \quad \text{is } R(4)R(5)N-C(X)--; \\
15 \quad X & \quad \text{is oxygen, S or N-R(6);} \\
R(4) & \quad \text{and } R(5) \\
& \quad \text{identically or differently, are } H, \text{(C}_1\text{-C}_6\text{)-alkyl, (C}_3\text{-C}_6\text{)-alkenyl} \\
\text{or } & \quad -C_nH_{2n}-R(7); \\
\quad n & \quad \text{is zero, 1, 2, 3 or 4;} \\
20 \quad R(7) & \quad \text{is (C}_5\text{-C}_7\text{-cycloalkyl or phenyl,} \\
& \quad \text{which is unsubstituted or substituted by 1 - 3} \\
& \quad \text{substituents selected from the group consisting} \\
& \quad \text{of F, Cl, CF₃, methoxy and (C}_1\text{-C}_4\text{)-alkyl;} \\
& \quad \text{or} \\
\end{align*}
\]

or
\[
\begin{align*}
R(4) & \quad \text{and } R(5) \\
& \quad \text{together are 4 or 5 methylene groups, of which one CH₂} \\
& \quad \text{group can be replaced by oxygen, S, NH, N-CH₃ or N-benzyl;} \\
R(6) & \quad \text{is defined as } R(4) \text{ or is amidine;} \\
\end{align*}
\]
R(2) is H, F, Cl, Br, I, (C₁-C₆)-alkyl, 1-alkenyl or 1-alkynyl,
(C₃-C₆)-cycloalkyl, (C₃-C₆)-cycloalkyl-(C₁-C₄)-alkyl, phenyl,
C₆H₅-(C₁-C₄)-alkyl, naphthyl, biphenyl, 1,1-diphenyl-(C₁-C₄)-alkyl,
cyclopentadienyl, pyridyl, thiopyridyl, pyrrolyl, furanyl, thienyl,
thiazolyl, oxazolyl, indenyl, quinolyl, indolyl, benzofuranyl, benzothienyl, benzothiazolyl, benzoxazolyl or -W-R(8);

W is oxygen, S or NR(9);

R(8) is H, (C₁-C₉)-alkyl, (C₅-C₇)-cycloalkyl, cyclohexylmethyl, cyclopentylmethyl, -(CH₂)mCₙF₂p₊₁ or -C₈H₂q-R(10);

m is zero or 1;

p is 1, 2 or 3;

q is zero, 1, 2, 3 or 4;

R(10) is phenyl, which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(11)R(12);

R(11) and R(12) are H or (C₁-C₄)-alkyl;

R(9) is H or (C₁-C₃)-alkyl;

or

R(8) and R(9) together are 4 or 5 methylene groups, of which one CH₂ group can be replaced by oxygen, S, NH, N-CH₃ or N-benzyl;

R(3) is H, F, Cl, Br, I, (C₁-C₉)-alkyl or -W-R(8) as defined for R(2), and their pharmaceutically acceptable salts;

(93/F 054 - NZ 250 919, EP- Offenlegungsschrift 612 723)
m) benzoyleguanidines of the formula I

\[
\begin{array}{c}
R(1) \\
\text{N} \quad \text{H} \\
R(2) \\
\text{N} \quad \text{H} \\
\text{R(3)} \\
\text{O} \\
\end{array}
\]

in which:

- R(1), R(2), R(3) are hydrogen, F, Cl, Br, I or (C\(_1\)-C\(_{12}\))-alkyl;
- one of the substituents R(1), R(2) and R(3) is N\(_3\), CN, OH or (C\(_1\)-C\(_{10}\))-alkyloxy, if at least one of the remaining substituents R(1), R(2) or R(3) is a sufficiently lipophilic alkyl radical having 3 to 12 carbon atoms;
- or
- one of the substituents R(1), R(2) and R(3) is R(4)-CH\(_2n\)-OM-;
  - m is zero or 1;
  - n is zero, 1, 2 or 3;
  - R(4) is C\(_p\)F\(_{2p+1}\);
  - p is 1, 2 or 3, if n is zero or 1;
  - or
  - R(4) is (C\(_3\)-C\(_{12}\))-cycloalkyl, phenyl, pyridyl, quinolyl or isoquinolyl, where the aromatic and heteroaromatic ring systems are unsubstituted or substituted by a substituent selected from the group consisting of F, Cl, CF\(_3\), methyl, methoxy and NR(5)R(6);
  - R(5) and R(6) are hydrogen or (C\(_1\)-C\(_4\))-alkyl;
- or one of the substituents R(1), R(2) and R(3) is -C=CR(5) or -C[R(6)] = CR(5);
R(5) is phenyl, which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy, hydroxyl, amino, methylamino and dimethylamino, (C₄-C₄)-heteroaryl, which is unsubstituted or substituted as phenyl, or R(5) is (C₅-C₆)-alkyl, which is unsubstituted or substituted by 1 - 3 OH; or R(5) is (C₆-C₈)-cycloalkyl, R(6) is hydrogen or methyl; and their pharmacologically acceptable salts;

(93/F 153 - EP- Offenlegungsschrift 627 413, NZ 260 660)

o) benzoylguanidines of the formula I

\[
\begin{align*}
\text{R}(1) & \quad \text{R}(2) \\
\text{R}(3) & \quad \text{R}(4) \\
\text{R}(5) & \quad \text{R}(6) \\
\end{align*}
\]

in which:

R(1) is hydrogen, F, Cl, Br, I, -NO₂, -C=N, X₅-(CH₂)₆-(CF₂)₇-CF₃, R(5)-SO₃, R(6)-CO⁻ or R(6)R(7)N-SO₂⁻, where

X is oxygen, S or NR(14);
m is zero, 1 or 2;
o is zero or 1;
p is zero, 1 or 2;
q is zero, 1, 2, 3, 4, 5 or 6;
R(5) and R(6) are (C₆-C₈)-alkyl, (C₃-C₆)-alkenyl, -C₅H₄n-R(8) or CF₃;
R(5) and R(6) are (C₆-C₈)-alkyl, (C₃-C₆)-alkenyl, -C₅H₄n-R(8) or CF₃;
R(8) is (C₃-C₇)-cycloalkyl or phenyl, which is not substituted or is substituted by 1 - 3
substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(9)R(10);
R(9) and R(10) are H or C₁-C₄-alkyl;
or
R(6) is H;
R(7) is H or (C₁-C₄)-alkyl;
or
R(6) and R(7) together are 4 or 5 methylene groups, of which one CH₂
R(2) is \(-Y\)\(\text{C}_{\text{h}}\)\(-\text{CHOH}\)\(_{\text{i}}\)-\(-\text{CH}_2\)\(_{\text{j}}\)-\(-\text{CHOH}\)\(_{\text{k}}\)-\(\text{R}(-11)\)
or
\(-Y\)\(\text{C}_{\text{h}}\)\(-\text{CHOH}\)\(_{\text{i}}\)-\(-\text{CH}_2\)\(_{\text{j}}\)-\(-\text{CHOH}\)\(_{\text{k}}\)-\(\text{R}(-11)\)
or
\(-Y\)\(\text{C}_{\text{h}}\)\(-\text{CHOH}\)\(_{\text{i}}\)-\(-\text{CH}_2\)\(_{\text{j}}\)-\(-\text{CHOH}\)\(_{\text{k}}\)-\(\text{R}(-11)\)
Y is oxygen, -S- or -NR(12)-;
R(11) and R(12) are hydrogen or (C₁-C₄)-alkyl;
h is zero or 1;
i, j and k

independently are zero, 1, 2, 3 or 4;

but where h, i and k are not simultaneous; zero,

R(3) is defined as R(1), or is (C\textsubscript{1}-C\textsubscript{6})-alkyl or -X-R(13);

5 \[ \begin{align*}
X & \text{ is oxygen, S or NR(14);} \\
R(14) & \text{ is H or (C\textsubscript{1}-C\textsubscript{3})-alkyl;} \\
R(13) & \text{ is H, (C\textsubscript{1}-C\textsubscript{6})-alkyl, (C\textsubscript{3}-C\textsubscript{6})-cycloalkyl or -C\textsubscript{6}H\textsubscript{2n}-R(15);} \\
\text{b} & \text{ is zero, 1, 2, 3 or 4;} \\
\text{or} & \\
R(13) & \text{ and R(14) together are 4 or 5 methylene groups, where one CH\textsubscript{2} group can be replaced by oxygen, S, NH, N-CH\textsubscript{3} or N-benzyl;} \\
R(15) & \text{ is phenyl,} \]

10 which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF\textsubscript{3}, methyl, methoxy and NR(9)R(10);

R(9) and R(10) are H or (C\textsubscript{1}-C\textsubscript{4})-alkyl;

15 R(4) is hydrogen, -OR(16) or -NR(16)R(17);

R(16) and R(17) independently are hydrogen or (C\textsubscript{1}-C\textsubscript{3})-alkyl;

and their pharmaceutically tolerable salts;

(HOE 93/F 154 - EP- Offenlegungsschrift 628 543, NZ 260 681)

20 p) benzoylguanidines of the formula I

\[
\begin{align*}
& \text{R(1)} \\
& \text{R(2) - R(5)} \\
& \text{R(3)} \\
& \text{R(4) - R(1)} \\
& \text{NH}_{2} \\
\end{align*}
\]

30 in which:
R(1) is R(6)-CO or R(7)R(8)N-CO;
R(6) is (C_1-C_8)-alkyl, (C_1-C_8)-perfluoroalkyl, (C_3-C_8)-alkenyl or
-C_nH_{2n-1}R(9);
n is zero, 1, 2, 3 or 4;
R(9) is (C_3-C_8)-cycloalkyl, phenyl, biphenylyl or naphthyl,
where the aromatics are not substituted or are
substituted by 1 - 3 substituents selected from
the group consisting of F, Cl, CF_3, methyl,
methoxy and NR(10)R(11);
R(10) and R(11)
are H, (C_1-C_8)-alkyl or (C_1-C_8)-perfluoro-
alkyl;
R(7) is H, (C_1-C_8)-alkyl, (C_1-C_8)-perfluoroalkyl, (C_3-C_8)-alkenyl or
-C_nH_{2n-1}R(12);
n is zero, 1, 2, 3 or 4;
R(12) is (C_3-C_8)-cycloalkyl, phenyl, biphenylyl or naphthyl,
where the aromatics are not substituted or are
substituted by 1 - 3 substituents selected from
the group consisting of F, Cl, CF_3, methyl,
methoxy and NR(13)R(14);
R(13) and R(14)
are H, (C_1-C_8)-alkyl or (C_1-C_8)-perfluoro-
alkyl;
R(8) is H, (C_1-C_8)-alkyl or (C_1-C_8)-perfluoroalkyl;
or
R(7) and R(8)
together are 4 or 5 methylene groups, of which one CH_2

group can be replaced by oxygen, S, NH, N-CH_3 or N-benzyl;
R(2) is defined as R(1), or is H, F, Cl, Br, I, CN, NO_2, (C_1-C_8)-alkyl,
(C_1-C_8)-perfluoroalkyl, (C_3-C_8)-alkenyl or -C_nH_{2n}R(15);
n is zero, 1, 2, 3, 4;
R(15) is (C_3-C_8)-cycloalkyl, phenyl, biphenylyl or naphthyl,
where the aromatics are not substituted or are
substituted by 1 - 3 substituents selected from the
group consisting of F, Cl, CF₃, methyl, methoxy and
NR(16)R(17);

R(16) and R(17)
are H, (C₁-C₄)-alkyl or (C₁-C₄)-perfluoro-
alkyl;
or
R(2) is (C₁-C₆)-heteroaryl,
which is linked via C or N and which is unsubstituted or
substituted by 1 - 3 substituents selected from the group
consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino,
methylamino and dimethylamino;
or
R(2) is SR(18), -OR(18), -NR(18)R(19), -CR(18)R(19)R(20);
R(18) is -C₆H₄-(C₁-C₆)-heteroaryl,
which is unsubstituted or substituted by 1 - 3
substituents selected from the group consisting of F,
Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino
and dimethylamino;
a is zero, 1 or 2;
R(19) and R(20)
are independently of one another are defined as R(18) or are
hydrogen, (C₁-C₄)-alkyl or (C₁-C₄)-perfluoroalkyl;
or
R(2) is R(21)-SOₘ or R(22)R(23)N-SO₂⁻;
m is 1 or 2;
R(21) is (C₁-C₆)-alkyl, (C₁-C₆)-perfluoroalkyl, (C₃-C₉)-alkenyl, -CₙH₂ₙ⁻
R(24),
n is zero, 1, 2, 3 or 4;
R(24) is (C₃-C₆)-cycloalkyl, phenyl, biphenyl or naphthyl,
substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(27)R(28); R(27) and R(28) are H, (C₁-C₄)-alkyl or (C₁-C₄)-perfluoroalkyl; 

R(22) is H, (C₁-C₈)-alkyl, (C₁-C₈)-perfluoroalkyl, (C₂-C₈)-alkenyl, -CₙH₂ₙ-R(29); 

n is zero, 1, 2, 3 or 4; 

R(29) is (C₃-C₈)-cycloalkyl, phenyl, biphenyl or naphthyl, where the aromatics are not substituted or are substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(30)R(31); 

R(30) and R(31) are H, (C₁-C₄)-alkyl or (C₁-C₄)-perfluoroalkyl; 

R(23) is H, (C₁-C₄)-alkyl or (C₁-C₄)-perfluoroalkyl; or 

R(22) and R(23) together are 4 or 5 methylene groups, of which one CH₂ group can be replaced by oxygen, S, NH, N-CH₃ or N-benzyl; or 

R(2) is R(33)X--; 

X is oxygen, S, NR(34), (D=O)A-, NR(34)C=MN(*)R(35)--; 

M is oxygen or S; 

A is oxygen or NR(34); 

D is C or SO; 

R(33) is (C₁-C₈)-alkyl, (C₃-C₈)-alkenyl, (CH₂)₃CₙF₂d+₁, -CₙH₂ₙ-R(36), 

b is zero or 1; 

d is 1, 2, 3, 4, 5, 6 or 7; 

n is zero, 1, 2, 3 or 4;
R(36) is \((C_3-C_8)\)-cycloalkyl, phenyl, biphenyl or naphthyl, where the aromatics are not substituted or are substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(37)R(38); R(37) and R(38) are H, \((C_1-C_4)\)-alkyl or \((C_1-C_4)\)-perfluoroalkyl; R(34) is H, \((C_1-C_4)\)-alkyl or \((C_1-C_4)\)-perfluoroalkyl; R(35) is defined as R(33); or R(33) and R(34) together are 4 or 5 methylene groups, of which one CH₂ group can be replaced by oxygen, S, NH, N-OH or N-benzyl; where A and N° are bonded to the phenyl nucleus of the benzoxylguanidine parent structure; or R(2) is -SR(40), -OR(40), -NHR(40), -NR(40)R(41), -CHR(40)R(42), -C[R(42)R(43)OH], -C=CR(45), -CR(46)=CHR(45), -[CR(47)R(48)]_u-\{(CO)\}-[CR49]R(50)]_v-R(44); R(40), R(41) identically or differently are -\((CH_2)_p\)-(CHOH)₉-(CH₂)₉-(CHOH)₉- R(51) or -(CH₂)ₚ-O-(CH₂CH₂O)₉-R(51); R(51) is hydrogen or methyl; u is 1, 2, 3 or 4; v is zero, 1, 2, 3 or 4; p, q, r identically or differently are zero, 1, 2, 3 or 4; t is 1, 2, 3 or 4; R(42) and R(43) identically or differently are hydrogen or \((C_1-C_6)\)-alkyl;
or
R(42) and R(43)
together with the carbon atom carrying them form a (C₃-C₈)-
cycloalkyl;

5 R(44) is H, (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl or -C₆H₂₉-R(45);
e is zero, 1, 2, 3 or 4;

R(45) is phenyl,
which is unsubstituted or substituted by 1 - 3
substituents from the group consisting of F, Cl, CF₃,
methyl, methoxy and NR(52)R(53) where
R(52) and R(53) are H or (C₁-C₄)-alkyl, or

R(45) is (C₁-C₆)-heteroaryl,
which is unsubstituted or substituted as phenyl;
or

15 R(45) is (C₁-C₆)-alkyl,
which is unsubstituted or substituted by 1 - 3 OH;

R(46), R(47), R(48), R(49) and R(50)
are hydrogen or methyl;
or

20 R(2) is R(55)-NH-SO₂⁻;
R(55) is R(56)R(57)N-(C=Y)-;
Y is oxygen, S or N-R(58);
R(56) and R(57)
identically or differently are H, (C₁-C₆)-alkyl, (C₃-C₆)-
alkenyl or -C₆H₂₉-R(59);
f is zero, 1, 2, 3 or 4;

R(59) is (C₅-C₇)-cycloalkyl or phenyl,
which is unsubstituted or substituted by 1
- 3 substituents selected from the group
consisting of F, Cl, CF₃, methoxy and
(C₁-C₄)-alkyl;
or
R(56) and R(57) together are 4 or 5 methylene groups, of which one CH$_2$ group can be replaced by oxygen, S, NH, N-CH$_3$ or N-benzyl;

R(58) is defined as R(56) or is amidine;

R(3), R(4) and R(5) independently of one another are defined as R(1) or R(2); and their pharmaceutically tolerable salts;

(HOE 93/F 220 - EP- Offenlegungsschrift 640 593, NZ 264 117)

q) benzoylguanidines of the form,

\[
\begin{align*}
R(1) & \quad R(2) \\
\text{NH} & \quad \text{NH}_2 \\
R(3) & \quad R(4) \\
\end{align*}
\]

in which:

R(1) is hydrogen, F, Cl, Br, I, -NO$_2$, -C=O, -X$_n$-(CH$_2$)$_p$-(CF$_2$)$_q$-CF$_3$,
R(5)-SO$_m$-, R(6)-CO-, R(6)R(7)N-CO- or R(6)R(7)N-SO$_2$-;
X is oxygen, -S- or NR(14);

m is zero, 1 or 2;
o is zero or 1;
p is zero, 1 or 2;
q is zero, 1, 2, 3, 4, 5 or 6;

R(5) and R(6) are (C$_1$-C$_9$)-alkyl, (C$_3$-C$_8$)-alkenyl, -C$_n$H$_{2n}$-R(8) or CF$_3$;

n is zero, 1, 2, 3 or 4;

R(8) is (C$_3$-C$_7$)-cycloalkyl, phenyl, which is not substituted or is substituted by 1 to
3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(9)R(10); R(9) and R(10) are H or (C₁₋C₄)-alkyl;

or

R(6) is hydrogen;

R(7) is hydrogen or (C₁₋C₄)-alkyl;

or

R(6) and R(7) together are 4 or 5 methylene groups, of which one CH₂ group can be replaced by oxygen, S, NH, N-CH₃ or N-benzyl;

R(2) is

$$\begin{align*}
\text{Y} & \quad \text{R(1)} \\
\text{Y} & \quad \text{R(1)} \\
\text{Y} & \quad \text{R(1)}
\end{align*}$$

R(11) is (C₁₋C₉)-heteroaryl, which is linked via C or N and which is unsubstituted or substituted by 1 to 3 substituents selected from the group consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino, dimethylamino and benzyl;

Y is oxygen, -S- or NR(12);

R(12) is H or (C₁₋C₄)-alkyl;

R(3) is defined as R(1);

or

R(3) is (C₁₋C₉)-alkyl or -X-R(13);

X is oxygen, -S- or NR(14);

R(14) is H or (C₁₋C₃)-alkyl;

R(13) is H, (C₁₋C₉)-alkyl, (C₃₋C₈)-cycloalkyl or -C₅H₂₅-R(15);

b is zero, 1, 2, 3 or 4;

or

R(13) and R(14)
together are 4 or 5 methylene groups, of which one
CH₂ group can be replaced by oxygen, S, NH, N-CH₃
or N-benzyl;

R(15) is phenyl,

which is unsubstituted or substituted by 1 - 3
substituents selected from the group consisting
of F, Cl, CF₃, methyl, methoxy and NR(9)R(10);
R(9) and R(10)
are H or (C₁-C₄)-alkyl;

R(4) is hydrogen, -OR(16), -NR(16)R(17) or CₓF₂r₊₁;
R(16) and R(17)
independently are hydrogen or (C₁-C₃)-alkyl;
r is 1, 2, 3 or 4;
and their pharmaceutically tolerable salts;

r) benzo-fused 5-membered ring heterocycles of the formula I

in which:

X is N or CR(6);
Y is oxygen, S or NR(7);
A, B together are a bond
or
A, B are both hydrogen, if X is simultaneously CR(6) and Y is NR(7);

one of the substituents R(1) to R(6) is a -CO-N=C(NH₂)₂ group;
the other substituents R(1) to R(6) in each case
are hydrogen, F, Cl, Br, I or (C₁-C₆)-alkyl;
up to two of the other substituents R(1) to R(6) are CN, NO₂, N₃, (C₁-C₄)-alkyloxy or CF₃;
up to one of the other substituents is R(8)-CₙH₂₂n-Z⁻;

n is zero to 10;
where the alkylene chain -CₙH₂ₙ- is straight-chain or branched and where one carbon atom can be replaced by an oxygen or sulfur atom or by a nitrogen atom;

R(8) is hydrogen, (C₂-C₈)-alkenyl or (C₃-C₁₀)-cycloalkyl,

which is unsubstituted or substituted by 1 to 4 methyl groups or an OH group, or can contain an ethylene group -CH=CH-, and in which one methylene group can be replaced by an oxygen or sulfur atom or by a nitrogen atom;

or

R(8) is phenyl,

which is unsubstituted or substituted by 1 to 3 substituents selected from the group consisting of F, Cl, Br, I, CF₃, CH₃-S(O)₂⁻ or R(9)-W⁻;

s is zero, 1 or 2;
R(9) is H, methyl, ethyl,
W can be oxygen or NR(10);

R(10) is H or methyl;
y is zero or 1;

or

R(8) is CₘF₂ᵐ⁻¹;

m is 1 to 3;

or

R(8) is 1- or 2-naphthyl, pyridyl, quinolyl or isoquinolyl;

Z is -CO-, -CH₂⁻ or -[CR(11)(OH)]ₙ⁻;

q is 1, 2 or 3;
R(11) is H or methyl;
or
Z is oxygen or -NR(12)-
R(12) is H or methyl;
or
5
Z is -S(O)₅⁻;
s is zero, 1 or 2;
or
Z is -SO₂-NR(13)-
R(13) is H or (C₁-C₄)-alkyl;
R(7) is hydrogen, (C₁-C₁₀)-alkyl, (C₂-C₁₀)-alkenyl or R(8)-CₙH₂ₙ⁻;
and their pharmaceutically tolerable salts;
(HOE 93/F 236 - EP- Offenlegungsschrift 638 548, NZ 264 216)
s) benzoylguanidines of the formula I

R(1), R(3) or R(4)
is -NR(6) C=X NR(7)R(8);
X is oxygen or S;
R(6) is hydrogen, (C₁-C₆)-alkyl, (C₁-C₆)-perfluoroalkyl,
(C₃-C₆)-alkenyl or -CₙH₂ₙ⁻R(9);
n is zero, 1, 2, 3 or 4;
R(9) is (C₃-C₆)-cycloalkyl, phenyl, biphenylyl or naphthyl,
where the aromatics are not substituted
or are substituted by 1 - 3 substituents
selected from the group consisting of F, Cl, CF₃, methyl, methoxy and
NR(10)R(11);
R(10) and R(11) are H, (C₁₋C₄)-alkyl or (C₁₋C₄)-perfluoroalkyl;

R(7) is hydrogen, (C₁₋C₆)-alkyl, (C₁₋C₆)-perfluoroalkyl, (C₃₋C₆)-alkenyl or -C₅H₂₀-R(12);
o is zero, 1, 2, 3 or 4;
R(12) is (C₅₋C₆)-cycloalkyl, phenyl, biphenylyl or naphthyl,

where the aromatics are not substituted or are substituted by 1-3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and

NR(13)R(14);
R(13) and R(14) are H, (C₁₋C₄)-alkyl or (C₁₋C₄)-perfluoroalkyl;
R(8) is defined as R(7);
or
R(7) and R(8) together are 4 or 5 methylene groups, of which one CH₂ group can be replaced by oxygen, S, NH, N-CH₃ or N-benzyl;

the remaining substituents R(2), R(3), R(4), R(5) or R(1), R(2), R(4), R(5) or R(1), R(2), R(3), R(5) in each case independently of one another are hydrogen, F, Cl, Br, I, -Oᵦ(C₁₋C₆)-alkyl, -Oᵦ(C₅₋C₆)-alkenyl,

-Οᵦ(CH₂)bC₆F₂d₁₋, -ΟᵦC₆H₂d₂R(18),
or up to 2 groups CN, NO₂, NR(16)R(17),
b is zero or 1;
d is 1, 2, 3, 4, 5, 6 or 7;
ta is zero or 1;
tb is zero or 1;
tc is zero or 1;
td is zero or 1;

5 p is zero, 1, 2, 3 or 4;

R(18) is (C₃-C₈)-cycloalkyl, phenyl, biphenyl or naphthyl,
where the aromatics are not substituted or are
substituted by 1 - 3 substituents selected from the

10 group consisting of F, Cl, CF₃, methyl, methoxy and
NR(19)R(20);

R(19) and R(20)

15 are hydrogen or (C₁-C₄)-alkyl or (C₁-C₄)-
perfluoroalkyl;

R(16) is hydrogen, (C₁-C₆)-alkyl, (C₁-C₈)-perfluoroalkyl, (C₃-C₈)-

20 alkenyl, -C₉H₂₉-R(21),
q is zero, 1, 2, 3 or 4;

25 R(21) is (C₃-C₈)-cycloalkyl, phenyl, biphenyl or naphthyl,
where the aromatics are not substituted or are
substituted by 1 - 3 substituents from the group

30 F, Cl, CF₃, methyl, methoxy or NR(22)R(23),
R(22) and R(23) are hydrogen, (C₁-C₄)-alkyl or

(C₁-C₄)-perfluoroalkyl;

R(17) is hydrogen, (C₁-C₈)-alkyl, (C₁-C₈)-perfluoroalkyl, (C₃-C₈)-

35 alkenyl, -C₁₉H₂₉-R(24);

R(24) is (C₃-C₈)-cycloalkyl, phenyl, biphenyl or naphthyl,
where the aromatics are not substituted or are
substituted by 1 - 3 substituents selected from
the group consisting of F, Cl, CF₃, methyl,

methoxy and NR(25)R(26);

30 R(25) and R(26)

R(25) and R(26)

are hydrogen, (C₁-C₄)-alkyl or (C₁-C₄)-
perfluoroalkyl;

or

R(16) and R(17)
together are 4 or 5 methylene groups, of which one CH₂

5
group can be replaced by oxygen, S, NH, N-CH₃ or N-aryl;

and their pharmaceutically tolerable salts;

(HOE 93/F 249 - EP- Offenlegungsschrift 640 587, NZ 264 282)
t) diacyl-substituted guanidines of the formula I

\[
\begin{align*}
X(1) & \quad NH \quad \equiv \quad NH \quad X(2) \\
\text{in which:} & \\
X(1) & \quad \text{and} \quad X(2) \\
R(A) & \quad \text{and} \quad R(B) \\
T_1 & \quad \text{is zero, 1, 2, 3 or 4;} \\
R(A) & \quad \text{and} \quad R(B) \\
\text{are hydrogen, F, Cl, Br, I, CN,} \\
\text{OR(106), (C₅-C₈)-alkyl, (C₃-C₆)-cycloalkyl, Oₙ(CH₂)ₙCₙFₙ₊₁,} \\
\text{NR(107)R(108), phenyl or benzyl,} \\
\text{where the aromatics are not substituted or are substituted by} \\
1 - 3 substituents selected from the group consisting of F, Cl, \\
\text{CF₃, methyl, methoxy and NR(109)R(110);} \\
\text{R(109) and R(110) are hydrogen, (C₃-C₈)-alkyl or (C₁-C₄)-perfluoroalkyl;} \\
\end{align*}
\]

z₁ is zero, 1, 2, 3 or 4;

zₖ is zero or 1;

zₐ is 1, 2, 3, 4, 5, 6, 7 or 8;
R(106)
is hydrogen, (C\textsubscript{1}-C\textsubscript{8})-alkyl, (C\textsubscript{1}-C\textsubscript{8})-perfluoroalkyl, (C\textsubscript{3}-C\textsubscript{8})-alkenyl, (C\textsubscript{3}-C\textsubscript{8})-cycloalkyl, phenyl or benzyl,
where the aromatics are not substituted or are substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF\textsubscript{3}, methyl, methoxy and NR(111)R(112);
R(111) and R(112)
are hydrogen, (C\textsubscript{1}-C\textsubscript{4})-alkyl or (C\textsubscript{1}-C\textsubscript{4})-perfluoroalkyl;
R(107) and R(108)
individually of one another are defined as R(106),
or R(107) and R(108)
together are 4 or 5 methylene groups, of which one CH\textsubscript{2} group can be replaced by oxygen, S, NH, N-CH\textsubscript{3} or N-benzyl;
or X(1) and X(2) are
\[
\begin{align*}
&\begin{array}{c}
\text{R(102)} \\
\text{R(103)} \\
\text{R(104)}
\end{array} \\
&\begin{array}{c}
\text{R(105)} \\
\text{X(1)} \\
\text{X(2)}
\end{array}
\end{align*}
\]
T\textsubscript{2}a and T\textsubscript{2}b independently of one another are zero, 1 or 2;
where the double bond can have the (E)- or (Z)-configuration;
or X(1) and X(2) are
T3 is zero, 1 or 2;
U, YY and Z independently of one another are C or N,
where U, YY, Z can carry the following number of substituents:

<table>
<thead>
<tr>
<th>U, YY or Z</th>
<th>Bonded in the ring to a double bond</th>
<th>Number of permitted substituents</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>yes</td>
<td>1</td>
</tr>
<tr>
<td>C</td>
<td>no</td>
<td>2</td>
</tr>
<tr>
<td>N</td>
<td>yes</td>
<td>0</td>
</tr>
<tr>
<td>N</td>
<td>no</td>
<td>1</td>
</tr>
</tbody>
</table>

R(D) is hydrogen, (C₁-C₆)-alkyl or (C₁-C₆)-perfluoroalkyl,
R(U1), R(U2), R(Y1), R(Y2), R(Z1), R(Z2)

independently of one another are hydrogen, F, Cl, Br, I, CN,
OR(114), (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl, O₉₁₉₁₁₉₁²₁₉₁₉₂₉₁₉₁₁₉₁₉₅₁, NR(115)R(116), phenyl or benzyl,

where the aromatics are not substituted or are substituted by

1 - 3 substituents selected from the group consisting of F, Cl,
CF₃, methyl, methoxy, NR(117)R(118),
R(117) and R(118)

are hydrogen, (C₁-C₆)-alkyl or (C₁-C₆)-perfluoroalkyl,

z₁₉₁ is zero or 1;
z₁₁ is zero, 1, 2, 3 or 4;
zma is 1, 2, 3, 4, 5, 6, 7 or 8;

R(114) is hydrogen, (C_1-C_9)-alkyl, (C_1-C_8)-perfluoroalkyl, (C_3-C_8)-alkenyl, (C_3-C_8)-cycloalkyl, phenyl or benzyl,

where the aromatics are not substituted or are substituted by 1-3 substituents selected from the group consisting of F, Cl, CF_3, methyl, methoxy and NR(119)R(120); R(119) and R(120)

are hydrogen, (C_1-C_4)-alkyl or (C_1-C_4)-perfluoroalkyl;

R(115) and R(116) independently of one another are defined as R(114); or

R(115) and R(116) together are 4 or 5 methylene groups, of which one CH_2 group can be replaced by oxygen, S, NH, N-CH_3 or N-benzyl;

but where the constitution of U is nitrogen (N), YY is nitrogen (N) and Z is carbon (C) is excluded,

R(101), R(102), R(103), R(104) and R(105)

independently of one another are hydrogen, F, Cl, Br, I, -C≡N, X_{zpa}-(CH_2)_{zpa}-(C_{zqa}F_{2zqa+1}), R(110a)-SO_{zbm}, R(110b)R(110c)N-CO, R(111a)-CO- or R(112a)R(113a)N-SO_2-

where the perfluoroalkyl group is straight-chain or branched,

X is oxygen, S or NR(114a);

R(114a)

is H or (C_1-C_5)-alkyl;

d is zero or 1;

zpa is zero, 1 or 2;

zqa is zero, 1, 2, 3 or 4;

R(110a), R(110b), R(111a) and R(112a)
dependently of one another are (C_{1-8})-alkyl, (C_{3-8})-alkenyl, -C_{zn}H_{2zn}\text{-}R(115a) or (C_{1-8})-perfluoroalkyl;

\[
z_n \text{ is zero, 1, 2, 3 or 4;} \]

R(115a)

is (C_{2-8})-cycloalkyl, phenyl, biphenylyl or naphthyl, where the aromatics are not substituted or are substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF_{3}, methyl, methoxy and N(R(116a)R(117a));

R(116a) and R(117a)

are hydrogen, (C_{1-4})-perfluoroalkyl or (C_{1-4})-alkyl;

or

R(110b), R(111a) and R(112a)

are hydrogen;

R(110c) and R(113a)

independently are hydrogen, (C_{1-4})-perfluoroalkyl or (C_{1-4})-alkyl;

or

R(110b) and R(110c) and R(112a) and R(113a)

together are 4 or 5 methylene groups, of which one CH_{2} group can be replaced by oxygen, sulfur, NH, N-CH_{3} or N-benzyl;

or

R(101), R(102), R(103), R(104), R(105)

independently of one another are (C_{1-8})-alkyl, -C_{zn}H_{2zn}\text{-}R(118a) or (C_{3-8})-alkenyl,

\[
zal \text{ is zero, 1, 2, 3 or 4;} \]

R(118a)

is (C_{3-8})-cycloalkyl, phenyl, biphenylyl or naphthyl, where the aromatics are not substituted or are substituted by 1 - 3 substituents from the group
consisting of F, Cl, CF₃, methyl, methoxy or 
NR(119a)R(119b);
R(119a) and R(119b) 
are hydrogen, (C₃-C₄)-alkyl or (C₃-C₄)- 
perfluoroalkyl;

or 
R(101), R(102), R(103), R(104), R(105) 
individually of one another are (C₁-C₉)-heteroaryl, which is linked via C or N and which is unsubstituted or 
substituted by 1 - 3 substituents from the group consisting of 
F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino and 
dimethylamino; 

or 
R(101), R(102), R(103), R(104), R(105) 
individually of one another are -C=C-R(193);
R(193) 
is phenyl which is not substituted or is substituted by 1 - 3 
substituents from the group consisting of F, Cl, CF₃, methyl, 
methoxy or NR(194)R(195); 

R(194) and R(195) 
are hydrogen or CH₃; 

or 
R(101), R(102), R(103), R(104), R(105) 
individually of one another are 
-Y-para-C₆H₄-(CO)ₜₜ(CHOH)ₜₜ(CH₂)ₜₜ(CHOH)₂ₜₜ(CH₂)₂ₜₜ(CHOH)ₜₜ-R(123),
-Y-meta-C₆H₄-(CO)ₜₜ(CHOH)ₜₜ(CH₂)ₜₜ(CHOH)₂ₜₜ(CH₂)₂ₜₜ(CHOH)ₜₜ-R(124) 
or 
-Y-ortho-C₆H₄-(CO)ₜₜ(CHOH)ₜₜ(CH₂)ₜₜ(CHOH)₂ₜₜ(CH₂)₂ₜₜ(CHOH)ₜₜ-R(125); 
Y is oxygen, -S- or -NR(122d)-; 

zh, zad, zah 
individually are zero or 1; 
zi, zj, zk, zae, zaf, zag, zao, zap and zak
independently are zero, 1, 2, 3 or 4;
but where in each case
zh, zi and zk are not simultaneously zero,
zad, zae and zag are not simultaneously zero, and
zah, zao and zak are not simultaneously zero,

R(123), R(124) R(125) and R(122d)
  independently are hydrogen or (C₁-C₃)-alkyl;
or
R(101), R(102), R(103), R(104) and R(105)
  independently of one another are SR(129), -OR(130),
  -NR(131)R(132) or -CR(133)R(134)R(135);
R(129), R(130), R(131) and R(133)
  independently are -C zabH₂zab-(C₁-C₉)-heteroaryl,
    which is unsubstituted or substituted by 1 - 3
  substituents from the group consisting of F, Cl, CF₃,
  CH₃, methoxy, hydroxyl, amino, methylamino and
  dimethylamino;
  zab is zero, 1 or 2;
R(132), R(134) and R(135)
  independently are defined as R(129) or are hydrogen, (C₁-
  C₄)-alkyl or (C₁-C₄)-perfluoroalkyl;
or
R(101), R(102), R(103), R(104) and R(105)
  independently of one another are -W-para-(C₆H₄)-R(196), -W-meta-
  (C₆H₄)-R(197) or -W-ortho-(C₆H₄)-R(198);
R(196), R(197) and R(198)
  independently of one another are (C₁-C₉)-heteroaryl,
    which is linked via C or N and which is unsubstituted
    or substituted by 1 to 3 substituents from the group
    consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl,
    amino, methylamino, dimethylamino and benzyl;
W is oxygen, S or NR(136)-;
R(136) is hydrogen or (C\textsubscript{1}-C\textsubscript{4})-alkyl;

or

R(101), R(102), R(103), R(104) and R(105) independently of one another are R(146)X(1a)-;

X(1a) is oxygen, S, NR(147), (D=O)A-, NR(148)C=NM(*)R(149)-;

M is oxygen or sulfur;

A is oxygen or NR(150);

D is C or SO;

R(146) is (C\textsubscript{1}-C\textsubscript{9})-alkyl, (C\textsubscript{3}-C\textsubscript{8})-alkenyl, (CH\textsubscript{2})\textsubscript{zxa}C\textsubscript{zdz}F\textsubscript{zdz+1} or -C\textsubscript{zxa}H\textsubscript{zdz}-R(151);

zbz is zero or 1;

zdz is 1, 2, 3, 4, 5, 6 or 7;

zxa is zero, 1, 2, 3 or 4;

R(151) is (C\textsubscript{3}-C\textsubscript{9})-cycloalkyl, phenyl, biphenylyl or naphthyl, where the aromatics are not substituted or are substituted by 1 - 3 substituents from the group consisting of F, Cl, CF\textsubscript{3}, methyl, methoxy and NR(152)R(153);

R(152) and R(153) are hydrogen, (C\textsubscript{1}-C\textsubscript{4})-alkyl or (C\textsubscript{1}-C\textsubscript{4})-perfluoroalkyl;

R(147), R(148) and R(150) independently are hydrogen, (C\textsubscript{1}-C\textsubscript{4})-alkyl, (C\textsubscript{1}-C\textsubscript{4})-perfluoroalkyl;

R(149) is defined as R(146),

or

R(146) and R(147), or R(146) and R(148) together are 4 or 5 methylene groups, of which one CH\textsubscript{2}
group can be replaced by oxygen, sulfur, NH, N-CH₃ or N-benzyl;

where A and N⁽ⁿ⁾ are bonded to the phenyl nucleus of the alkanoyl parent structure;

or

R(101), R(102), R(103), R(104) and R(105) independently of one another are -SR(164), -OR(165), -NHR(166), -NR(167)R(168), -CHR(169)R(170), -CR(154)R(155)OH, -C=CR(156), -CR(158)=CR(157) or

-[CR(159)R(160)]ₙu -(C=O)-[CR(161)R(162)]ₙv -R(163);

R(164), R(165), R(166), R(167), R(169) identically or differently are -(CH₂)ₙz-(CHOH)ₙz-(CH₂)ₙaa -(CHOH)ₙz-R(171) or -(CH₂)ₙab-O-(CH₂-CH₂O)ₙzc-R(172);

R(171) and R(172) are hydrogen or methyl;

zu is 1, 2, 3 or 4;

zv is zero, 1, 2, 3 or 4;

zy, zz, zaa, zab, zac identically or differently are zero, 1, 2, 3 or 4;

zt is 1, 2, 3 or 4;

R(168), R(170), R(154), R(155) identically or differently are hydrogen or (C₁-C₆)-alkyl,

or

R(169) and R(170), or R(154) and R(155) together with the carbon atom carrying them are a (C₃-C₆)-cycloalkyl;

R(163) is hydrogen, (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl or -CₙzebH₂zeb-R(173);

zub is zero, 1, 2, 3 or 4;

R(156), R(157) and R(173) independently are phenyl which is unsubstituted or is
substituted by 1-3 substituents from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(174)R(175); R(174) and R(175) are hydrogen or (C₁-C₄)-alkyl;

or

R(156), R(157) and R(173) independently are (C₁-C₆)-heteroaryl, which is unsubstituted or substituted as phenyl;

R(158), R(159), R(160), R(161) and R(162) are hydrogen or methyl;

or

R(101), R(102), R(103), R(104), R(105) independently of one another are R(176)-NH-SO₂⁻;

R(176) is R(177)R(178)N-(C=Y')⁻;

Y' is oxygen, S or N-R(179);

R(177) and R(178) identically or differently are hydrogen, (C₁-C₆)-alkyl, (C₃-C₆)-alkenyl or -CZFₐHZFₐ-R(180);

z₁ is zero, 1, 2, 3 or 4;

R(180) is (C₅-C₇)-cycloalkyl or phenyl, which is unsubstituted or substituted by 1-3 substituents selected from the group consisting of F, Cl, CF₃, methoxy or (C₁-C₄)-alkyl;

or

R(177) and R(178) together are 4 or 5 methylene groups, of which one CH₂ group can be replaced by oxygen, sulfur, NH, N-CH₃ or N-benzyl;
is defined as R(177) or is amidine,

or

R(101), R(102), R(103), R(104), R(105)
individually of one another are NR(184a)R(185), OR(184b),
SR(184c) or \(-C_{z_{mx}}H_{2z_{mx}}-R(184d)\);
z_{mx} is zero, 1, 2, 3 or 4;

R(184d) is \((C_3-C_7)\)-cycloalkyl or phenyl,

which is not substituted or substituted by 1 - 3
substituents from the group consisting of F, Cl, CF₃,
methyl, methoxy and NR(116k)R(117k);
R(116k) and R(117k)
are hydrogen or C₁-C₄-alkyl;

R(184a), R(184b), R(184c), R(185)
individually of one another are hydrogen, \((C_1-C_9)\)-alkyl,
\((C_1-C_9)\)-perfluoroalkyl or \((CH_2)_{z_{ao}}-R(184g)\);
z_{ao} is zero, 1, 2, 3 or 4;

R(184g) is \((C_3-C_7)\)-cycloalkyl or phenyl,

which is not substituted or substituted by 1 - 3
substituents from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(184u)R(184v);
R(184u) and R(184v)
are hydrogen or C₁-C₄-alkyl;
or

R(184a) and R(185)
together are 4 or 5 methylene groups, of
which one CH₂ group can be replaced by

oxygen, sulfur, NH, N-CH₃ or N-benzyl;

and their pharmaceutically tolerable salts;

(HOE 93/F 254 - EP-Offenlegungsschrift 640 588, NZ 264 307)
u) benzoylguanidines of the formula I

\[
\text{R(1)} \text{N NH}_2 \\
\text{R(2)} \\
\text{R(3)} \text{R(4) O} \\
\text{N NH}_2
\]

in which:

1. **R(1)** is H, F, Cl, Br, I, CN, NO\(_2\), \((C_1-C_4)\)-alkyl, \((C_3-C_6)\)-cycloalkyl or \(X_a(CH_2)_b(CF_2)_cCF_3\); 
   - **X** is oxygen, S or NR(5); 
   - **a** is zero or 1; 
   - **b** is zero, 1 or 2; 
   - **c** is zero, 1, 2 or 3; 
   - **R(5)** is H, \((C_1-C_4)\)-alkyl or \(-C_6H_{2d}R(6)\); 
   - **d** is zero, 1, 2, 3 or 4; 
   - **R(6)** is \((C_3-C_6)\)-cycloalkyl, phenyl, biphenyl or naphthyl, 
2. where the aromatics are not substituted or are substituted by 1 to 3 substituents selected from the group consisting of F, Cl, CF\(_3\), methyl, methoxy and NR(7)R(8); 
   - **R(7) and R(8)** independently are H or \((C_1-C_4)\)-alkyl; 
3. or **R(1)** is -SR(10), -OR(10) or -CR(10)R(11)R(12); 
   - **R(10)** is \(-C_6H_{2r}(C_3-C_6)\)-cycloalkyl, \(-(C_1-C_6)\)-heteroaryl or phenyl, 
4. where the aromatic systems are unsubstituted or substituted by one to 3 substituents selected from the group consisting of F, Cl, CF\(_3\), CH\(_3\), methoxy, hydroxyl,
amino, methylamino and dimethylamino;

f is zero, 1 or 2;

R(11) and R(12)

independently of one another are defined as R(10) or are hydrogen or (C<sub>1</sub>-C<sub>4</sub>)-alkyl;

or

R(1) is phenyl, naphthyl, biphenylyl or (C<sub>1</sub>-C<sub>9</sub>)-heteroaryl,

the latter linked via C or N,

and which are unsubstituted or substituted by 1 to 3 substituents selected from the group consisting of F, Cl, CF<sub>3</sub>, CH<sub>3</sub>, methoxy, hydroxyl, amino, methylamino and dimethylamino;

or

R(1) is -SR(13), -OR(13), -NHR(13), -NR(13)R(14), -CHR(13)R(15), -C[R(15)R(16)]OH, -C=CR(18), -C[R(19)]=CR(18), -[CR(20)R(21)]k-(CO)-[CR(22)R(23)R(24)];

R(13) and R(14)

identically or differently are -(CH<sub>2</sub>)<sub>g</sub>-(CHOH)<sub>h</sub>-(CH<sub>2</sub>)<sub>j</sub>-(CHOH)<sub>j</sub>-

R(17),

R(17) is hydrogen or methyl;

-(CH<sub>2</sub>)<sub>g</sub>-O-(CH<sub>2</sub>-CH<sub>2</sub>O)<sub>h</sub>-R(24),

g, h, i

identically or differently are zero, 1, 2, 3 or 4;

j is 1, 2, 3 or 4;

R(15) and R(16)

identically or differently are hydrogen, (C<sub>1</sub>-C<sub>9</sub>)-alkyl or together with the carbon atom carrying them are a (C<sub>3</sub>-C<sub>9</sub>)-cycloalkyl;

R(18) is phenyl,

which is unsubstituted or substituted by 1 to 3 substituents selected from the group consisting of F, Cl, CF<sub>3</sub>, methyl, methoxy and NR(25)R(26);
R(25) and R(26) are H or (C₁-C₄)-alkyl;

or

R(18) is (C₁-C₆)-alkyl, which is unsubstituted or substituted by 1 to 3 OH;

or

R(18) is (C₁-C₆)-alkyl, which is unsubstituted or substituted as phenyl;

or

R(18) is (C₃-C₆)-cycloalkyl;

R(19), R(20), R(21), R(22) and R(23) are hydrogen or methyl;

k is zero, 1, 2, 3 or 4;

l is zero, 1, 2, 3 or 4;

m is 1, 2, 3 or 4;

R(24) is H, (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl or -CₘH₂ₘ-R(18);

and their pharmaceutically tolerable salts;

v) acylguanidines of the formula I

\[
\begin{align*}
R(1) : & \quad \text{R}(1) \text{ and } \text{R}(3) \text{ independently of one another are defined as } \text{R}(1); \\
R(4) : & \quad \text{R}(4) \text{ is } \text{(C₁-C₃)-alkyl, F, Cl, Br, I, CN or } -(\text{CH}_2)_n-(\text{CF}_2)_m-\text{CF}_3; \\
n : & \quad \text{is zero or } 1; \\
o : & \quad \text{is zero, } 1 \text{ or } 2;
\end{align*}
\]

(HOE 93/F 436 - EP-Offenlegungsschrift 659 748), NZ 270 264)
unsubstituted or substituted by hydroxyl, (C$_3$-$C_6$)-cycloalkyl, phenyl, which is unsubstituted or substituted by 1 - 3 substituents from the group F, Cl, CF$_3$, CH$_3$, methoxy, hydroxyl, amino, methylamino or dimethylamino, 

R(2) is H, (C$_1$-$C_4$)-alkyl, and their pharmaceutically tolerable salts;

(HOE 94/F 014 K - EP-Offenlegungsschrift 666 252, NZ 270 370)

w) phenyl-substituted alkycarboxylic acid guanidides, carrying perfluoroalkyl groups, of the formula I

\[
\begin{align*}
\text{R}(A) & \quad \text{is hydrogen, F, Cl, Br, I, CN, OR}(6), (C$_1$-$C_6$)-alkyl, (C$_3$-$C_6$)-cycloalkyl, \\
\text{O}(_2\text{CH}_2)_a\text{C}_b\text{F}_{2b+1} & \text{or NR}(7)\text{R}(8); \\
\text{r} & \quad \text{is zero or 1}; \\
\text{a} & \quad \text{is zero, 1, 2, 3 or 4}; \\
\text{b} & \quad \text{is 1, 2, 3, 4, 5, 6, 7 or 8}; \\
\text{R}(6) & \quad \text{is hydrogen, (C$_1$-$C_6$)-alkyl, (C$_3$-$C_6$)-alkenyl, (C$_3$-$C_6$)-cycloalkyl, phenyl or benzyl,} \\
\text{where the aromatics are not substituted or are} \\
\text{substituted by 1 - 3 substituents selected from the} \\
\text{group consisting of F, Cl, CF}_3, \text{methyl, methoxy and} \\
\text{NR}(9)\text{R}(10); \\
\text{R}(9) & \text{and R}(10) \\
\text{are H, (C$_1$-$C_4$)-alkyl or (C$_1$-$C_4$)-perfluoroalkyl;} \\
\text{R}(7) & \text{and R}(8)
\end{align*}
\]
independently of one another are defined as R(6);
R(B) independently is defined as R(A);
X is 1, 2 or 3;
R(1) is hydrogen, \((C_1-C_8)\)-alkyl, \((C_3-C_9)\)-cycloalkyl, \(-O_1(CH_2)_aC_6F_{2a+1}\), F, Cl, Br, I or CN;
t is zero or 1;
d is zero, 1, 2, 3 or 4;
e is 1, 2, 3, 4, 5, 6, 7 or 8;
R(2), R(3), R(4) and R(5) independently of one another are defined as R(1);
but with the condition
that at least one of the substituents R(1), R(2), R(3), R(4), R(5), R(A) and R(B) is an \(-O_1(CH_2)_aC_6F_{2a+1}\) or an \(-Ot(CH_2)_dC_bF_{2b+1}\) group,
and their pharmaceutically tolerable salts;

x) heteroaroylguanidines of the formula I

\[
\begin{array}{c}
\text{R(1)} \\
\text{R(4)} \\
\text{HA} \\
\text{R(5)} \\
\text{R(2)} \\
\text{R(3)}
\end{array}
\]

in which:
HA is \(SO_m\), O or NR(5);
m is zero, 1 or 2;
R(5) is hydrogen, \((C_1-C_8)\)-alkyl or \(-C_{am}H_{2am}\)R(81);
am is zero, 1 or 2;
R(81) is \((C_3-C_9)\)-cycloalkyl or phenyl,
which is not substituted or is substituted by 1 - 3 substituents selected from the

group consisting of F, Cl, CF₃, methyl, methoxy and NR(82)R(83);
R(82) and R(83)
Is H or CH₃;

or

R(81) is (C₁-C₉)-heteroaryl,
which is linked via C or N and which is

unsubstituted or substituted by 1 - 3

substituents selected from the group consisting
of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino,
methylamino and dimethylamino;

one of the two substituents R(1) and R(2)

is -CO-N=C(NH₂)₂;

and the other in each case

is hydrogen, F, Cl, Br, I, (C₁-C₃)-alkyl, -OR(6), C₇F₂ᵣ₊₁, -CO-
N=C(NH₂)₂ or -NR(6)R(7);

R(6) and R(7)

are independently hydrogen or (C₁-C₃)-alkyl;

r is 1, 2, 3 or 4;

R(3) and R(4)

are independently of one another hydrogen, F, Cl, Br, I, -C≡N, X-
(CH₂)ᵦ₋₁(Cₙ₋₁F₂ᵦ₊₁), R(8)-SOₐ₋₁ᵦ, R(9)R(10)N-CO, R(11)-CO- or

R(12)R(13)N'-SO₂₋₁ᵦ, R(14)R(15)N'-SO₂₋₁ᵦ, R(16)R(17)N'-SO₂₋₁ᵦ,
where the perfluoroalkyl group is straight-chain or branched,

X is oxygen, S or NR(14);

R(14) is H or (C₁-C₃)-alkyl;

b₁ is zero, 1 or 2;

p is zero, 1 or 2;

q is zero, 1, 2, 3, 4, 5 or 6;

R(8), R(9), R(11) and R(12)

are independently (C₁-C₉)-alkyl, (C₃-C₉)-alkenyl, -Cₙ₋₁H₂₋₁ᵦR(15),
CF₃;

R(15) is (C₃-C₇)-cycloalkyl or phenyl;

which is not substituted or is substituted by 1 - 3
substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy or NR(16)R(17); R(16) and R(17) are H or C₁-C₄-alkyl;

5 or 
R(9), R(11) and R(12) are H;
R(10) and R(13) independently are H or (C₁-C₄)-alkyl;

10 or 
R(9) and R(10), and R(12) and R(13) together are 4 or 5 methylene groups, of which one CH₂ group can be replaced by oxygen, S, NH, N-CH₃ or N-benzyl,
or 
15 R(3) and R(4) independently of one another are (C₁-C₈)-alkyl or -C₅H₅nR(18); al is zero, 1 or 2;
R(18) is (C₃-C₈)-cycloalkyl or phenyl;
which is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(19)R(20);
R(19) and R(20) are H or CH₃;
or 
20 R(3) and R(4) independently of one another are (C₁-C₉)-heteroaryl, which is linked via C or N and which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino and dimethylamino;
or 
25 R(3) and R(4)
independently of one another are

\[
-Y\underbrace{-(\text{C} \text{h}-(\text{CHOH})\text{i}-(\text{CH}_2)\text{j}-(\text{CHOH})\text{k}}_{-R(23)}-\text{R}(23)
\]

or

\[
-Y\underbrace{-(\text{C} \text{d}-(\text{CHOH})\text{a}-(\text{CH}_2)\text{e}-(\text{CHOH})\text{g}}_{-R(24)}-\text{R}(24)
\]

or

\[
-Y\underbrace{-(\text{C} \text{h}-(\text{CHOH})\text{a}-(\text{CH}_2)\text{p}-(\text{CHOH})\text{k}}_{-R(25)}-\text{R}(25)
\]

\(Y\) is oxygen, -S- or -NR(22)-;

\(h\), ad, ah independently are zero or 1;

\(i, j, k, ae, af, ag, ao, ap\) and \(ak\) independently are zero, 1, 2, 3, ...,

but where in each case

\(h, i\) and \(k\) are not simultaneously zero,

ad, ae and ag are not simultaneously zero,

\(ah, ao\) and \(ak\) are not simultaneously zero,

\(R(23), R(24)\) \(R(25)\) and \(R(22)\)

independently are hydrogen or \((\text{C}_1-\text{C}_3)\)-alkyl;

or

\(R(3)\) and \(R(4)\)

independently are hydrogen, F, Cl, Br, I, CN, \((\text{C}_1-\text{C}_3)\)-alkyl, \((\text{C}_1-\text{C}_6)\)-perfluoroalkyl, \((\text{C}_3-\text{C}_6)\)-alkenyl or \(-\text{C}_9\text{H}_{2g}\) \(R(26)\);

\(g\) is zero, 1, 2, 3 or 4;

\(R(26)\) is \((\text{C}_3-\text{C}_6)\)-cycloalkyl, phenyl, biphenylyl or naphthyl,

where the aromatics are not substituted or are

substituted by 1 - 3 substituents selected from the

\(\text{group consisting of F, Cl, CF}_3,\) methyl, methoxy and

\(\text{NR(27)R(28)}\);

\(R(27)\) and \(R(28)\)

are H, \((\text{C}_1-\text{C}_4)\)-alkyl or \((\text{C}_1-\text{C}_6)\)-perfluoroalkyl;
or

\[ \text{R(3) and R(4)} \]

independently of one another are \( SR(29), -OR(30), -NR(31)R(32) \) or

\( -CR(33)R(34)R(35) \);

\[ \text{R(29), R(30), R(31) and R(33)} \]

independently of one another are \( -C_{6}H_{2a}-(C_{1}-C_{9}) \)-heteroaryl,

which is unsubstituted or substituted by 1 - 3

substituents selected from the group consisting of F,

Cl, CF\(_{3}\), CH\(_{3}\), methoxy, hydroxyl, amino, methylamino

and dimethylamino;

\[ a \]

is zero, 1 or 2;

\[ \text{R(32), R(34) and R(35)} \]

independently of one another are defined as R(29) or are hydrogen, \( (C_{1}-C_{4}) \)-alkyl or \( (C_{1}-C_{4}) \)-perfluoroalkyl;

or

\[ \text{R(3) and R(4)} \]

independently of one another are

\[ \begin{array}{c}
-\text{w}-\text{R(96)} \\
-\text{w}-\text{R(97)} \\
-\text{w}-\text{R(98)}
\end{array} \]

\[ \text{R(96), R(97) and R(98)} \]

independently are \( (C_{1}-C_{6}) \)-heteroaryl,

which is linked via C or N and which is unsubstituted

or substituted by 1 to 3 substituents selected from the

group consisting of F, Cl, CF\(_{3}\), CH\(_{3}\), methoxy, hydroxyl,

amino, methylamino, dimethylamino or benzyl;

\[ W \]

is oxygen, S or NR(36)-;

\[ \text{R(36)} \]

is H or \( (C_{1}-C_{4}) \)-alkyl;

or

\[ \text{R(3) and R(4)} \]

independently of one another are \( R(37)-SO_{cm} \) or \( R(38)R(39)N-SO_{2}^{-} \);

\[ cm \]

is 1 or 2;
R(37) is (C₁-C₈)-alkyl, (C₁-C₈)-perfluoroalkyl, (C₃-C₈)-alkenyl or
-C₆H₂₆R(40);

s is zero, 1, 2, 3 or 4;

R(40) is (C₃-C₈)-cycloalkyl, phenyl, biphenyl or naphthyl,
where the aromatics are not substituted or are
substituted by 1 - 3 substituents selected from
the group consisting of F, Cl, CF₃, methyl,
methoxy and NR(41)R(42);

R(41) and R(42) are H, (C₁-C₄)-alkyl or (C₁-C₄)-
perfluoroalkyl;

R(38) is H, (C₁-C₈)-alkyl, (C₁-C₈)-perfluoroalkyl, (C₃-C₈)-alkenyl or
-C₆H₂₆-R(43);

w is zero, 1, 2, 3 or 4;

R(43) is (C₃-C₈)-cycloalkyl, phenyl, biphenyl or naphthyl,
where the aromatics are not substituted or are
substituted by 1 - 3 substituents selected from
the group consisting of F, Cl, CF₃, methyl,
methoxy and NR(44)R(45);

R(44) and R(45) are H, (C₁-C₄)-alkyl or (C₁-C₄)-
perfluoroalkyl;

R(39) is H, (C₁-C₄)-alkyl or (C₁-C₄)-perfluoroalkyl;

or

R(38) and R(39) together are 4 or 5 methylene groups, of which one CH₂
group can be replaced by oxygen, S, NH, N-CH₃ or N-benzyl;

or

R(3) and R(4) independently of one another are R(46)X(1)-;

X(1) is oxygen, S, NR(47), (D=O)A-, NR(48)C=MN(49)R(49)-,
M is oxygen or S;
A is oxygen or NR(50);
D is C or SO;
R(46) is (C₁₋C₉)-alkyl, (C₃₋C₈)-alkenyl, (CH₂)₅CF₂-d₁ or -CₓH₂ₓ-R(51);
b is zero or 1;
5 d is 1, 2, 3, 4, 5, 6 or 7;
x is zero, 1, 2, 3 or 4;
R(51) is (C₅₋C₆)-cycloalkyl, phenyl, biphenyl or naphthyl, where the aromatics are not substituted or are substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(52)R(53);
R(52) and R(53) are H, (C₁₋C₄)-alkyl or (C₁₋C₄)-perfluoroalkyl;
15 R(47), R(48) and R(50) independently are hydrogen, (C₁₋C₄)-alkyl or (C₁₋C₄)-perfluoroalkyl;
R(49) is defined as R(46);
or
20 R(46) and R(47), or R(46) and R(48) together are 4 or 5 methylene groups, of which one CH₂ group can be replaced by oxygen, S, NH, N-CH₃ or N-benzyl, where A and N(*) are bonded to the phenyl nucleus of the benzoylguanidine parent structure;
or
R(3) and R(4) independently of one another are -SR(64), -OR(65), -NHR(66), -NR(67)R(68), -CHR(69)R(70), -C(OH)R(54)R(55), -C=CR(56), -CR(58)=CHR(57), -[CR(59)R(60)]ₙ-[CO]-[CR(61)R(62)]ₙ-R(63);
30 R(64), R(65), R(66), R(67) and R(69) identically or differently are -(CH₂)ₙ-(CHOH)ₙ-(CH₂)ₙₐs-
(CH₂OH)ₜ-R(71) or -(CH₂)₁₆-O-(CH₂-CH₂O)₉₆-R(72),

R(71) and R(72)

are hydrogen or methyl;

u is 1, 2, 3 or 4;

v is zero, 1, 2, 3 or 4;

y, z, aa

identically or differently are zero, 1, 2, 3 or 4;

t is 1, 2, 3 or 4;

R(68), R(70), R(54) and R(55)

identically or differently are hydrogen, (C₁-C₆)-alkyl;

or

R(69) and R(70), or R(54) and R(55)

together with the carbon atom carrying them are a (C₃-C₈)-
cycloalkyl;

R(63)

is H, (C₁-C₆)-alkyl, (C₃-C₈)-cycloalkyl or -C₆H₄-R(73);

e is zero, 1, 2, 3 or 4;

R(56), R(57) and R(73)

independently are phenyl,

which are unsubstituted or substituted by 1 - 3
substituents selected from the group consisting of F,
Cl, CF₃, methyl, methoxy and NR(74)R(75);

R(74) and R(75)

are H or (C₁-C₄)-alkyl;

or

R(56), R(57) and R(73)

independently are (C₁-C₆)-heteroaryl,

which is unsubstituted or substituted as phenyl;

R(58), R(59), R(60), R(61) and R(62)

are hydrogen or methyl,

or

R(3) and R(4)
independently of one another are \( R(76) \)-NH-SO\(_2\)\(^{-}\);

\( R(76) \) is \( R(77) \)R(78)N-(C=Y')\(^{-}\);

\( Y' \) is oxygen, S or N-R(79);

\( R(77) \) and \( R(78) \) identically or differently are H, (C\(_1\)-C\(_8\))-alkyl, (C\(_3\)-C\(_6\))-alkenyl, -C\(_{1}\)H\(_{2\text{f}}\)-R(80);

\( f \) is zero, 1, 2, 3 or 4;

\( R(80) \) is (C\(_5\)-C\(_7\))-cycloalkyl or phenyl, which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF\(_3\), methoxy and (C\(_1\)-C\(_4\))-alkyl;

or \( R(77) \) and \( R(78) \) together are 4 or 5 methylene groups, of which one CH\(_2\) group can be replaced by oxygen, S, NH, N-CH\(_3\) or N-benzyl;

\( R(79) \) is defined as \( R(77) \) or is amidine;

or \( R(3) \) and \( R(4) \) independently of one another are NR(84)R(85);

\( R(84) \) and \( R(85) \) independently of one another are H, (C\(_1\)-C\(_4\))-alkyl, or together are 4 or 5 methylene groups, of which one CH\(_2\) group can be replaced by oxygen, S, NH, N-CH\(_3\) or N-benzyl; or of which one or two CH\(_2\) groups can be replaced by CH-C\(_{dm}\)H\(_{2dm+1}\), and their pharmaceutically tolerable salts;

(HOE 94/F 123 - EP-Offenlegungsschrift 682 017, NZ 272 058)
y) bicyclic heteroarylguanidines of the formula I

in which:

T, U, V, W, X, Y and Z

independently of one another are nitrogen or carbon;

but with the restriction

that X and Z are not simultaneously nitrogen,

and that T, U, V, W, X, Y and Z carry no substituents if they are

nitrogen,

and that no more than four of them are simultaneously nitrogen,

R(1) and R(2)

independently of one another are hydrogen, F, Cl, Br, I, (C₁₋C₃)-

alkyl, (C₁₋C₃)-perfluoroalkyl, OR(8), NR(8)R(9) or C(=O)N=C(NH₂)₂;

R(8) and R(9)

independently of one another are hydrogen or (C₁₋C₃)-alkyl,

or

R(8) and R(9)

together are 4 or 5 methylene groups, of which one CH₂

group can be replaced by oxygen, S, NH, N-CH₃ or N-benzyl;

R(3), R(4), R(5), R(6) and R(7)

independently of one another are hydrogen, F, Cl, Br, I, -C≡N, X⁺⁻

(CH₂)ₚ₋(C₉F₂q₊₁), R(10a)-SO₃⁻, R(10b)R(10c)N-CO, R(11)-CO-

or

R(12)R(13)N⁻⁻SO₂⁻,

where the perfluoroalkyl group is straight-chain or branched;

X is oxygen, S or NR(14);
R(14) is H or (C₁-C₅)-alkyl;

bₘ is zero, 1 or 2;

p is zero, 1 or 2;

k is zero or 1;

q is 1, 2, 3, 4, 5 or 6;

R(10a), R(10b), R(11) and R(12)

independently of one another are (C₁-C₅)-alkyl,
(C₃-C₇)-alkenyl, -C₆H₄R(15) or (C₁-C₅)-perfluoroalkyl;

n is zero, 1, 2, 3 or 4;

R(15) is (C₃-C₇)-cycloalkyl or phenyl, which is not substituted
or is substituted by 1 - 3 substituents selected from the

group consisting of F, Cl, CF₃, methyl, methoxy and

NR(16)R(17);

R(16) and R(17)

are H or C₁-C₄-alkyl;

or

R(10b), R(11) and R(12)

are hydrogen;

R(10c) and R(13)

independently are hydrogen or (C₁-C₅)-alkyl;

or

R(10b) and R(10c) and R(12) and R(13)

together are 4 or 5 methylene groups, of which one CH₂

group can be replaced by oxygen, sulfur, NH, N-CH₃ or

N-benzyl;

or

R(3), R(4), R(5), R(6) and R(7)

independently of one another are (C₁-C₅)-alkyl, -C₆H₄R(18) or (C₃-C₅)

-C₆H₄alkenyl;

al is zero, 1 or 2;

R(18) is (C₃-C₆)-cycloalkyl, phenyl, biphenyl or naphthyl, where

the aromatics are not substituted or are substituted by 1 - 3
substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(19a)R(19b); R(19a) and R(19b) are hydrogen, (C₇-C₉)-alkyl or (C₇-C₉)-perfluoroalkyl;

or

R(3), R(4), R(5), R(6) and R(7) independently of one another are (C₇-C₉)-heteroaryl, which is linked via C or N and which is unsubstituted or substituted by 1 - 3 substituents from the group consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino or dimethylamino;

or

R(3), R(4), R(5), R(6) and R(7)

\[
\begin{align*}
-Y- & \quad \left( C \right) _{h} \left( \text{CHOH} \right) _{i} \left( \text{CH}_{2} \right) _{j} \left( \text{CHOH} \right) _{k} - R (23)
\end{align*}
\]

independently of one another are

\[
\begin{align*}
\text{or} \quad & \quad \left( C \right) _{ah} \left( \text{CHOH} \right) _{ao} \left( \text{CH}_{2} \right) _{ap} \left( \text{CHOH} \right) _{ak} - R (25) \\
\text{or} \quad & \quad \left( C \right) _{ad} \left( \text{CHOH} \right) _{ae} \left( \text{CH}_{2} \right) _{af} \left( \text{CHOH} \right) _{ag} - R (24)
\end{align*}
\]

\[Y\] is oxygen, -S- or -NR(22)-; h, ad, ah independently of one another are zero or 1; i, j, k, ae, af, ag, ao, ap and ak independently of one another are zero, 1, 2, 3 or 4; but where in each case

h, i and k are not simultaneously zero, ad, ae and ag are not simultaneously zero, and
ah, ao and ak are not simultaneously zero, 

\[ R(23), R(24) R(25) \text{ and } R(22) \]

independently of one another are hydrogen or \((C_1-C_3)\)-alkyl;

or

\[ \text{R(3), R(4), R(5), R(6) and R(7)} \]

independently of one another are \(SR(29), -OR(30), -NR(31)R(32)\) or \(-CR(33)R(34)R(35)\);

\[ R(29), R(30), R(31) \text{ and } R(33) \]

independently of one another are \(-C_9H_{2a}(C_1-C_9)\)-heteroaryl, which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino and dimethylamino;

\[ a \text{ is zero, 1 or 2;} \]

\[ \text{R(32), R(34) and R(35)} \]

independently of one another are defined as \(R(29)\) or are hydrogen, \((C_1-C_4)\)-alkyl or \((C_1-C_4)\)-perfluoroalkyl;

or

\[ \text{R(3), R(4), R(5), R(6) and R(7)} \]

independently of one another are

\[ \text{W} \text{---}_{R(96)} \text{---}_{R(97)} \text{ or } \text{W} \text{---}_{R(96)} \text{---}_{R(98)} \]

\[ \text{R(96), R(97) and R(98)} \]

independently of one another are \((C_1-C_9)\)-heteroaryl, which is linked via C or N and which is unsubstituted or substituted by 1 to 3 substituents from the group consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino, dimethylamino or benzyl;

\[ W \text{ is oxygen, S or NR(36)-;} \]

\[ R(36) \text{ is H or } (C_1-C_3)\)-alkyl;

or
R(3), R(4), R(5), R(6) and R(7) independently of one another are R(46)X(1)-;

X(1) is oxygen, S, NR(47), (D=O)A- or NR(48)C=NM[*]R(49)-;

M is oxygen or sulfur;

A is oxygen or NR(50);

D is C or SO;

R(46) is (C₁-C₈)-alkyl, (C₃-C₈)-alkenyl, (CH₂)bC₆F₂d₊₁ or -C₆H₂x-R(51);

b is zero or 1;

d is 1, 2, 3, 4, 5, 6 or 7;

x is zero, 1, 2, 3 or 4;

R(51) is (C₃-C₈)-cycloalkyl, phenyl, biphenyl or naphthyl,
where the aromatics are not substituted or are substituted by 1-3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(52)R(53);

R(52) and R(53)
are hydrogen, (C₁-C₄)-alkyl or (C₁-C₄)-perfluoroalkyl;

R(47), R(48) and R(50) independently
are hydrogen, (C₁-C₄)-alkyl or (C₁-C₄)-perfluoroalkyl;

R(49) is defined as R(46);

or

R(46) and R(47), or R(46) and R(48)
together are 4 or 5 methylene groups, of which one CH₂ groups can be replaced by oxygen, sulfur, NH, N-CH₃ or N-benzyl;

where A and N[*] are bonded to the phenyl nucleus of the heteroaroylguanidine parent structure;

or

R(3), R(4), R(5), R(6) and R(7) independently of one another are -SR(64), -OR(65), -NHR(66), -NR(67)R(68), -CHR(69)R(70) or -CR(54)R(55)OH, -C≡CR(56), -
\text{CR(58)=CR(57) or -[CR(59)R(60)]_v-CO-[CR(61)R(62)]_v-R(63);} \\
R(64), R(65), R(66), R(67) and R(69) 

identically or differently are 
\text{-(CH}_2)_{y}(\text{CHOH})_z-(\text{CH}_2)_{aa}-(\text{CHOH})_t-R(71) \text{ or} \\
\text{-(CH}_2)_{ab}O-(\text{CH}_2\text{-CH}_2O)_{ac}-R(72); \\
R(71) \text{ and } R(72) 

independently of one another are hydrogen or methyl; \\
u \text{ is } 1, 2, 3 \text{ or } 4; \\
v \text{ is zero, } 1, 2, 3 \text{ or } 4; \\
y, z, aa \text{ identically or differently} \\
is zero, 1, 2, 3 \text{ or } 4; \\
t \text{ is } 1, 2, 3 \text{ or } 4; \\
R(68), R(70), R(54) \text{ and } R(55) 

identically or differently are hydrogen or \text{(C}_1\text{-C}_6\text{-alkyl;}

\text{or}

R(69) \text{ and } R(70), \text{ or } R(54) \text{ and } R(55) 

together with the carbon atom carrying them are \text{(C}_3\text{-C}_6\text{-cycloalkyl;}

R(63) 

is hydrogen, \text{(C}_1\text{-C}_6\text{-alkyl, (C}_3\text{-C}_6\text{-cycloalkyl or -C}_6H_{2e}-R(73);}

e \text{ is zero, } 1, 2, 3 \text{ or } 4; \\
R(56), R(57) \text{ and } R(73) \text{ independently} 

are phenyl, which is unsubstituted or substituted by 1 - 3 
substituents selected from the group consisting of F, Cl, CF\text{,} 

methyl, methoxy and NR(74)R(75); \\
R(74) \text{ and } R(75) 

are hydrogen or \text{(C}_1\text{-C}_4\text{-alkyl;}

\text{or}

R(56), R(57) \text{ and } R(73) \text{ independently} 

are \text{(C}_1\text{-C}_9\text{-heteroaryl, which is unsubstituted or substituted as phenyl;}

R(58), R(59), R(60), R(61) \text{ and } R(62)
are hydrogen or methyl;

or

R(3), R(4), R(5), R(6) and R(7)

independently of one another are R(76)-NH-SO₂-;

R(76) is R(77)R(78)N-(C=Y')-;
Y' is oxygen, S or N-R(79);

R(77) and R(78)

identically or differently are hydrogen, (C₁-C₇)-alkyl,
(C₃-C₆)-alkenyl or -C₆H₄-R(80);

f is zero, 1, 2, 3 or 4;

R(80) is (C₅-C₇)-cycloalkyl or phenyl, which is
unsubstituted or substituted by 1 - 3
substituents selected from the group consisting
of F, Cl, CF₃, methoxy and (C₁-C₄)-alkyl;

or

R(77) and R(78)
together are 4 or 5 methylene groups, of which one
CH₂ group can be replaced by oxygen, sulfur, NH,
N-CH₃ or N-benzyl;

R(79) is defined as R(77) or is amidine;

or

R(3), R(4), R(5), R(6) and R(7)

independently of one another are NR(84a)R(85), OR(84b), SR(84c)
or -C₆H₄-R(84d);

n is zero, 1, 2, 3 or 4;

R(84d) is (C₃-C₇)-cycloalkyl or phenyl, which is not substituted
or is substituted by 1 - 3 substituents from the group
consisting of F, Cl, CF₃, methyl, methoxy and
NR(16)R(17);

R(16) and R(17)

are hydrogen or C₁-C₄-alkyl;

R(84a), R(84b), R(84c) and R(85)
independently of one another are hydrogen, (C₁-C₆)-alkyl,
(C₁-C₆)-perfluoroalkyl or (CH₂)ₐₓ-R(84g);

R(84g) is (C₃-C₅)-cycloalkyl or phenyl, which is not
substituted or is substituted by 1 - 3
substituents selected from the group consisting
of F, Cl, CF₃, methyl, methoxy and
NR(84u)R(84v);

R(84u) and R(84v) are hydrogen or C₁-C₄-alkyl;
or

R(84a) and R(85) together are 4 or 5 methylene groups, of which one CH₂
group can be replaced by oxygen, sulfur, NH, N-CH₃ or
N-benzyl,
and their pharmaceutically tolerable salts;

(HOE 94/F 134 - EP-Offenlegungsschrift 686 627, NZ 272 103)
z) benzoylguanidines of the formula I

\[
\begin{align*}
R(1) & \quad \text{is } R(6)-SO_m; \\
m & \quad \text{is zero, 1 or 2;}
R(6) & \quad \text{is perfluoroalkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, which,}
& \quad \text{is straight-chain or branched;}
R(2) & \quad \text{and } R(3)
\end{align*}
\]

independently of one another are hydrogen, F, Cl, Br, I, alkyl having
1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms
or phenoxy,

which is unsubstituted or substituted by 1 - 3 substituents
selected from the group consisting of F, Cl, methyl and
methoxy;

or

R(2) and R(3)

independently of one another are pyrrol-1-yl, pyrrol-2-yl or pyrrol-3-yl,

which is not substituted or is substituted by 1 to 4

substituents selected from the group consisting of F, Cl, Br, I,
CN, alkanoyl having 2, 3, 4, 5, 6, 7 or 8 carbon atoms,
alkoxycarbonyl having 2, 3, 4, 5, 6, 7 or 8 carbon atoms,
formyl, carboxyl, CF$_3$, methyl and methoxy;

R(4) and R(5)

independently of one another are hydrogen, alkyl having 1, 2 or 3
carbon atoms, F, Cl, Br, I, CN, OR(7), NR(8)R(9) or -(CH$_2$)$_n$-(CF$_2$)$_o$-
CF$_3$;

R(7), R(8) and R(9)

independently of one another are hydrogen or alkyl having 1,
2, 3 or 4 carbon atoms;

n is zero or 1;

o is zero, 1 or 2;

and their pharmacologically acceptable salts;
ab) Phenyl-substituted alkenylcarboxylic acid guanidides, carrying perfluoroalkyl groups, of the formula I

\[
\text{R(A)} \quad \text{is hydrogen, F, Cl, Br, I, CN, OH, OR(6), (C}_1\text{-C}_8\text{-)alkyl, O}_x(\text{CH}_2)_y\text{C}_z\text{-alkyl, (C}_3\text{-C}_8\text{-cycloalkyl or NR(7)R(8);} \\
\text{r} \quad \text{is zero or 1;} \\
\text{a} \quad \text{is zero, 1, 2, 3 or 4;} \\
\text{b} \quad \text{is 1, 2, 3, 4, 5, 6, 7 or 8;} \\
\text{R(6)} \quad \text{is (C}_1\text{-C}_8\text{-alkyl, (C}_1\text{-C}_4\text{-)perfluoroalkyl, (C}_3\text{-C}_8\text{-alkenyl,} \\
\text{(C}_3\text{-C}_8\text{-cycloalkyl, phenyl or benzyl;}} \\
\text{where the aromatics are not substituted or are substituted by 1 - 3 substituents from the group consisting of F, Cl, CF}_3\text{, methyl, methoxy and} \\
\text{NR(9)R(10);} \\
\text{R(9) and R(10) are H, (C}_1\text{-C}_4\text{-)alkyl or (C}_1\text{-C}_4\text{-perfluoroalkyl;}} \\
\text{R(7) and R(8) independently of one another are defined as R(6);} \\
\text{or} \\
\text{R(7) and R(8) together are 4 or 5 methylene groups, of which one CH}_2
group can be replaced by oxygen, sulfur, NH, N-CH₃ or N-benzyl;

R(B) independently is defined as R(A);

x is zero, 1 or 2;

y is zero, 1 or 2;

R(C) is hydrogen, F, Cl, Br, I, CN, OR(12), (C₁₋₃₋₅₋₇₋₉₋₁₁₋₁₃₋₁₅₋₁₇₋₁₉₋₂₁₋₂₃₋₂₅₋₂₇₋₂₉₋₃₁₋₃₃₋₃₅₋₃₇₋₃₉₋₄₁₋₄₃₋₄₅₋₄₇₋₄₉₋₅₁₋₅₃₋₅₅₋₅₇₋₅₉₋₆₁₋₆₃₋₆₅₋₆₇₋₆₉₋₇₁₋₇₃₋₇₅₋₇₇₋₇₉₋₈₁₋₈₃₋₈₅₋₈₇₋₈₉₋₉₁₋₉₃₋₉₅₋₉₇₋₉₉₋₁₀₁₋₁₀₃₋₁₀₅₋₁₀₇₋₁₀₉₋₁₁₁₋₁₁₃₋₁₁₅₋₁₁₇₋₁₁₉₋₁₂₁₋₁₂₃₋₁₂₅₋₁₂₇₋₁₂₉₋₁₃₁₋₁₃₃₋₁₃₅₋₁₃₇₋₁₃₉₋₁₄₁₋₁₄₃₋₁₄₅₋₁₄₇₋₁₄₉₋₁₅₁₋₁₅₃₋₁₅₅₋₁₅₇₋₁₅₉₋₁₆₁₋₁₆₃₋₁₆₅₋₁₆₇₋₁₆₉₋₁₇₁₋₇₃₋₇₅₋₇₇₋₇₉₋₈₁₋₈₃₋₈₅₋₈₇₋₈₉₋₉₁₋₉₃₋₉₅₋₉₇₋₉₉₋₁₀₁₋₁₀₃₋₁₀₅₋₁₀₇₋₁₀₉₋₁₁₁₋₁₁₃₋₁₁₅₋₁₁₇₋₁₁₉₋₁₂₁₋₁₂₃₋₁₂₅₋₁₂₇₋₁₂₉₋₁₃₁₋₁₃₃₋₁₃₅₋₁₃₇₋₁₃₉₋₁₄₁₋₁₄₃₋₁₄₅₋₁₄₇₋₁₄₉₋₁₅₁₋₁₅₃₋₁₅₅₋₁₅₇₋₁₅₉₋₁₆₁₋₁₆₃₋₁₆₅₋₁₆₇₋₁₆₉₋₁₇₁₋₇₃₋₇₅₋₇₇₋₇₉₋₈₁₋₈₃₋₈₅₋₈₇₋₈₉₋₉₁₋₉₃₋₉₅₋₉₇₋₉₉₋₁₀₁₋₁₀₃₋₁₀₅₋₁₀₇₋₁₀₉₋₁₁₁₋₁₁₃₋₁₁₅₋₁₁₇₋₁₁₉₋₁₂₁₋₁₂₃₋₁₂₅₋₁₂₇₋₁₂₉₋₁₃₁₋₁₃₃₋₁₃₅₋₁₃₇₋₁₃₉₋₁₄₁₋₁₄₃₋₁₄₅₋₁₄₇₋₁₄₉₋₁₅₁₋₁₅₃₋₁₅₅₋₁₅₇₋₁₅₉₋₁₆₁₋₁₆₃₋₁₆₅₋₁₆₇₋₁₆₉₋₁₇₁₋₇₃₋₇₅₋₇₇₋₇₉₋₈₁₋₈₃₋₈₅₋₈₇₋₈₉₋₉₁₋₉₃₋₉₅₋₉₇₋₉₉₋₁₀₁₋₁₀₃₋₁₀₅₋₁₀₇₋₁₀₉₋₁₁₁₋₁₁₃₋₁₁₅₋₁₁₇₋₁₁₉₋₁₂₁₋₁₂₃₋₁₂₅₋₁₂₇₋₁₂₉₋₁₃₁₋₁₃₃₋₁₃₅₋₁₃₇₋₁₃₉₋₁₄₁₋₁₄₃₋₁₄₅₋₁₄₇₋₁₄₉₋₁₅₁₋₁₅₃₋₁₅₅₋₁₅₇₋₁₅₉₋₁₆₁₋₁₆₃₋₁₆₅₋₁₆₇₋₁₆₉₋₁₇₁₋₇₃₋₇₅₋₇₇₋₇₉₋₈₁₋₈₃₋₈₅₋₈₇₋₈₉₋₉₁₋₉₃₋₉₅₋₉₇₋₉₉₋₁₀₁₋₁₀₃₋₁₀₅₋₁₀₇₋₁₀₉₋₁₁₁₋₁₁₃₋₁₁₅₋₁₁₇₋₁₁₉₋₁₂₁₋₁₂₃₋₁₂₅₋₁₂₇₋₁₂₉₋₁₃₁₋₁₃₃₋₁₃₅₋₁₃₇₋₁₃₉₋₁₄₁₋₁₄₃₋₁₄₅₋₁₄₇₋₁₄₉₋₁₅₁₋₁₅₃₋₁₅₅₋₁₅₇₋₁₅₉₋₁₆₁₋₁₆₃₋₁₆₅₋₁₆₇₋₁₆₉₋₁₇₁₋₇₃₋₇₅₋₇₇₋₇₉₋₈₁₋₈₃₋₈₅₋₈₇₋₈₉₋₉₁₋₉₃₋₉₅₋₉₇₋₉₉₋₁₀₁₋₁₀₃₋₁₀₅₋₁₀₇₋₁₀₉₋₁₁₁₋₁₁₃₋₁₁₅₋₁₁₇₋₁₁₉₋₁₂₁₋₁₂₃₋₁₂₅₋₁₂₇₋₁₂₉₋₁₃₁₋₁₃₃₋₁₃₅₋₁₃₇₋₁₃₉₋₁₄₁₋₁₄₃₋₁₄₅₋₁₄₇₋₁₄₉₋₁₅₁₋₁₅₃₋₁₅₅₋₁₅₇₋₁₅₉₋₁₆₁₋₁₆₃₋₁₆₅₋₁₆₇₋₁₆₉₋₁₇₁₋₇₃₋₇₅₋₇₇₋₇₉₋₈₁₋₈₃₋₈₅₋₈₇₋₈₉₋₉₁₋₉₃₋₉₅₋₉₇₋₉₉₋₁₀₁₋₁₀₃₋₁₀₅₋₁₀₇₋₁₀₉₋₁₁₁₋₁₁₃₋₁₁₅₋₁₁₇₋₁₁₉₋₁₂₁₋₁₂₃₋₁₂₅₋₁₂₇₋₁₂₉₋₁₃₁₋₁₃₃₋₁₃₅₋₁₃₇₋₁₃₉₋₁₄₁₋₁₄₃₋₁₄₅₋₁₄₇₋₁₄₉₋₁₅₁₋₁₅₃₋₁₅₅₋₁₅₇₋₁₅₉₋₁₆₁₋₁₆₃₋₁₆₅₋₁₆₇₋₁₆₉₋₁₇₁₋₇₃₋₇₅₋₇₇₋₇₉₋₈₁₋₈₃₋₈₅₋₈₇₋₈₉₋₉₁₋₉₃₋₉₅₋₉₇₋₉₉₋₁₀₁₋₁₀₃₋₁₀₅₋₁₀₇₋₁₀₉₋₁₁₁₋₁₁₃₋₁₁₅₋₁�
and their pharmaceutically tolerable salts;
(HOE 94/F 182 - EP-Offenlegungsschrift 690 048, NZ 272 449)
ac) ortho-amino-substituted benzoylguanidines of the formula I

\[
\begin{array}{c}
\text{R}(1) \text{R}(2) \text{R}(3) \text{R}(4) \\
\text{R}(5) \text{R}(6) \text{R}(7) \\
\text{R}(8) \text{R}(9) \text{R}(10) \\
\end{array}
\]

in which:
R(1) is NR(50)R(6),
R(50) and R(6)

independently of one another are hydrogen, (C₁₋₅)-alkyl or
(C₁₋₃)-perfluoroalkyl;

R(2), R(3), R(4) and R(5)
independently of one another are R(10)-SO₂⁻, R(11)R(12)N-CO⁻,
R(13)-CO⁻ or R(14)R(15)N-SO₂⁻;

a is zero, 1 or 2,
R(10), R(11), R(12), R(13), R(14) and R(15)
independently of one another are (C₁₋₅)-alkyl, (C₁₋₃)-perfluoroalkyl,
(C₃₋₅)-alkenyl or -CₐbH₂ab-R(16);

ab is zero, 1, 2, 3 or 4;
R(16) is (C₃₋₇)-cycloalkyl, phenyl,
which is not substituted or is substituted by 1 - 3
substituents selected from the group consisting of F,
Cl, CF₃, methyl, methoxy and NR(17)R(18);
R(17) and R(18)
independently of one another are H, CF₃ or
(C₁₋₄)-alkyl;
or
R(11), R(12), and also R(14) and R(15)
together are 4 or 5 methylene groups, of which one
CH₂ group can be replaced by oxygen, S, NH, N-CH₃ or N-benzyl;

or

R(11), R(12), R(14) and R(15)

independently of one another are hydrogen;

or

R(2), R(3), R(4) and R(5)

independently of one another are SR(21), -OR(22), -NR(23)R(24) or -CR(25)R(26)R(27);

R(21), R(22), R(23) and R(25)

independently of one another are \(-C₆H₄-\)heteroaryl, which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino and dimethylamino;

b is zero, 1 or 2;

R(24), R(26) and R(27)

independently of one another are hydrogen, \((C₁-C₄)\)-alkyl or \((C₁-C₄)\)-perfluoroalkyl;

or

R(2), R(3), R(4) and R(5)

independently of one another are hydrogen, F, Cl, Br, I, CN, -(Xa)dg-C₆H₄-(-(Xb)dh-(CH₂)db-C₆F₂dh+1, (C₃-C₈)\)-alkenyl or -C₆H₂dfR(30);

(Xa) is O, S or NR(33);

R(33)

is H, \((C₁-C₄)\)-alkyl or \((C₁-C₄)\)-perfluoroalkyl;

dg is zero or 1;

(Xb) is O, S or NR(34);

R(34)

is H, \((C₁-C₄)\)-alkyl or \((C₁-C₄)\)-perfluoroalkyl;

dh is zero or 1;

da is zero, 1, 2, 3, 4, 5, 6, 7, 8;
db is zero, 1, 2, 3, 4;
dc is zero, 1, 2, 3, 4, 5, 6, 7;
df is zero, 1, 2, 3, 4;

R(30)

5 is (C₃-C₈)-cycloalkyl, phenyl, biphenylyl or naphthyl, where
the aromatics phenyl, biphenylyl or naphthyl are not
substituted or are substituted by 1 - 3 substituents selected
from the group consisting of F, Cl, CF₃, methyl, methoxy and
NR(31)R(32);

10 R(31) and R(32)

are H, (C₁-C₄)-alkyl or (C₁-C₄)-perfluoroalkyl;

or

R(2), R(3), R(4) and R(5)

independently of one another are NR(40)R(41) or -(Xe)-

(CH₂)₉R(45);

R(40) and R(41)

independently of one another are hydrogen, (C₁-C₄)-alkyl,
(C₁-C₈)-perfluoroalkyl or (CH₂)₉-R(42);

e is zero, 1, 2, 3 or 4;

R(42)

is (C₃-C₇)-cycloalkyl, phenyl, which is not substituted or
is substituted by 1 - 3 substituents selected from the
group consisting of F, Cl, CF₃, methyl, methoxy and
NR(43)R(44);

25 R(43) and R(44)

independently of one another are H, CF₃ or
(C₁-C₄)-alkyl;

or

R(40) and R(41)

30 together are 4 or 5 methylene groups, of which one CH₂
group can be replaced by oxygen, sulfur, NH, N-CH₃ or
N-benzyl;
(Xe) is O, S or NR(47);
R(47)
is H, (C₃₋C₄)-alkyl or (C₁₋C₄)-perfluoroalkyl;

eb is zero, 1, 2, 3 or 4;

R(45) is (C₃₋C₇)-cycloalkyl, phenyl, which is not substituted or is
substituted by 1 - 3 substituents selected from the group
consisting of F, Cl, CF₃, methyl, methoxy, NR(50)R(51) and
-(Xfa)-(CH₂)ₑ₋ₓ-(Xfb)R(46);
Xfa is CH₂, O, S or NR(48);
Xfb is O, S or NR(49);
ed is 1, 2, 3 or 4;

R(46)
is H, (C₁₋C₄)-alkyl or (C₁₋C₄)-perfluoroalkyl;
R(48), R(49), R(50) and R(51)
independently of one another are H or (C₁₋C₄)-alkyl or
(C₁₋C₄)-perfluoroalkyl;

where R(3) and R(4), however, cannot be hydrogen,
and their pharmaceutically tolerable salts;
(HOE 94/F 265 - NZ 272 946, EP-Offenlegungsschrift 700 904)

ad) benzoylguanidines of the formula I

in which:

one of the three substituents R(1), R(2) and R(3)
is (C₃₋C₆)-heteroaryl-N-oxide,
which is linked via C or N and which is unsubstituted or
substituted by 1 - 3 substituents selected from the group
consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino and dimethylamino;

or

one of the three substituents R(1), R(2) and R(3)

5  is -SR(10), -OR(10), -NR(10)R(11) or -CR(10)R(11)R(12);
R(10)
is -C₆H₄-(C₁₋C₉)-heteroaryl-N-oxide, 
which is unsubstituted or substituted by 1 - 3
substituents selected from the group consisting of F,

10  Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino
and dimethylamino;

a  is zero, 1 or 2;
R(11) and R(12)

are hydrogen or (C₁₋C₄)-alkyl;

and the other substituents R(1), R(2) and R(3) in each case

independently of one another are defined as R(10),

15  are hydrogen or (C₁₋C₄)-alkyl;

and the other substituents R(1), R(2) and R(3) in each case

independently of one another are (C₁₋C₉)-alkyl, (C₂₋C₉)-alkenyl or
-C₉H₈mR(14);

20  m  is zero, 1 or 2;
R(14) is (C₃₋C₉)-cycloalkyl or phenyl,

which is not substituted or is substituted by 1 - 3
substituents selected from the group consisting
of F, Cl, CF₃, methyl, methoxy and
NR(15)R(16),

25  R(15) and R(16)

are hydrogen or CH₃;

or

the other substituents R(1), R(2) and R(3) in each case

independently of one another are hydrogen, F, Cl, Br, I, -C≡N,

30  X-(CH₂)ₚ-(C₉F₂q₋₁), R(22)-SO₄, R(23)R(24)N-CO, R(25)-CO- or
R(26)R(27)N-SO₂⁻,

where the perfluoroalkyl group is straight-chain or branched;
X is a bond, oxygen, S or NR(28);
n is zero, 1 or 2;
p is zero, 1 or 2;
q is zero, 1, 2, 3, 4, 5 or 6;
R(22), R(23), R(25) and R(26)
individually are (C\textsubscript{1}-C\textsubscript{6})-alkyl, (C\textsubscript{2}-C\textsubscript{6})-alkenyl, -C\textsubscript{n}H\textsubscript{2n}-R(29)
or CF\textsubscript{3};
n is zero, 1, 2, 3 or 4;
R(28) is hydrogen or (C\textsubscript{1}-C\textsubscript{6})-alkyl;
R(29) is (C\textsubscript{3}-C\textsubscript{7})-cycloalkyl or phenyl;
which is not substituted or is substituted by 1 - 3
substituents selected from the group consisting
of F, Cl, CF\textsubscript{3}, methyl, methoxy and
NR(30)R(31);
R(30) and R(31)
are hydrogen or C\textsubscript{1}-C\textsubscript{4}-alkyl,
or
R(23), R(25) and R(26)
are also hydrogen;
R(24) and R(27)
individually of one another are hydrogen or (C\textsubscript{1}-C\textsubscript{4})-alkyl;
or
R(23) and R(24), and also R(26) and R(27) together are 4 or 5
methylene groups, of which one CH\textsubscript{2} group can be replaced by
oxxygen, S, NH, N-CH\textsubscript{3} or N-benzyl;
or
the other substituents R(1), R(2) and R(3) in each case
individually of one another are OR(35) or NR(35)R(36);
R(35) and R(36)
independently of one another are hydrogen or (C\textsubscript{1}-C\textsubscript{6})-alkyl;
or
R(35) and R(36)
together are 4 - 7 methylene groups, of which one CH2 group can be replaced by oxygen, S, NH, N-CH3 or N-benzyl,

R(4) and R(5)

independently of one another are hydrogen, (C1-C4)-alkyl, F, Cl,

-OR(32), -NR(33)R(34) or C1F2r+1;

R(32), R(33) and R(34)

independently of one another are hydrogen or (C1-C2)-alkyl;

r is 1, 2, 3 or 4;

and their pharmaceutically tolerable salts;

(HOE 94/F 266 - EP-Offenlegungsschrift 702 001, NZ 272 948)

ae) benzoylguanidines of the formula I

in which:

R(1) is hydrogen, F, Cl, Br, I, CN, NO2, OH, (C1-C6)-alkyl, (C3-C6)-cycloalkyl, Oa-(CH2)b-(CF2)c-CF3;

a is zero or 1;

b is zero, 1 or 2;

c is zero, 1 or 2 or 3;

or

R(1) is R(5)-SOm or R(6)R(7)N-SO2-;

m is zero, 1 or 2;

R(5) and R(6) independently of one another are (C1-C6)-alkyl, (C3-C6)-alkenyl, CF3 or CnH2n-R(8);

n is zero, 1, 2, 3 or 4;

R(7) is hydrogen or (C1-C4)-alkyl;
R(8) is \((C_3\text{-}C_7)\text{-cycloalkyl or phenyl,}
\)
which is not substituted or is substituted by 1 - 3
substituents selected from the group consisting of F,
Cl, CF₃, methyl, methoxy and NR(9)R(10);
\R(9) and R(10) independently of one another
are hydrogen or \((C_1\text{-}C_4)\text{-alkyl;}
\)
or
R(6) is H;
or R(6) and R(7)
together are 4 or 5 methylene groups, of which one CH₂
group can be replaced by oxygen, S, NH, N-CH₃ or N-benzyl,
or
R(1) is -SR(11), -OR(11) or -CR(11)R(12)R(13);
R(11) is \(-C_6H_{2p}(C_3\text{-}C_9)\text{-cycloalkyl, -(C}_1\text{-}C_9)\text{-heteroaryl or phenyl,}
\)
where the aromatic systems are unsubstituted
or substituted by 1 - 3 substituents selected
from the group consisting of F, Cl, CF₃, CH₃,
methoxy, hydroxyl, amino, methylamino and
dimethylamino;
\R(12), R(13) independently of one another
are defined as R(11) or are hydrogen or
\((C_1\text{-}C_4)\text{-alkyl;}
\)
p is zero, 1 or 2;
or
R(1) is phenyl, naphthyl, biphenylyl or \((C_1\text{-}C_9)\text{-heteroaryl, the latter linked}
via C or N,
which are unsubstituted or substituted by 1 - 3 substituents
selected from the group consisting of F, Cl, CF₃, CH₃,
methoxy, hydroxyl, amino, methylamino and dimethylamino;
\R(2) is -CF₂R(14), -CF[R(15)][R(16)], -CF[(CF₂)ₚCF₃][R(15)],
-C[(CF₂)ₚCF₃]=CR(15)R(16);
R(14) is \((C_1\text{-}C_4)\text{-alkyl or (C}_3\text{-}C_6)\text{-cycloalkyl;}
\)
R(15) and R(16) independently of one another are hydrogen or (C₁-C₄)-alkyl;

q is zero, 1 or 2;

r is zero, 1 or 2;

R(3) is defined as R(1);

R(4) is hydrogen, (C₁-C₃)-alkyl, F, Cl, Br, I, CN, -(CH₂)ₓ-(CF₂)ᵧ-CF₃;

s is zero or 1;

t is zero, 1 or 2;

and their pharmaceutically tolerable salts;

(HOE 94/F 267 - EP-Offenlegungsschrift 700 899, NZ 272 947; (HOE 94/F 267 - EP-Offenlegungsschrift 700 899, NZ 272 947

af) benzoylguanidines of the formula I

R(1) NH₂

R(2) R(3) R(4) R(5)

in which:

one of the three substituents R(1), R(2) and R(3) is -Y-4-[(CH₂)ₓ-CHR(7)-(C=O)R(8)]-phenyl, -Y-3-[(CH₂)ₓ-CHR(7)-(C=O)R(8)]-phenyl or -Y-2-[(CH₂)ₓ-CHR(7)-(C=O)R(8)]-phenyl, where the phenyl in each case is unsubstituted or substituted by 1 - 2 substituents from the group F, Cl, -CF₃, methyl, hydroxyl, methoxy, or -NR(37)R(38);

R(37) and R(38) independently of one another are hydrogen or -CH₃;

Y is a bond, oxygen, -S- or -NR(9);

R(9) is hydrogen or -(C₁-C₄)-alkyl;

R(7) is -OR(10) or -NR(10)R(11);
R(10) and R(11)
individually of one another are hydrogen, -(C₁₋₈)-alkyl, -(C₁₋₈)-alkanoyl, -(C₁₋₈)-alkoxycarbonyl, benzyl, benzyloxy carbonyl;

or

R(10) is trityl;
R(8) is -OR(12) or -NR(12)R(13);
R(12) and R(13)
independently of one another are hydrogen, -(C₁₋₈)-alkyl or benzyl;

k is zero, 1, 2, 3 or 4;

and the other radicals R(1), R(2) and R(3) in each case
individually of one another are -(C₁₋₈)-alkyl, -(C₂₋₈)-alkenyl or -(CH₂)ₘR(14);

m is zero, 1 or 2;
R(14) is -(C₃₋₈)-cycloalkyl or phenyl,
which is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F, Cl, -CF₃, methyl, methoxy and -NR(15)R(16);
R(15) and R(16)
are hydrogen or -CH₃;

or

the other radicals R(1), R(2) and R(3) in each case
individually of one another are R(18)R(19)N-(C=Y')-NH-SO₂⁻;

Y' is oxygen, -S- or -N-R(20);
R(18) and R(19)
independently of one another are hydrogen, -(C₁₋₈)-alkyl, -(C₃₋₈)-alkenyl or -(CH₂)ₜR(21);
t is zero, 1, 2, 3 or 4;
R(21) is -(C₅₋₇)-cycloalkyl or phenyl,
which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F,
Cl, -CF₃, methoxy and -(C₁₋₄)-alkyl;

or

R(18) and R(19) together are 4 or 5 methylene groups, of which one CH₂ group can be replaced by oxygen, -S-, -NH-, -N-CH₃ or -N-benzyl;

R(20) is defined as R(18) or is amidine;

or

the other radicals R(1), R(2) and R(3) in each case independently of one another are hydrogen, F, Cl, Br, I, -C≡N, X-(CH₂)ᵢ-(C₄F₂₋₄₋), R(22)-SO₂⁻, R(23)R(24)N-CO⁻, R(25)-CO⁻ or R(26)R(27)N-SO₂⁻, where the perfluoroalkyl group is straight-chain or branched;

X is a bond, oxygen, -S- or -NR(28);

u is zero, 1 or 2;

p is zero, 1 or 2;

q is 1, 2, 3, 4, 5 or 6;

R(22), R(23), R(25) and R(26) independently of one another are -(C₁₋₃)-alkyl,

-(C₃₋₆)-alkenyl, -(CH₂)ₙ-R(29) or -CF₃;

n is zero, 1, 2, 3 or 4;

R(28) is hydrogen or -(C₁₋₃)-alkyl;

R(29) is -(C₃₋₉)-cycloalkyl or phenyl, which is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F, Cl, -CF₃, methyl, methoxy and -NR(30)R(31);

R(30) and R(31) are hydrogen or -(C₁₋₄)-alkyl;

or

R(23), R(25) and R(26) are hydrogen;
R(24) and R(27) independently of one another are hydrogen or -(C_1-C_4)-alkyl;

or

R(23) and R(24), and also R(26) and R(27) together are 4 or 5 methylene groups, of which one CH\_2 group can be replaced by oxygen, -S-, -NH-, -N-CH\_3 or -N-benzyl;

or

the other radicals R(1), R(2) and R(3) in each case independently of one another are -OR(35) or -NR(35)R(36);

R(35) and R(36) independently of one another are hydrogen or -(C_1-C_4)-alkyl;

or

R(35) and R(36) together are 4 - 7 methylene groups, of which one CH\_2 group can be replaced by oxygen, -S-, -NH-, -N-CH\_3 or -N-benzyl;

R(4) and R(5) independently of one another are hydrogen, -(C_1-C_4)-alkyl, F, Cl, -OR(32), -NR(33)R(34) or -C\_rF\_2r+;

R(32), R(33) and R(34) independently of one another are hydrogen or -(C_1-C_4)-alkyl;

r is 1, 2, 3 or 4;

and their pharmaceutically tolerable salts;

(HOE 94/F 352 - EP-Offenlegungsschrift 713 684, NZ 280 517)

ag) benzoylguanidines of the formula I

\[
\begin{align*}
\text{R(1)} & \\
\text{R(2)} & \\
\text{R(3)} & \\
\text{R(4)} & \\
\text{R(5)} & \\
\end{align*}
\]

in which:
R(1) is R(6)-CO or R(7)R(8)N-CO;

R(6) is (C_1-C_8)-alkyl, (C_1-C_8)-perfluoroalkyl, (C_3-C_8)-alkenyl or -C_nH_{2n}-R(9),

n is zero, 1, 2, 3 or 4;

R(9) is (C_3-C_8)-cycloalkyl, phenyl, biphenylyl or naphthyl,

where the aromatics are not substituted or are substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF_3, methyl, methoxy and NR(10)R(11), R(10) and R(11) are H, (C_1-C_4)-alkyl or (C_1-C_4)-perfluoroalkyl;

R(7) is H, (C_1-C_8)-alkyl, (C_1-C_8)-perfluoroalkyl, (C_3-C_8)-alkenyl or -C_nH_{2n}-R(12);

n is zero, 1, 2, 3 or 4;

R(12) is (C_3-C_8)-cycloalkyl, phenyl, biphenylyl or naphthyl,

where the aromatics are not substituted or are substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF_3, methyl, methoxy and NR(13)R(14);

R(13) and R(14) are H, (C_1-C_4)-alkyl or (C_1-C_4)-perfluoroalkyl;

R(8) is H, (C_1-C_4)-alkyl or (C_1-C_4)-perfluoroalkyl;
or

R(7) and R(8) together are 4 or 5 methylene groups, of which one CH_2 group can be replaced by oxygen, S, NH, N-CH_3 or N-benzyl;
R(2) is defined as R(1), or is H, OH, F, Cl, Br, I, CN, NO₂, (C₁-C₈)-alkyl, (C₁-C₈)-perfluoroalkyl, (C₃-C₈)-alkenyl or -CₙH₂ₙR(15);

R(15) is (C₃-C₈)-cycloalkyl, phenyl, biphenyl or naphthyl,

where the aromatics are not substituted or are substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(16)R(17);

R(16) and R(17) are H, (C₁-C₄)-alkyl or (C₁-C₄)-perfluoroalkyl;

or

R(2) is (C₁-C₈)-heteroaryl,

which is linked via C or N and which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino and dimethylamino;

or

R(2) is SR(18), -OR(18), -NR(18)R(19) or -OR(18)R(18)R(20);

R(18) is CₙH₂ₙ-(C₁-C₈)-heteroaryl,

which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino, dimethylamino;

a is zero, 1 or 2;

R(19) and R(20) independently of one another are defined as R(18) or are hydrogen, (C₁-C₄)-alkyl or (C₁-C₄)-perfluoroalkyl;

or

R(2) is R(21)-SOₘ or R(22)R(23)N-SO₂⁻;

m is 1 or 2;

R(21) is (C₁-C₈)-alkyl, (C₁-C₈)-perfluoroalkyl, (C₃-C₈)-alkenyl or -CₙH₂ₙR(24);

n is zero, 1, 2, 3 or 4;
R(24) is \((C_3-C_8)\)-cycloalkyl, phenyl, biphenyl or naphthyl, where the aromatics are not substituted or are substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(27)R(28);

R(27) and R(28) are H, \((C_1-C_4)\)-alkyl or \((C_1-C_4)\)-perfluoroalkyl;

R(22) is H, \((C_1-C_8)\)-alkyl, \((C_1-C_8)\)-perfluoroalkyl, \((C_3-C_8)\)-alkenyl or \(-C_nH_{2n}\); where \(n\) is zero, 1, 2, 3 or 4;

R(29) is \((C_3-C_8)\)-cycloalkyl, phenyl, biphenyl or naphthyl, where the aromatics are not substituted or are substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(30)R(31);

R(30) and R(31) are H, \((C_1-C_4)\)-alkyl or \((C_1-C_4)\)-perfluoroalkyl;

R(23) is hydrogen, \((C_1-C_4)\)-alkyl or \((C_1-C_4)\)-perfluoroalkyl; or R(22) and R(23) together are 4 or 5 methylene groups, of which one \(CH_2\) group can be replaced by oxygen, S, NH, N-CH₃ or N-benzyl; or

R(2) is R(33)X-;

X is oxygen, S, NR(34), \((D=O)A^-\) or \(NR(34)C=NM^{(\alpha)}R(35)\); M is oxygen or S;

A is oxygen or NR(34);

D is C or SO;

R(33) is \((C_1-C_8)\)-alkyl, \((C_3-C_8)\)-alkenyl, \((CH_2)_{n}C_6F_{2n+1}\) or
-C\(_n\)H\(_{2n}\)-R(36);

b is zero or 1;
d is 1, 2, 3, 4, 5, 6 or 7;
n is zero, 1, 2, 3, or 4;

5

R(36) is (C\(_3\)-C\(_8\))-cycloalkyl, phenyl, biphenyl or naphthyl,

where the aromatics are not substituted or are substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF\(_3\), methyl,

methoxy and NR(37)R(38);

R(37) and R(38)

are H, (C\(_1\)-C\(_4\))-alkyl or (C\(_1\)-C\(_4\))-perfluoroalkyl;

R(34) is hydrogen, (C\(_1\)-C\(_4\))-alkyl or (C\(_1\)-C\(_4\))-perfluoroalkyl;

10

R(35) is defined as R(33);

or

R(33) and R(34)
together are 4 or 5 methylene groups, of which one CH\(_2\) group can be replaced by oxygen, S, NH, N-CH\(_3\)

or N-benzyl;

where A and N\(^{+}\) are bonded to the phenyl nucleus of the benzoxyguanidine parent structure;

or

R(2) is -SR(40), -OR(40), -NHR(40), -NR(40)R(41), -CHR(40)R(42),

25

-CR(42)R(43)OH, -C=CR(45), -CR(46)=CR(45) or

-[CR(47)R(48)]\(_u\)-CO-[C(R49)R(50)]\(_v\)-R(44);

R(40) and R(41)
independently of one another are -(CH\(_2\))\(_p\)-(CHOH)\(_q\)-(CH\(_2\))\(_r\)-(CHOH)\(_t\)-R(51) or -(CH\(_2\))\(_p\)-O-(CH\(_2\)-CH\(_2\)O)\(_q\)-R(51);

30

R(51) is hydrogen or methyl;

u is 1, 2, 3 or 4;

v is zero, 1, 2, 3 or 4;
p, q and r

independently of one another are zero, 1, 2, 3 or 4;

t is 1, 2, 3 or 4;

R(42) and R(43)

independently of one another are hydrogen or (C<sub>1</sub>-C<sub>6</sub>)-alkyl;

or

R(42) and R(43)

together with the carbon atom carrying them are a (C<sub>3</sub>-C<sub>6</sub>)-cycloalkyl;

R(44) is hydrogen, (C<sub>1</sub>-C<sub>6</sub>)-alkyl, (C<sub>3</sub>-C<sub>6</sub>)-cycloalkyl, -C<sub>6</sub>H<sub>2</sub>-R(45);

e is zero, 1, 2, 3 or 4;

R(45) is phenyl,

which is unsubstituted or substituted by 1-3 substituents selected from the group consisting of F,

Cl, CF<sub>3</sub>, methyl, methoxy and NR(52)R(53);

R(52) and R(53)

are H or (C<sub>1</sub>-C<sub>4</sub>)-alkyl;

or

R(45) is (C<sub>1</sub>-C<sub>6</sub>)-heteroaryl,

which is unsubstituted or substituted as phenyl;

or

R(45) is (C<sub>1</sub>-C<sub>6</sub>)-alkyl,

which is unsubstituted or substituted by 1-3 OH;

R(46), R(47), R(48), R(49) and R(50)

independently of one another are hydrogen or methyl;

or

R(2) is R(55)-NH-SO<sub>2</sub>-;

R(55) is R(56)R(57)N-(C=Y)-;

Y is oxygen, S or N-R(58);

R(56) and R(57)

independently of one another are hydrogen, (C<sub>1</sub>-C<sub>6</sub>)-alkyl,

(C<sub>3</sub>-C<sub>6</sub>)-alkenyl or -C<sub>6</sub>H<sub>2</sub>-R(59);
f is zero, 1, 2, 3 or 4;

R(59) is (C₅₋C₇)-cycloalkyl, phenyl,

which is unsubstituted or substituted by

1-3 substituents selected from the

group consisting of F, Cl, CF₃, methoxy

and (C₁₋C₄)-alkyl;

or

R(56) and R(57)
together are 4 or 5 methylene groups, of which one CH₂

group can be replaced by oxygen, S, NH, N-CH₃ or N-benzyl;

R(58)
is defined as R(56) or is amidine;

R(3), R(4) and R(5) are independently of one another defined as R(1) or

R(2), but where at least one of the substituents R(2), R(3), R(4) and R(5)
must be OH;

and their pharmaceutically tolerable salts;

(HOE 95/F 007 K - EP-Offenlegungsschrift 723 956, NZ 280 887)

ah) benzoylguanidines of the formula I

in which:

one of the three substituents R(1), R(2) and R(3)
is R(6)-A-B-D-;

R(6) is a basic protonatable radical, i.e. an amino group

-NR(7)R(8), an amidino group R(7)R(8)N-C[=N-R(9)]- or a

guanidino group
R(7), R(8), R(9) and R(10) independently of one another are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

or

R(7) and R(8)
together are C\textsubscript{a}H\textsubscript{2a};
a is 4, 5, 6 or 7;
where if a = 5, 6 or 7 a methylene group of the group C\textsubscript{a}H\textsubscript{2a} can be replaced by a heteroatom group O, SO\textsubscript{m} or NR(11),

or

R(8) and R(9) or R(9) and R(10) or R(7) and R(10) are a group C\textsubscript{a}H\textsubscript{2a};
a is 2, 3, 4 or 5;
where if a = 3, 4 or 5 a methylene group of the group C\textsubscript{a}H\textsubscript{2a} can be replaced by a heteroatom group O, SO\textsubscript{m} or NR(11);
m is zero, 1 or 2;

or

R(11) is hydrogen or methyl;

or

R(6) is a basic heteroaromatic ring system having 1 - 9 carbon atoms;
A is C\textsubscript{b}H\textsubscript{2b};
b is 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10;
where in the group C\textsubscript{b}H\textsubscript{2b} one or two methylene groups can be replaced by one of the groupings selected from
the group consisting of -O-, -CO-, -CH[OR(20)]-, -SO_n^-, -NR(20)-, -NR(20)-CO-, -NR(20)-CO-NH-, -NR(20)-CO-NH-SO_2^- 
\[
\begin{array}{c}
\text{R} \text{(20) N-S-} \\
\text{NR(19) } \text{b b}
\end{array}
\]

and -SO_{aa}[NR(19)]_{bb}^-;

and where in the group C_{bb}H_{2b} a methylene group can be replaced by -CH-R(99), where R(99) together with R(7) forms a pyrrolidine or piperidine ring;

\( \text{aa} \) is 1 or 2;
\( \text{bb} \) is 0 or 1;
\( \text{aa} + \text{bb} = 2; \)

R(19) is hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

R(20) is hydrogen or methyl;

B is a phenylene or naphthylene radical

\[
\begin{array}{c}
\text{R(12)} \\
\text{R(13)}
\end{array}
\]

R(12) and R(13) independently of one another are hydrogen, methyl, F, Cl, Br, I, CF_3 or -SO_n^-R(14);

R(14) is methyl or NR(15)R(16);

R(15) and R(16) independently of one another are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;
w is zero, 1 or 2;

D is \(-C_dH_{2d}-X_f\);

d is zero, 1, 2, 3 or 4;

X is \(-O-, -CO-, -CH[OR(21)], -SO_m- or -NR(21)-\);

f is zero or 1;

R(21) is hydrogen or methyl;

m is zero, 1 or 2;

and the other substituents R(1) and R(2) and R(3) in each case independently of one another are hydrogen, F, Cl, Br, I, -CN,

\(-(C_1-C_8)-alkyl, -(C_2-C_8)-alkenyl, -NR(35)R(36) or R(17)-C_9H_{2g}Z_n^{-}\);  
g is zero, 1, 2, 3 or 4;

h is zero or 1;

R(35) and R(36) independently of one another are hydrogen or alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms;

or

R(35) and R(36)

together are 4 - 7 methylene groups, of which one CH₂ group can be replaced by oxygen, -S-, -NH-, -NCH₃ or -N-benzyl;

Z is \(-O-, -CO-, -SO_\alpha-, -NR(18), -NR(18)-CO-, -NR(18)-CO-NH-, or -NR(18)-SO_\beta^{-}\);

R(18) is hydrogen or methyl;

v is zero, 1 or 2;

R(17) is hydrogen, cycloalkyl having 3, 5 or 6 carbon atoms or \(C_kF_{2k+1}^{-}\);

k is 1, 2 or 3;

or

R(17) is pyrrol-1-yl, pyrrol-2-yl or pyrrol-3-yl, which is not substituted or is substituted by 1 - 4 substituents selected from the group consisting of F, Cl, Br, I, -CN, (C₂₋C₈)-alkanoyl, (C₂₋C₈)-alkoxycarbonyl, formyl, carboxyl, -CF₃, methyl and methoxy;
or

R(17) -is (C₃-C₆)-cycloalkyl or phenyl,

which is not substituted or is substituted by 1 - 3
substituents selected from the group consisting of F
and Cl, -CF₃, methyl, hydroxyl, methoxy,
-NR(37)R(38), CH₃SO₂⁻ and H₂NO₂⁻;
R(37) and R(38)
are hydrogen or -CH₃;

R(4) and R(5)

independently of one another are hydrogen, alkyl having 1, 2, 3 or 4
carbon atoms, F, Cl, -OR(32), -NR(33)R(34) or -C₆F₁₃⁺;
R(32), R(33) and R(34)

independently of one another are hydrogen or alkyl having 1, 2 or 3 carbon atoms;

r is 1, 2, 3 or 4;

and their pharmacologically tolerable salts;

(HOE 95/F 072 - EP-Offenlegungsschrift 738 712, NZ 286 380)

ai) indenoylguanidines of the formula I

in which:
R(1) and R(2)

independently of one another are hydrogen, alkyl having 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 carbon atoms, cycloalkyl having 3, 4, 5 or 6
carbon atoms, O-alkyl having 1, 2, 3 or 4 carbon atoms, O-C(=O)-alkyl having 1, 2, 3 or 4 carbon atoms or C₉₋₁₈NR(12)R(13);
R(12) and R(13) independently of one another are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;
m is zero, 1, 2, 3 or 4;

5
NH-C(=O)-NH₂, C(=O)-O-alkyl having 1, 2, 3 or 4 carbon atoms,
C(=O)-NH₂, C(=O)-NH-alkyl having 1, 2, 3 or 4 carbon atoms,
C(=O)-N(alkyl)₂ having 1, 2, 3 or 4 carbon atoms in each alkyl group,
alkenyl having 2, 3, 4, 5, 6, 7, 8, 9 or 10 carbon atoms, alkynyl
having 2, 3, 4, 5, 6, 7, 8, 9 or 10 carbon atoms, alkylaryl having 1, 2,
3 or 4 carbon atoms in the alkyl group, alkenylaryl having 2, 3, 4, 5,
6, 7, 8, 9 or 10 carbon atoms in the alkenyl group, alkynylaryl having
2, 3, 4, 5, 6, 7, 8, 9 or 10 carbon atoms in the alkynyl group, C₁⁻C₄⁻
alkyl-substituted aryl, C₁⁻C₄⁻alkylheteroaryl, C₁⁻C₄⁻alkenylnheteroaryl,
aminoalkylaryl having 1, 2, 3 or 4 carbon atoms in the alkyl group,
15
substituted aryl, heteroaryl and substituted heteroaryl;

R(3), R(4), R(5) and R(6)

independently of one another are hydrogen, alkyl having 1, 2, 3, 4,
5, 6, 7, 8, 9 or 10 carbon atoms, O-alkyl having 1, 2, 3, 4, 5, 6, 7, 8,
9 or 10 carbon atoms, halogen, (such as F, Cl, Br, I), OH, aryl,
20
substituted aryl, heteroaryl, substituted heteroaryl, O-lower alkyl,
O-aryl, O-lower alkyaryl, O-substituted aryl, O-lower alkyl-
substituted aryl, O-C(=O)-C₁⁻C₄⁻alkylaryl, O-C(=O)-NH-C₁⁻C₄⁻alkyl,
O-C(=O)-N(C₁⁻C₄⁻alkyl)₂, NO₂, CN, CF₃, NH₂, NH-(=O)-C₁⁻C₄⁻alkyl,
NH-C(=O)-NH₂, COOH, C(=O)-O-C₁⁻C₄⁻alkyl, C(=O)-NH₂, C(=O)-
25
NH-C₁⁻C₄⁻alkyl, C(=O)-N(C₁⁻C₄⁻alkyl)₂, C₁⁻C₄⁻COOH, C₁⁻C₄⁻alkyl-
C(=O)-O-C₁⁻C₄⁻alkyl, SO₂H, SO₂-alkyl, SO₂-alkylaryl, SO₂-N-(alkyl)₂,
SO₂-N(alkyl)(alkylaryl), C(=O)-R(11), C₁⁻C₁₀⁻alkyl-C(=O)-R(11), C₂⁻
C₁₀⁻alkenyl-C(=O)-R(11), C₂⁻C₁₀⁻alkenyln-C(=O)-R(11), NH-C(=O)-C₁⁻
30
C₁₀⁻alkyl-C(=O)-R(11), O-C₁⁻C₁₁⁻alkyl-C(=O)-R(11);

R(11) is C₁⁻C₄⁻alkyl, C₁⁻C₄⁻alkynyl, aryl, substituted aryl, NH₂, NH-C₁⁻C₄⁻
alkyl, N-(C₁⁻C₄⁻alkyl)₂, SO₂H, SO₂-alkyl, SO₂-alkylaryl, SO₂-N-(alkyl)₂,
SO₂-N(alkyl)(alkylaryl);
X is O, S or NH;
R(7), R(8), R(9) and R(10) independently of one another are hydrogen, alkyl, cycloalkyl, aryl, alkylaryl;

or

R(8) and R(9) together are part of a 5, 6 or 7-membered heterocyclic ring;
A is absent or is a nontoxic organic or inorganic acid.

(HOE 95/F 109 - EP 748 795, NZ 266 583)

10 ak) benzyloxy carbonyl guanidines of the formula I

![](image)

in which:

R(1), R(2) and R(3)

independently of one another are -Y-[4-R(8)-phenyl], -Y-[3-R(8)-phenyl] or -Y-[2-R(8)-phenyl],

where the phenyl is in each case unsubstituted or substituted by 1 - 2 substituents from the group consisting of F, Cl, -CF₃,
methyl, hydroxyl, methoxy and -NR(96)R(97);

R(96) and R(97) independently of one another are hydrogen or -CH₃;

Y is a bond, CH₂, oxygen, -S- or -NR(9);
R(9) is hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;
R(8) is SO₃[NR(98)]bNR(99)R(10);

30 a is 1 or 2;
b is 0 or 1;
a + b = 2;
R(98), R(99) and R(10) independently of one another are hydrogen, -(C_1-C_8)-alkyl, benzyl, -(C_2-C_8)-alkylene-NR(11)R(12), (C_2-C_8)-alkylene-NR(13)-(C_2-C_8)-alkylene-NR(37)R(38) or (C_0-C_8)-alkylene-CR(39)R(40)CR(41)R(42)(C_0-C_8)-alkylene-NR(43)R(44);

R(11), R(12), R(13), R(37), R(38), R(43) and R(44) independently of one another are hydrogen, -(C_1-C_8)-alkyl or benzyl:

R(39), R(40), R(41) and R(42) independently of one another are hydrogen, -(C_1-C_8)-alkyl or -(C_0-C_3)-alkylene-phenyl, where the phenyl is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F, Cl, -CF_3, methyl and methoxy;

or

R(99) and R(10) together are 4 - 6 methylene groups, of which one CH_2 group can be replaced by oxygen, -S-, -NH-, -N-CH_3 or -N-benzyl;

or

R(8) is SO_a[NR(98)]_bNR(95)-C[=N-R(94)]-NR(93)R(92);

R(92), R(93), R(94) and R(95) independently of one another are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

or

R(1), R(2) and R(3) independently of one another are pyrrol-1-yl, pyrrol-2-yl or pyrrol-3-yl, which is not substituted or is substituted by 1 - 4 substituents selected from the group consisting of F, Cl, Br, I, -CN,
\[(\text{C}_2\text{-C}_8)\text{-alkanoyl, (C}_2\text{-C}_8)\text{-alkoxycarbonyl, formyl, carboxyl, -CF}_3, \text{methyl, methoxy;}
\]

or

\[\text{R(1), R(2) and R(3) independently of one another are hydrogen, -(C}_1\text{-C}_8)\text{-alkyl, -(C}_2\text{-C}_8)\text{-alkenyl or -(CH}_2\text{)}_m\text{R(14); m is zero, 1 or 2;}
\]

\[\text{R(14) is -(C}_3\text{-C}_6)\text{-cycloalkyl or phenyl,}
\]

which is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F and -Cl, -CF\(_3\), methyl, methoxy and -NR(15)R(16);

\[\text{R(15) and R(16) are hydrogen or -CH}_3;\]

or

\[\text{R(1), R(2) and R(3) independently of one another are -Q-4-[(CH}_2\text{)}_k\text{-CHR(17)-(C=O)R(20)}]\text{-phenyl, -Q-3-[(CH}_2\text{)}_k\text{-CHR(17)-(C=O)R(20)}]\text{-phenyl or -Q-2-[(CH}_2\text{)}_k\text{-CHR(17)-(C=O)R(20)}]\text{-phenyl,}
\]

where the phenyl in each case is unsubstituted or substituted by 1 - 2 substituents from the group F, Cl, -CF\(_3\), methyl, hydroxyl, methoxy and -NR(35)R(36);

\[\text{R(35) and R(36) independently of one another are hydrogen or -CH}_3;\]

\[\text{Q is a bond, oxygen, -S- or -NR(18);}\]

\[\text{R(18) is hydrogen or -(C}_1\text{-C}_4)\text{-alkyl;}
\]

\[\text{R(17) is -OR(21) or -NR(21)R(22);}
\]

\[\text{R(21) and R(22) independently of one another are hydrogen, -(C}_1\text{-C}_8)\text{-alkyl, -(C}_1\text{-C}_8)\text{-alkanoyl, -(C}_1\text{-C}_8)\text{-alkoxycarbonyl, benzyl, benzyloxy carbonyl;}
\]

or

\[\text{R(21) is trityl;}\]
R(20) is -OR(23) or -NR(23)R(24);
R(23), R(24) independently of one another are hydrogen, -(C_1\text{-}C_8)-alkyl or benzyl;

k is zero, 1, 2, 3 or 4;

or

R(1), R(2) and R(3)
individually of one another are (C_1\text{-}C_9)-heteroaryl,
which is linked via C or N and which is unsubstituted or substituted by 1 - 3 substituents from the group F, Cl, CF_3,

CH_3, methoxy, hydroxyl, amino, methylamino and dimethylamino;

or

R(1), R(2) and R(3)
are -SR(25), -OR(25), -NR(25)R(26), -CR(25)R(26)R(27);
R(25) is -C_H\_2\text{-}(C_1\text{-}C_9)-heteroaryl,
which is unsubstituted or substituted by 1 - 3 substituents from the group F, Cl, CF_3, CH_3, methoxy, hydroxyl, amino, methylamino and dimethylamino;

f is zero, 1 or 2;

R(26) and R(27)
individually of one another are defined as R(25) or are hydrogen or (C_1\text{-}C_4)-alkyl,

or

R(1), R(2) and R(3)
individually of one another are (C_1\text{-}C_9)-heteroaryl-N-oxide,
which is linked via C or N and which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF_3, CH_3, methoxy, hydroxyl, amino, methylamino and dimethylamino;

or

R(1), R(2) and R(3)
individually of one another are -SR(28), -OR(28), -NR(28)R(29)
or -CR(28)R(29)R(30);
R(28) is -C₉H₉-(C₁₋C₅)-heteroaryl-N-oxide,
    which is unsubstituted or substituted by 1 - 3
    substituents selected from the group consisting of F,
    Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino
    and dimethylamino;
    g is zero, 1 or 2;
    R(29), R(30) independently of one another are defined as R(28),
    hydrogen or (C₁₋C₄)-alkyl;

or
R(1), R(2) and R(3) independently of one another are hydrogen, F, Cl, Br, I, -C≡N,
T-(CH₂)ₙ-(CF₂)ₙ₋₁, R(31)SO₂, R(32)R(33)N-CO-, R(34)-CO- or
R(45)R(46)N-SO₂, where the perfluoroalkyl group is straight-chain or branched;
T is a bond, oxygen, -S- or -NR(47);
I is zero, 1 or 2;
h is zero, 1 or 2;
i is 1, 2, 3, 4, 5 or 6;
R(31), R(32), R(34) and R(45) independently of one another are -(C₁₋C₅)-alkyl, -(C₃₋C₆)-
alkenyl, (CH₂)ₙR(48) or -CF₃;
n is zero, 1, 2, 3 or 4;
R(47) is hydrogen or alkyl with 1, 2 or 3 carbon atoms;
R(48) is -(C₃₋C₇)-cycloalkyl or phenyl,
    which is not substituted or is substituted by 1 - 3
    substituents selected from the group consisting
    of F, Cl, -CF₃, methyl, methoxy and
    -NR(49)R(50);
R(49) and R(50) are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;
or

R(32), R(34) and R(45)

are hydrogen;

R(33) and R(46)

independently of one another are hydrogen or alkyl having 1,
2, 3 or 4 carbon atoms;

or

R(32) and R(33), and R(45) and R(46)

together are 5 or 6 methylene groups, of which one CH₂

group can be replaced by oxygen, -S-, -NH-, -NCH₃ or
-N-benzyl;

or

R(1), R(2) and R(3)

independently of one another are R(51)-A-G-D-;

R(51) is a basic protonatable radical, i.e. an amino group
-NR(52)R(53), an amidino group R(52)R(53)N-C[=N-R(54)]-
or a guanidino group R(52)R(53)N-C[=N-R(54)]-NR(55)-;

R(52), R(53), R(54) and R(55)

independently of one another are hydrogen or alkyl having 1,
2, 3 or 4 carbon atoms;

or

R(52) and R(53) are

a group CₐH₂ₐ;

α is 4, 5, 6 or 7;

where if α = 5, 6 or 7 a carbon atom of the group
CₐH₂ₐ can be replaced by a heteroatom group O, SO₄,
or NR(56),

or

R(53) and R(54) or R(54) and R(55) or R(52) and R(55) are

a group CᵣH₂ᵣ;

γ is 2, 3, 4 or 5;

where if γ = 3, 4 or 5 a carbon atom of the group CᵣH₂ᵣ,
can be replaced by a heteroatom group O, SO₂ or NR(56);

d is zero, 1 or 2;

R(56) is hydrogen or methyl;

or

R(51) is a basic heteroaromatic ring system having 1 - 9 carbon atoms;

A is a group C₆H₆,;

e is zero, 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10;

where in the group C₆H₆ a carbon atom can be replaced by one of the groupings -O-, -CO-, -CH[OR(57)]-, -SO₂-,
-NR(57)-, -NR(57)-CO-, -NR(57)-CO-NH-, -NR(57)-CO-NH-
-SO₂- or -NR(57)-SO₂-;

r is zero, 1 or 2;

G is a phenylene radical

R(58) and R(59)

independently of one another are hydrogen, methyl,
methoxy, F, Cl, Br, I, CF₃ or -SO₂-R(60);

R(60) is methyl or NR(61)R(62);

R(61) and R(62)

independently of one another are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

D is -C₆H₆v-Ew-;

v is zero, 1, 2, 3 or 4;

E is -O-, -CO-, -CH[OR(63)]-, -SO₂- or -NR(63)-;

w is zero or 1;

aa is zero, 1 or 2
R(63) is hydrogen or methyl,

or

R(1), R(2) and R(3)

independently of one another are -CF₂R(64), -CF[R(65)][R(66)],

-CF[(CF₂)ₚ-CF₃][R(65)], -C[(CF₂)ₚ-CF₃]=CR(65)R(66);

R(64) is alkyl having 1, 2, 3 or 4 carbon atoms or cycloalkyl having

3, 4, 5, 6 or 7 carbon atoms;

R(65) and R(66) independently of one another are hydrogen or alkyl

having 1, 2, 3 or 4 carbon atoms;

q is zero, 1 or 2;

p is zero, 1 or 2;

or

R(1), R(2) and R(3)

independently of one another are -OR(67) or -NR(67)R(68);

R(67) and R(68) independently of one another are hydrogen or alkyl having 1,

2, 3, 4, 5 or 6 carbon atoms;

or

R(67) and R(68)

together are 4, 5, 6 or 7 methylene groups, of which one CH₂

group can be replaced by oxygen, -S-, SO₂, -NH-, -NCH₃ or

-N-benzyl;

R(4) and R(5)

independently of one another are hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms, F, Cl, -OR(69), -NR(70)R(71) or -C₂F₂z₊₁;

R(69), R(70) and R(71)

independently of one another are hydrogen or alkyl having 1,

2 or 3 carbon atoms;

z is 1, 2, 3 or 4;

R(6) and R(7)

independently of one another are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;
X is oxygen or NR(72);

R(72) is hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

and their pharmaceutically tolerable salts;

(HOE 95/F 115 - EP 744 397, NZ 286 622)

a) alkenylcarboxylic acid guanidides, carrying fluorophenyl groups, of the

formula I

\[
\begin{array}{c}
R(1) \\
R(2) \\
R(3) \\
R(4) \\
R(5) \\
R(6) \\
R(7)
\end{array}
\]

in which:

R(6) is hydrogen, (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl or phenyl,

where the phenyl group is not substituted or is substituted by

1 - 3 substituents selected from the group consisting of F, Cl,

CF₃, methyl, methoxy and NR(9)R(10);

R(9) and R(10) are hydrogen, (C₁-C₄)-alkyl or (C₁-C₄)-perfluoroalkyl;

R(7) independently is defined as R(6);

R(1), R(2), R(3), R(4) and R(5) independently of one another are hydrogen or F;

where, however, at least one of the radicals R(1), R(2), R(3), R(4)

and R(5) must be fluorine;

and their pharmaceutically tolerable salts;

(HOE 95/F 167 - NZ 299 015)

am)

benzoylguanidines

of the formula I
in which:

- \( R(1) \) is \( R(4)\text{-SO}_m \) or \( R(5)\text{-R(6)N-SO}_2 \);
  - \( m \) is 1 or 2;
- \( R(4) \) and \( R(5) \) independently of one another are alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, alkenyl having 3, 4, 5 or 6 carbon atoms, \( \text{CF}_3 \) or \( -\text{C}_n\text{H}_{2n-}\text{-R(7)} \);
  - \( n \) is zero, 1, 2, 3 or 4;
- \( R(6) \) is H or alkyl having 1, 2, 3 or 4 carbon atoms;
- \( R(7) \) is cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms or phenyl, which is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of \( \text{F}, \text{Cl}, \text{CF}_3, \text{methyl}, \text{methoxy} \) and \( \text{NR}(8)\text{-R(9)} \);
  - \( R(8) \) and \( R(9) \) are H or alkyl having 1, 2, 3 or 4 carbon atoms;
- \( R(5) \) is also hydrogen;
- or \( R(5) \) and \( R(6) \) together are 4 or 5 methylene groups, of which a \( \text{CH}_2 \) group can be replaced by oxygen, \( \text{S}, \text{NH}, \text{N-CH}_3 \) or \( \text{N-benzyl} \);
- or \( R(1) \) is \( -\text{O}_p\text{-}(\text{CH}_2)_q\text{-}(\text{CF}_2)_r\text{-CF}_3 \);
  - \( p \) is zero or 1;
q is zero, 1 or 2;

r is zero, 1, 2 or 3;

or

\( R(1) \) is \(-SR(10), -OR(10)\) or \(-CR(10)R(11)R(12)\);

\( R(10), R(11) \) and \( R(12) \)

independently of one another are hydrogen, alkyl

having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, \(-C_\text{a}H_{2\text{a}}-(C_\text{b}-C_\text{c})\)-cycloalkyl or an aromatic system selected from the

group consisting of pyridyl, pyrrolyl, quinolyl,

isoquinolyl, imidazolyl or phenyl;

s is zero, 1 or 2;

where the aromatic systems pyridyl, pyrrolyl, quinolyl,

isoquinolyl, imidazolyl and phenyl are unsubstituted or

substituted by 1 - 3 substituents selected from the

group consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl,

amino, methylamino and dimethylamino;

\( R(2) \) is \(-(CH_2)_t-(CF_3)_u-CF_3\);

t is zero, 1, 2 or 3;

u is zero or 1;

\( R(3) \) is hydrogen or independently is defined as \( R(1) \);

and their pharmaceutically tolerable salts;

(HOE 95/F 173 - NZ 299 052)

an) substituted cinnamic acid guanidides of the formula

\[
\begin{align*}
\text{R}(3) & \quad \text{R}(2) \\
\text{R}(4) & \quad \text{R}(1) \\
\text{R}(5) & \quad \text{R}(6) \\
\text{R}(7) & \quad \text{NH}_2 \\
\text{NH}_2 & \quad \text{I}
\end{align*}
\]

in which:

at least one of the substituents \( R(1), R(2), R(3), R(4) \) and \( R(5) \) is

\(-X_a-Y_b-L_n-U\);
$X$ is \( CR(16)R(17), O, S \) or \( NR(18) \);  
\( R(16), R(17) \) and \( R(18) \) independently of one another are \( H, \text{alkyl having 1, 2, 3 or 4 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms} \);  
\( a \) is zero or \( 1 \);  
\( Y \) is \( \text{alkylene having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, alkyene-T having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms in the alkyene group, T, T-alkylene having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms in the alkyene group} \);  
\( T \) is \( NR(20), O, S \) or phenylene, where the phenylene is not substituted or is substituted by \( 1 - 3 \) substituents selected from the group consisting of \( F, \text{Cl, CF}_3 \), methyl, methoxy and \( NR(21)R(22) \);  
\( R(20), R(21) \) and \( R(22) \) independently of one another are \( H, \text{alkyl having 1, 2, 3 or 4 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms} \);  
\( b \) is zero or \( 1 \);  
\( L \) is \( O, S, NR(23) \) or \( C_kH_{2k} \);  
\( k \) is \( 1, 2, 3, 4, 5, 6, 7, 8 \);  
\( n \) is zero or \( 1 \);  
\( U \) is \( NR(24)R(25) \) or an \( N \)-containing heterocycle having \( 1, 2, 3, 4, 5, 6, 7, 8 \) or \( 9 \) carbon atoms;  
\( R(24) \) and \( R(25) \) independently of one another are hydrogen, alkyl having \( 1, 2, 3, 4, 5, 6, 7 \) or \( 8 \) carbon atoms or perfluoroalkyl having \( 1, 2, 3, 4, 5, 6, 7 \) or \( 8 \) carbon atoms;  
\( \) or
R(24) and R(25) together are 4 or 5 methylene groups, of which one CH₂ group can be replaced by oxygen, S, NH, N-CH₃ or N-benzyl;

where the N-containing heterocycles are N- or C-bridged and are not substituted or are substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(27)R(28);

R(23), R(27) and R(28) independently of one another are H, alkyl having 1, 2, 3 or 4 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;

and the other substituents R(1), R(2), R(3), R(4) and R(5) in each case independently of one another are H, F, Cl, Br, I, CN, -Oₙ-CₘH₂ₙ₊₁,

-Oₚ-(CH₂)ₚ-CₚF₂ₙ₊₁ or -CₚH₂ₙ,R(10);

n is zero or 1;

m is zero 1, 2, 3, 4, 5, 6, 7 or 8;

p is zero or 1;

q is 1, 2, 3, 4, 5, 6, 7 or 8;

s is zero, 1, 2, 3 or 4;

r is zero, 1, 2, 3 or 4;

R(10) is cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, or phenyl, where the phenyl is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(11)R(12);

R(11) and R(12) independently of one another are H, alkyl having 1, 2, 3 or 4 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;

R(6) and R(7) independently of one another are hydrogen, F, Cl, Br, I, CN, alkyl
having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, perfluoroalkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, or phenyl,

which is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(14)R(15);

R(14) and R(15)

independently of one another are H, alkyl having 1, 2, 3 or 4 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;

and their pharmaceutically tolerable salts;

(HOE 95/F 220 - NZ 299 052)

ao) benzoylguanidines of the formula I

\[
\begin{align*}
\text{I} & \\
R(1) & \\
R(2) & R(3) R(4) \text{O NH}_2 \\
R(5) & R(6) \text{NH}_2 \\
\end{align*}
\]

in which:

at least one of the substituents R(1), R(2) and R(3)

is R(6)-C(OH)₂⁻;

R(6) is perfluoroalkyl having 1, 2 or 3 carbon atoms, which is straight-chain or branched;

and the other substituents R(1), R(2) and R(3)

independently of one another are hydrogen, OH, F, Cl, Br, I, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, cycloalkyl with 3, 4, 5 or 6 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms or phenoxy, which is unsubstituted or is substituted by 1 - 3 substituents selected from the group consisting of F, Cl, methyl and methoxy;
110

or

the other substituents \( R(1), R(2) \) and \( R(3) \)

independently of one another are alkyl-\( \text{SO}_x \), \( -\text{CR}(7)=\text{CR}(8)R(9) \) or \( -\text{C}_x=\text{CR}(9) \);

\( x \) is zero, 1 or 2;

\( R(7) \) is hydrogen or methyl;

\( R(8) \) and \( R(9) \)

independently of one another are hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms or phenyl, which is unsubstituted or is substituted by 1 - 3 substituents selected from the group consisting of F, Cl, \( \text{CF}_3 \), methyl and methoxy;

or

the other substituents \( R(1), R(2) \) and \( R(3) \)

independently of one another are phenyl, \( \text{C}_6\text{H}_5-(\text{C}_1-\text{C}_4)\)-alkyl, naphthyl, biphenylyl, quinolinyl, isoquinolinyl or imidazolyl, where quinolinyl, isoquinolinyl or imidazolyl are bonded via C or N and where phenyl, \( \text{C}_6\text{H}_5-(\text{C}_1-\text{C}_4)\)-alkyl, naphthyl, biphenylyl, quinolinyl, isoquinolinyl and imidazolyl are unsubstituted or are substituted by 1 - 3 substituents selected from the group consisting of F, Cl, \( \text{CF}_3 \), \( \text{CH}_3 \), methoxy, hydroxyl, amino, methylamino and dimethylamino;

or

the other substituents \( R(1), R(2) \) and \( R(3) \)

independently of one another are SR(10), -OR(10), -\( \text{CR}(10)R(11)R(12) \);

\( R(10) \)

is \(-\text{C}_1\text{H}_2-(\text{C}_3-\text{C}_9)\)-cycloalkyl, quinolinyl, isoquinolinyl, pyridinyl, imidazolyl or phenyl, where the aromatic systems quinolinyl, isoquinolinyl, pyridinyl, imidazolyl and phenyl are unsubstituted or
are substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino and dimethylamino;

\[ f \] is zero, 1 or 2;

\[ \text{R}(11) \] and \[ \text{R}(12) \]

independently of one another are defined as \[ \text{R}(10) \], hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

\[ \text{R}(4) \] and \[ \text{R}(5) \]

independently of one another are hydrogen, alkyl having 1, 2 or 3 carbon atoms, F, Cl, Br, I, CN, OR(13), NR(14)R(15), -(CH₂)n-(CF₂)ₙ-CF₃;

\[ \text{R}(13), \text{R}(14) \] and \[ \text{R}(15) \]

independently of one another are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

\[ \text{n} \] is zero or 1;

\[ \text{o} \] is zero, 1 or 2;

and their pharmacologically acceptable salts;

(HOE 95/F 253 - NZ 299 682)

ap) sulfonimidamides of the formula \( I \)

\[
\begin{align*}
\text{O} & \equiv \text{S} & \equiv \text{R}_2 \\
\text{N} \quad \text{R}_3 & \equiv \text{N} \quad \text{R}_4
\end{align*}
\]

in which:

\[ \text{at least one of the three substituents } \text{R}(1), \text{R}(2) \] and \[ \text{R}(3) \]

is a benzoylguanidine,

which is unsubstituted or substituted in the phenyl moiety by
1 - 4 radicals selected from the group consisting of alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, alkenyl having 2, 3, 4, 5, 6, 7 or 8 carbon atoms, \(-(\text{CH}_2)_m\)-R(14), F, Cl, Br, I, -C≡N, CF\(_3\), R(22)SO\(_2\)-, R(23)R(24)N-CO-, R(25)-CO-, R(26)R(27)N-SO\(_2\), -OR(35), -SR(35) or -NR(35)R(36); m is zero, 1 or 2;

R(14) is -(C\(_3\)-C\(_9\))-cycloalkyl or phenyl, which is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F and Cl, -CF\(_3\), methyl, methoxy and -NR(15)R(16);

R(15) and R(16) independently of one another are hydrogen or -CH\(_3\);

R(22), R(23), R(25) and R(26) independently of one another are alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, alkenyl having 2, 3, 4, 5, 6, 7 or 8 carbon atoms, \((\text{CH}_2)_n\)R(29) or -CF\(_3\);

n is zero, 1, 2, 3 or 4;

R(29) is -(C\(_3\)-C\(_7\))-cycloalkyl or phenyl, which is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F, Cl, -CF\(_3\), methyl, methoxy and -NR(30)R(31);

R(30) and R(31) are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

or

R(23), R(25) and R(26) are hydrogen;

R(24) and R(27)
independently of one another are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

or

R(23) and R(24), and also R(26) and R(27)

5 together are 5 or 6 methylene groups, of which one CH$_2$ group can be replaced by oxygen, -S-, -NH-, -NCH$_3$ or -N-benzyl;

R(35) and R(36)

independently of one another are hydrogen or alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms;

or

R(35) and R(36)

together are 4 - 7 methylene groups, of which one CH$_2$ group can be replaced by oxygen, -S-, -NH-, -NCH$_3$ or -N-benzyl;

or

R(35)

is phenyl,

which is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F, Cl, -CF$_3$, methyl, methoxy, SO$_2$R(5), SO$_2$NR(6)R(7) and -NR(32)R(33);

R(5) is alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms

25 R(6) and R(7)

independently of one another are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

R(32) and R(33)

independently of one another are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;
or

R(35)

is C₁-C₅-heteroaryl,

which is unsubstituted or substituted by 1 - 3

substituents selected from the group consisting

of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino,

methylamino and dimethylamino;

and the other substituents R(1), R(2) and R(3) in each case

independently of one another are alkyl having 1, 2, 3, 4, 5, 6, 7 or 8

carbon atoms, (CH₂)ₚR(1),

p is zero, 1, 2, 3 or 4;

R(10) is phenyl,

which is not substituted or is substituted by 1 - 3

substituents selected from the group consisting of F,

Cl, -CF₃, methyl, methoxy, -SO₂NR(17)R(8) and

-SO₂R(9);

R(17) and R(8)

independently of one another are hydrogen or

alkyl having 1, 2, 3 or 4 carbon atoms;

R(9) is alkyl having 1, 2, 3 or 4 carbon atoms;

or the other radicals R(1) and R(3) in each case

are hydrogen,

R(4) is hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

and their pharmaceutically tolerable salts;

(HOE 95/F 265 - NZ 299 739)

aq)

benzoxyguanidines

of the formula I
in which:

\[ R(1) \] is alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms or NR(7)R(8);
\[ R(7) \] and \[ R(8) \] independently of one another are hydrogen or alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms;

\[ R(2) \] is hydrogen, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms or \[-SO_2R(9)\];
\[ R(9) \] independently is defined as \[ R(1) \];

\[ R(3) \] is hydrogen, -SR(25), -OR(25), -NR(25)R(26) or -CR(25)R(26)R(27);
\[ R(25) \] is hydrogen, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, or phenyl,
which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino and dimethylamino;

or \[ R(25) \]

\[ R(26) \] and \[ R(27) \]

independently of one another are defined as \[ R(25) \] or are hydrogen or alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms;

\[ R(4) \] is hydrogen, F, Cl, Br, I, OH, -C=N, CF₃, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms or \(-\text{CH}_2\)ₙR(14);
\[ m \] is zero, 1 or 2;
R(14) is -(C₃₋C₈)-cycloalkyl or phenyl, which is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F and Cl, -CF₃, methyl, methoxy and -NR(15)R(16); R(15) and R(16) independently of one another are hydrogen or -CH₃;

R(5) and R(6) independently of one another are hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms, F, Cl, -OR(32), -NR(33)R(34) or CF₃;

R(32), R(33) and R(34) independently of one another are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

and their pharmaceutically tolerable salts;

(HOE 95/F 269 K)

benzenedicarboxylic acid diguanidides of the formula I

in which:

one of the radicals R(1), R(2), R(3) and R(4) is -CO-N=C(NH₂)₂;

and the other radicals R(1), R(2), R(3) and R(4) in each case are:

R(1) is hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms, F, Cl, Br, I, -OR(32), -NR(33)R(34) or CF₃;

R(32), R(33) and R(34) independently of one another are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

R(2) and R(4) independently of one another are hydrogen, F, Cl, Br, I, OH, -CN,
CF₃, -CO-N=C(NH₂)₂, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, alkenyl having 2, 3, 4, 5, 6, 7 or 8 carbon atoms or -(CH₂)ₘR(14);

ₘ is zero, 1 or 2;

R(14) is -(C₃₋C₆)-cycloalkyl or phenyl,

which is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F and Cl, -CF₃, methyl, methoxy and -NR(15)R(16);

R(15) and R(16) are hydrogen or -CH₃;

or

R(2) and R(4) independently of one another are pyrrol-1-yl, pyrrol-2-yl or pyrrol-3-yl,

not which is not substituted or is substituted by 1 - 4 substituents selected from the group consisting of F, Cl, Br, I, -CN, (C₂₋C₅)-alkanoyl, (C₂₋C₅)-alkoxycarbonyl, formyl, carboxyl, -CF₃, methyl, methoxy;

or

R(2) and R(4) independently of one another are R(22)-SO₂-, R(23)R(24)N-CO-, R(28)-CO- or R(29)R(30)N-SO₂;

R(22) and R(28) independently of one another are methyl or -CF₃;

R(23), R(24), R(29) and R(30) independently of one another are hydrogen or methyl;

or

R(2) and R(4) independently of one another are -OR(35) or -NR(35)R(36);

R(35) and R(36) independently of one another are hydrogen or alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms;
or
R(35) and R(36)

together are 4 - 7 methylene groups, of which one CH₂ group
can be replaced by oxygen, -S-, -NH-, -NCH₃ or -N-benzyl;

R(3) is hydrogen, -SR(25), -OR(25), -NR(25)R(26), -CR(25)R(26)R(27);
R(25) is hydrogen, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms
or phenyl,

which is unsubstituted or substituted by 1 - 3
substituents selected from the group consisting of F,
Cl, CF₃, CH₃ methoxy, hydroxyl, amino, methylamino
and dimethylamino;

or
R(25) is -(C₁-C₉)-heteroaryl,

which is unsubstituted or substituted by 1 - 3
substituents selected from the group consisting of F,
Cl, CF₃, CH₃ methoxy, hydroxyl, amino, methylamino
and dimethylamino;

R(26) and R(27)

independently of one another are defined as R(25) or are
hydrogen or alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms;
R(5) is alkyl having 1, 2, 3 or 4 carbon atoms, F, Cl, Br, I, X-(CH₂)ₙ-CF₃ or
phenyl,

which is not substituted or is substituted by 1 - 3 substituents
selected from the group consisting of F and Cl, -CF₃, methyl,
methoxy and -NR(6)R(7);
R(6) and R(7)

independently of one another are hydrogen or -CH₃;
X is a bond or oxygen;
y is zero, 1 or 2;

and their pharmaceutically tolerable salts;
(HOE 95/F 269 BK)
as) benzenedicarboxylic acid diguanidides of the formula I
in which:

one of the radicals R(1), R(2), R(3) and R(5) is -CO-N=C(NH₂)₂;

and the other radicals R(1), R(2), R(3) and R(5) in each case are:

R(1) and R(5) independently of one another are hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms, F, Cl, -OR(32), -NR(33)R(34) or CF₃;

R(32), R(33) and R(34) independently of one another are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

R(2) is hydrogen, F, Cl, Br, I, OH, -CN, CF₃, -CO-N=C(NH₂)₂, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, alkenyl having 2, 3, 4, 5, 6, 7 or 8 carbon atoms or -(CH₂)mR(14);

m is zero, 1 or 2;

R(14) is -(C₃₋₅-C₅)ₖ-cycloalkyl or phenyl, which is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F and Cl, -CF₃, methyl, methoxy and -NR(15)R(16);

R(15) and R(16) independently of one another are hydrogen or -CH₃;

or

R(2) is R(22)-SO₂-, R(23)R(24)N-CO-, R(28)-CO- or R(29)R(30)N-SO₂;

R(22) and R(28) independently of one another are methyl or -CF₃;

R(23), R(24), R(29) and R(30) independently of one another are hydrogen or methyl;
or
R(2) is -OR(35) or -NR(35)R(36);
R(35) and R(36) independently of one another are hydrogen or alkyl having 1,
2, 3, 4, 5 or 6 carbon atoms;
or
R(35) and R(36) together are 4 - 7 methylene groups, of which one CH₂ group
can be replaced by oxygen, -S-, -NH-, -NCH₃ or -N-benzyl;
R(3) is hydrogen, -SR(25), -OR(25), -NR(25)R(26), -CR(25)R(26)R(27);
R(25) is hydrogen, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms
or phenyl,
which is unsubstituted or substituted by 1 - 3
substituents selected from the group consisting of F,
Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino
and dimethylamino;
or
R(25) is -(C₁-C₉)-heteroaryl,
which is unsubstituted or substituted by 1 - 3
substituents selected from the group consisting of F,
Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino
and dimethylamino;
R(26) and R(27) independently of one another are defined as R(25) or are
hydrogen or alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms;
R(4) is CF₃, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, alkenyl
having 2, 3, 4, 5, 6, 7 or 8 carbon atoms, -(C₃-C₆)-cycloalkyl or
-(CH₂)ₘR(14);
m is 1 or 2;
R(14) is -(C₃-C₆)-cycloalkyl or phenyl,
which is not substituted or is substituted by 1 - 3
substituents selected from the group consisting of F
and Cl, -CF₃, methyl, methoxy and -NR(15)R(16); R(15) and R(16) independently of one another are hydrogen or -CH₃; or

R(4) is phenyl, which is substituted by 2, 3, 4 or five substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and -NR(15)R(16); R(15) and R(16) independently of one another are hydrogen or CH₃; and their pharmaceutically tolerable salts; (HOE 96/F 013)

at) diaryldicarboxylic acid diguanidides of the formula I

\[
\begin{align*}
\text{R}_1 & \quad \text{R}_2 \\
\text{R}_3 & \quad \text{R}_4 \\
\text{R}_5 & \quad \text{R}_6 \\
\text{R}_7 & \quad \text{R}_8 \\
\text{R}_9 & \quad \text{R}_{10}
\end{align*}
\]

in which:

one of the radicals R(1), R(2), R(3), R(4) and R(5) is -CO-N=C(NH₂)₂;

the other radicals R(1) and R(5) in each case independently of one another are hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms, F, Cl, -OR(32), -NR(33)R(34) or CF₃; R(32), R(33) and R(34) independently of one another are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

the other radicals R(2) and R(4) in each case independently of one another are hydrogen, F, Cl, Br, I, OH, -CN, CF₃, -CO-N=C(NH₂)₂, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon
atoms, alkenyl having 2, 3, 4, 5, 6, 7 or 8 carbon atoms or
\[-(CH_2)_mR(14);\]
\[m\] is zero, 1 or 2;
\[R(14)\] is \(-(C_3-C_8)-\)cycloalkyl or phenyl,
which is not substituted or is substituted by 1 - 3
substituents selected from the group consisting of F
and Cl, -CF_3, methyl, methoxy and -NR(15)R(16);
\[R(15)\] and \[R(16)\]
are hydrogen or -CH_3;

or

the other radicals \(R(2)\) and \(R(4)\) in each case
independently of one another are pyrrol-1-yl, pyrrol-2-yl or
pyrrol-3-yl,
which is not substituted or is substituted by 1 - 4 substituents
selected from the group consisting of F, Cl, Br, I, -CN,
(C_2-C_9)-alkanoyl, (C_2-C_9)-alkoxycarbonyl, formyl, carboxyl,
-CF_3, methyl, methoxy;

or

the other radicals \(R(2)\) and \(R(4)\) in each case
are \(R(22)-SO_2-,\) \(R(23)R(24)N-CO-,\) \(R(28)-CO-\) or \(R(29)R(30)N-SO_2;\n\[R(22)\] and \[R(28)\]
independently of one another are methyl or -CF_3;
\[R(23), R(24), R(29)\] and \[R(30)\]
independently of one another are hydrogen or methyl;

or

the other radicals \(R(2)\) and \(R(4)\) in each case
independently of one another are -OR(35) or -NR(35)R(36);
\[R(35)\] and \[R(36)\]
independently of one another are hydrogen or alkyl having 1,
2, 3, 4, 5 or 6 carbon atoms;
or
\[R(35)\] and \[R(36)\]
to 4 - 7 methylene groups, of which one CH₂ group can be replaced by oxygen, -S-, -NH-, -NCH₃ or -N-benzyl;

the other radical R(3) in each case

is hydrogen, -SR(25), -OR(25), -NR(25)R(26), -CR(25)R(26)R(27);

R(25) is hydrogen, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms or phenyl,

which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, CH₃ methoxy, hydroxyl, amino, methylamino and dimethylamino;

or

R(25) is -(C₁-C₉)-heteroaryl,

which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, CH₃ methoxy, hydroxyl, amino, methylamino and dimethylamino;

R(26) and R(27) independently of one another are defined as R(25) or are hydrogen or alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms;

one of the radicals R(6), R(7), R(8), R(9) and R(10) is -CO-N=C(NH₂)₂;

the other radicals R(6) and R(10) in each case independently of one another are hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms, F, Cl, -OR(132), -NR(133)R(134) or CF₃;

R(132), R(133) and R(134) independently of one another are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

the other radicals R(7) and R(9) in each case independently of one another are hydrogen, F, Cl, Br, I, OH, -CN, CF₃, -CO-N=C(NH₂)₂, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, alkenyl having 2, 3, 4, 5, 6, 7 or 8 carbon atoms or -(CH₂)ₙmR(114);
\( \text{mm is zero, 1 or 2; R(114)} \)

\( \text{is } -(\text{C}_3\text{-C}_8)\text{-cycloalkyl or phenyl,} \)

\( \text{which is not substituted or is substituted by 1 - 3} \)

\( \text{substituents selected from the group consisting of F} \)

\( \text{and Cl, -CF}_3, \text{methyl, methoxy and -NR(115)R(116);} \)

\( \text{R(115) and R(116)} \)

\( \text{are hydrogen or } -\text{CH}_3; \)

\( \text{or} \)

\( \text{the other radicals R(7) and R(9) in each case} \)

\( \text{independently of one another are pyrrol-1-yl, pyrrol-2-yl or pyrrol-3-yl,} \)

\( \text{which is not substituted or is substituted by 1 - 4 substituents} \)

\( \text{selected from the group consisting of F, Cl, Br, I, -CN,} \)

\( \text{(C}_2\text{-C}_8)\text{-alkanoyl, (C}_2\text{-C}_8)\text{-alkoxycarbonyl, formyl, carboxyl,} \)

\( -\text{CF}_3, \text{methyl and methoxy;} \)

\( \text{or} \)

\( \text{the other radicals R(7) and R(9) in each case} \)

\( \text{are R(122)-SO}_2\text{-, R(123)R(124)N-CO-, R(128)-CO- or} \)

\( \text{R(129)R(130)N-SO}_2\text{;} \)

\( \text{R(122) and R(128)} \)

\( \text{independently of one another are methyl or } -\text{CF}_3; \)

\( \text{R(123), R(124), R(129) and R(130)} \)

\( \text{independently of one another are hydrogen or methyl;} \)

\( \text{or} \)

\( \text{the other radicals R(7) and R(9) in each case} \)

\( \text{independently of one another are } -\text{OR(135)} \text{ or } -\text{NR(135)R(136);} \)

\( \text{R(135) and R(136)} \)

\( \text{independently of one another are hydrogen or alkyl having 1,} \)

\( 2, 3, 4, 5 \text{ or 6 carbon atoms;} \)

\( \text{or} \)

\( \text{R(135) and R(136)} \)
together are 4 - 7 methylene groups, of which one CH₂ group can be replaced by oxygen, -S-, -NH-, -NCH₃ or -N-benzyl;

the other radical R(8) in each case

is hydrogen, -SR(125), -OR(125), -NR(125)R(126) or

-CR(125)R(126)R(127);

R(125) is hydrogen, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms or phenyl,

which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino and dimethylamino;

or

R(125) is -(C₆₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁₋₋₁

R(126) and R(127) independently of one another are defined as R(125) or are hydrogen or alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms;

A is absent or is -NR(11)-CO-, -NR(12)-CO-NR(13)-,
-NR(17)-CO-NR(18)-SO₂-, -NR(19)-SO₂-, -SO₂-NR(19)-SO₂-,
-SO₂-NR(19)-CO-, -O-CO-NR(19)-SO₂- or -CR(20)=CR(21)-;

R(11), R(12), R(13), R(17), R(18), R(19), R(20) and R(21) independently of one another are hydrogen or alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms and their pharmaceutically tolerable salts;
(HOE 96/F 026)

au) substituted thiophenylalkenylicarboxylic acid guanidides of the formula I

in which:

at least one of the substituents R(1), R(2) and R(3)

is \(-O_\text{p}-(\text{CH}_2)_s-C_\text{q}F_{2q+1}, R(40)\text{CO- or } R(31)\text{SO}_\text{k}-\);

\(p\) is zero or 1;

\(s\) is zero, 1, 2, 3 or 4;

\(q\) is 1, 2, 3, 4, 5, 6, 7 or 8;

\(k\) is zero, 1 or 2;

R(40) is alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms,
perfluoroalkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms,
cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, or phenyl,

which is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl and methoxy;

R(31) is alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms,
perfluoroalkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms,
cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, or phenyl,

which is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl or methoxy;

or

R(31) is NR(41)R(42);

R(41) and R(42)

independently of one another are hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms, perfluoroalkyl having
1, 2, 3 or 4 carbon atoms,

or

R(41) and R(42)

together are 4 or 5 methylene groups, of which one

CH₂ group can be replaced by oxygen, S, NH, N-CH₃

or N-benzyl;

and the other substituents R(1), R(2) and R(3) in each case

independently of one another are H, F, Cl, Br, I, CN, -O_nα-C_mαH_{2mα+1}

or -O_nαC_rαH_{2rα}R(10);

na is zero or 1;

ma is zero, 1, 2, 3, 4, 5, 6, 7 or 8;

gα is zero or 1;

ra is zero, 1, 2, 3 or 4;

R(10) is cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms or phenyl,

where the phenyl is not substituted or is substituted by

1 - 3 substituents selected from the group consisting of

F, Cl, CF₃, methyl and methoxy;

R(4) and R(5)

independently of one another are hydrogen, F, Cl, Br, I, CN, alkyl

having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, perfluoroalkyl having 1,

2, 3, 4, 5, 6, 7 or 8 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7 or 8

carbon atoms or phenyl,

which is not substituted or is substituted by 1 - 3 substituents

selected from the group consisting of F, Cl, CF₃, methyl,

methoxy and NR(14)R(15);

R(14) and R(15)

independently of one another are H, alkyl having 1, 2,

3 or 4 carbon atoms or perfluoroalkyl having 1, 2, 3 or

4 carbon atoms;

and their pharmaceutically tolerable salts;
av) ortho-substituted benzoylguanidines of the formula I

\[
\begin{align*}
F & \\
R(2) & \\
R(3) & \\
Cl & \\
O & \\
N & \\
\text{NH}_2 & \\
\end{align*}
\]

in which:
R(2) and R(3) independently of one another are hydrogen, Cl, Br, I, \((\text{C}_1-\text{C}_8)-\text{alkyl}, (\text{C}_3-\text{C}_8)-\text{cycloalkyl}\) or 
\(\text{d}\) is zero, 1 or 2;

where one of the two substituents R(2) and R(3) is always hydrogen but both substituents R(2) and R(3) are not simultaneously hydrogen, and their pharmaceutically tolerable salts;

aw) benzoylguanidines of the formula I

\[
\begin{align*}
R(1) & \\
R(2) & \\
R(3) & \\
\text{NH}_2 & \\
\text{NH}_2 & \\
\text{OR}(4) & \\
\end{align*}
\]

in which:
R(1) is H, F, Cl, Br, I, CN, NO\(_2\), alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, alkoxy having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, cycloalkoxy having 3, 4, 5, 6, 7 or 8 carbon atoms or \(X_a-(\text{CH}_2)_b-(\text{CF}_2)_c-\text{CF}_3\);
X is oxygen, S, NR(5),
a is zero or 1;
b is zero, 1 or 2;
c is zero, 1, 2 or 3;
R(5) is H, alkyl having 1, 2, 3 or 4 carbon atoms or 
-C₆H₁₂R(6);

d is zero, 1, 2, 3 or 4;

R(6) is cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, phenyl, biphenylyl or naphthyl, 

where the aromatics phenyl, biphenylyl or naphthyl are not substituted or are substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(7)R(8);

R(7) and R(8) independently are H or alkyl having 1, 2, 3 or 4 carbon atoms;

or

R(1) is -SR(10), -OR(10) or -CR(10)R(11)R(12);

R(10) is -C₅H₁₀-cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms in the cycloalkyl ring, or phenyl, 

where phenyl is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, CH₃ methoxy, hydroxyl, amino, methylamino and dimethylamino;

f is zero, 1 or 2;

R(11) and R(12) independently of one another are defined as R(10) or are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

or

R(1) is phenyl, naphthyl, biphenylyl or heteroaryl having 1, 2, 3, 4, 5, 6, 7, 8 or 9 carbon atoms, with the latter being linked via a carbon atom or a nitrogen atom of the ring, 

which are in each case unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino and
dimethylamino,

or

R(1) is -SR(13), -OR(13), -NHR(13), -NR(13)R(14), -CHR(13)R(15), -C[R(15)R(16)OH], -C=CR(18), -C[R(19)]=CHR(18), -C[R(20)R(21)]-R(22), -(CO)-[CR(22)R(23)]-R(24),

dimethylamino,

or

R(1) is -SR(13), -OR(13), -NHR(13), -NR(13)R(14), -CHR(13)R(15), -C[R(15)R(16)OH], -C=CR(18), -C[R(19)]=CHR(18), -C[R(20)R(21)]-R(22), -(CO)-[CR(22)R(23)]-R(24),

k is zero, 1, 2, 3 or 4;

l is zero, 1, 2, 3 or 4;

R(13) and R(14)

identically or differently are -(CH2)g-(CHOH)h-(CH2)i-(CHOH)j-R(17) or -(CH2)g-O-(CH2-CH2O)h-R(24);

R(17) is hydrogen or methyl,

g, h and i

identically or differently are zero, 1, 2, 3 or 4;

j is 1, 2, 3 or 4;

R(15) and R(16)

identically or differently are hydrogen, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms or, together with the carbon atom carrying them, are cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms;

R(18)

is phenyl,

which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF3, methyl, methoxy and NR(25)R(26);

R(25) and R(26)

are H or alkyl having 1, 2, 3 or 4 carbon atoms;

or

R(18) is heteroaryl having 1, 2, 3, 4, 5, 6, 7, 8 or 9 carbon atoms,

which is unsubstituted or substituted as phenyl;

or

R(18) is alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms,

which is unsubstituted or substituted by 1 - 3 OH;
or

R(18)

is cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms;

R(19), R(20), R(21), R(22) and R(23)

identically or differently are hydrogen or methyl;

R(24) is H, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, cycloalkyl

having 3, 4, 5, 6, 7 or 8 carbon atoms or \(-C_mH_{2m}-\)R(18);

\(m\) is 1, 2, 3 or 4;

R(2) and R(3)

are defined as R(1);

R(4) is alkyl having 1, 2, 3 or 4 carbon atoms;

and their pharmaceutically tolerable salts;

(HOE 96/F 043)

ax) ortho-substituted benzoylguanidines of the formula I

\[
\begin{align*}
\text{R(1)} & \quad \text{R(2)} \\
\text{R(3)} & \quad \text{R(4)} \\
\text{N} & \quad \text{N} \\
\text{NH} & \quad \text{NH}_2 \\
\text{O} & \quad \text{NH}_2
\end{align*}
\]

in which:

R(1) is H, F, Cl, Br, I, CN, NO\(_2\), alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, alkoxy having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, cycloalkyl

having 3, 4, 5, 6, 7 or 8 carbon atoms, cycloalkoxy having 3, 4, 5, 6, 7 or 8 carbon atoms or X\(_a\)-(CH\(_2\))\(_b\)-(CF\(_2\))\(_c\)-CF\(_3\);

\(X\) is oxygen, S, \(\text{NR(5)}\),

\(a\) is zero or 1;

\(b\) is zero, 1 or 2;

\(c\) is zero, 1, 2 or 3;

R(5) is H, alkyl having 1, 2, 3 or 4 carbon atoms or

\(-C_dH_{2d}-\)R(6);

d is zero, 1, 2, 3 or 4.
R(6) is cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, phenyl, biphenylyl or naphthyl,

where the aromatics phenyl, biphenylyl or naphthyl are unsubstituted or

substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃,
methyl, methoxy and NR(7)R(8);

R(7) and R(8)

independently are H or alkyl

having 1, 2, 3 or 4 carbon atoms;

or

R(1) is -SR(10), -OR(10) or -CR(10)R(11)R(12);

R(10) is -C₆H₄-cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms in the cycloalkyl ring, or phenyl,

where phenyl is unsubstituted or substituted by 1 - 3

substituents selected from the group consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino and dimethylamino;

f is zero, 1 or 2;

R(11) and R(12) independently of one another are defined as R(10), or hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

or

R(1) is phenyl, naphthyl, biphenylyl or heteroaryl having 1, 2, 3, 4, 5, 6, 7,

8 or 9 carbon atoms, with the latter being linked via a carbon atom or a nitrogen atom of the ring,

which are in each case unsubstituted or substituted by 1 - 3

substituents selected from the group consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino and

dimethylamino;

or

R(1) is -SR(13), -OR(13), -NHR(13), -NR(13)R(14), -CHR(13)R(15),
-C[R(15)R(16)OH], -C=CR(18), -C[R(19)]=CHR(18),
-C[R(20)R(21)]_k-(CO)-[CR(22)R(23)]_l-R(24),
k is zero, 1, 2, 3 or 4;
l is zero, 1, 2, 3 or 4;

R(13) and R(14)
identically or differently are -(CH_2)_g-(CHOH)_h-(CH_2)_i-(CHOH)_j-R(17) or -(CH_2)_g-O-(CH_2-CH_2O)_h-R(24);
R(17) is hydrogen or methyl,
g, h and i
identically or differently are zero, 1, 2, 3 or 4;
j is 1, 2, 3 or 4;

R(15) and R(16)
identically or differently are hydrogen, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms or, together with the carbon atom carrying them, are cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms;

R(18)
is phenyl,
which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF_3, methyl, methoxy and NR(25)R(26);
R(25) and R(26)
are H or alkyl having 1, 2, 3 or 4 carbon atoms;
or

R(18) is heteroaryl having 1, 2, 3, 4, 5, 6, 7, 8 or 9 carbon atoms,
which is unsubstituted or substituted as phenyl;
or

R(18) is alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms,
which is unsubstituted or substituted by 1 - 3 OH;
or

R(18) is cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms;
R(19), R(20), R(21), R(22) and R(23) identically or differently are hydrogen or methyl;
R(24) is H, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms or -C_mH_{2m}-R(18);

m is 1, 2, 3 or 4;

one of the two substituents R(2) and R(3) is hydroxyl;

and

the other of the substituents R(2) and R(3) in each case is defined as R(1);

R(4) is alkyl having 1, 2, 3 or 4 carbon atoms; alkoxy having 1, 2, 3 or 4 carbon atoms, F, Cl, Br, I or -(CH_2)_n-(CF_2)_o-CF_3;
n is zero or 1;
o is zero or 1;

and their pharmaceutically tolerable salts;

(HOE 96/F 135)

bisortho-substituted benzoylguanidines of the formula I

in which:

R(1), R(2) and R(3) independently of one another are R(10)-SO_a- or R(14)R(15)N-SO_2-;
a is zero, 1 or 2,

R(10), R(14) and R(15) independently of one another are alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, perfluoroalkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, alkenyl having 3, 4, 5 or 6 carbon atoms or -C_{a+b}H_{2a+b}-R(16);
ab is zero, 1, 2, 3 or 4;
R(16) is cycloalkyl having 3, 4, 5, 6 or 7 carbon atoms or phenyl, which is unsubstituted or substituted by 1-3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(17)R(18);
R(17) and R(18) independently of each other are hydrogen, CF₃ or alkyl having 1, 2, 3 or 4 carbon atoms;
or
R(14) and R(15) together are 4 or 5 methylene groups, of which one CH₂ group can be replaced by oxygen, sulfur, NH, N-CH₃ or N-benzyl;
or
R(14) and R(15) are hydrogen;
or
R(1), R(2) and R(3) independently of each other are SR(21), -OR(22), -NR(23)R(24) or -CR(25)R(26)R(27);
R(21), R(22), R(23) and R(25) independently of one another are -C₉H₂₆-(C₁-C₉)-heteroaryl, which is unsubstituted or substituted by 1-3 substituents selected from the group consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino and dimethylamino;
b is zero, 1 or 2;
R(24), R(26) and R(27) independently of each other are hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;
or
R(1), R(2) and R(3)
independently of one another are hydrogen, F, Cl, Br, I, CN, -\((Xa)_{ag}C_{db}H_{2da+1}\), \(-(Xb)_{dh}(CH_{2})_{db}C_{de}F_{2de+1}\), alkenyl having 3, 4, 5, 6, 7 or 8 carbon atoms or \(-C_{df}H_{2df}R(30)\);

\((Xa)\) is oxygen, sulfur or \(NR(33)\);

\(R(33)\) is hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;

dg is zero or 1;

\((Xb)\) is oxygen, sulfur or \(NR(34)\);

\(R(34)\) is hydrogen, alkyl having 1, 2, 3, or 4 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;

dh is zero or 1;

da is zero, 1, 2, 3, 4, 5, 6, 7 or 8;

db is zero, 1, 2, 3 or 4;

de is zero, 1, 2, 3, 4, 5, 6 or 7;

df is zero, 1, 2, 3 or 4;

\(R(30)\) is cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, phenyl, biphenyl or naphthyl,

where the aromatics phenyl, biphenyl or naphthyl are not substituted or substituted by 1-3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and \(NR(31)R(32)\);

\(R(31)\) and \(R(32)\) are hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;

or

\(R(1), R(2)\) and \(R(3)\) independently of one another are \(NR(40)R(41)\) or \(-(Xe)-(CH_{2})_{ar}R(45)\);

\(R(40)\) and \(R(41)\) independently of one another are hydrogen, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, perfluoroalkyl having 1, 2, 3,
4, 5, 6, 7 or 8 carbon atoms or (CH$_2$)$_e$-R(42);
e is zero, 1, 2, 3 or 4;
R(42) is cycloalkyl having 3, 4, 5, 6 or 7 carbon atoms or phenyl,

which is not substituted or substituted by 1-3 substituents selected from the group consisting of F, Cl, CF$_3$, methyl, methoxy and NR(43)R(44);
R(43) and R(44)

independently of one another are hydrogen, CF$_3$ or alkyl having 1, 2, 3 or 4 carbon atoms;

or
R(40) and R(41)

together are 4 or 5 methylene groups, of which one CH$_2$ group can be replaced by oxygen, sulfur, NH, N-CH$_3$ or N-benzyl;

(Xe) is oxygen, sulfur or NR(47);
R(47) is hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;

eb is zero, 1, 2, 3 or 4;
R(45) is cycloalkyl having 3, 4, 5, 6 or 7 carbon atoms or phenyl,

which is not substituted or substituted by 1-3 substituents selected from the group consisting of F, Cl, CF$_3$, methyl, methoxy, NR(50)R(51) and -(Xfa)-(CH$_2$)$_{ed}$-(Xfb)R(46);

Xfa is CH$_2$, oxygen, sulfur or NR(48);
Xfb is oxygen, sulfur or NR(49);
R(48), R(49), R(50) and R(51)
independently of one another are hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;
ed is 1, 2, 3 or 4;
R(46) is hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or
perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;

or

$R(1), R(2)$ and $R(3)$ independently of one another are $-\text{CHR}(52)R(53)$;

$R(52)$ is $-(\text{CH}_2)_g-(\text{CHOH})_h-(\text{CH})_i-(\text{CHOH})_k-R(54)$ or $-(\text{CH}_2)_g-O-(\text{CH}_2-\text{CH}_20)_h-R(54)$;

$R(54)$ is hydrogen or methyl;

$g, h, i$ are identical or different and are zero, 1, 2, 3 or 4;

$k$ is 1, 2, 3 or 4;

$R(53)$ is hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

or

$R(1), R(2)$ and $R(3)$ independently of one another are $-\text{C(OH)}R(55)R(56)$;

$R(55)$ and $R(56)$ are identical or different and are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

or

$R(55)$ and $R(56)$ together are cycloalkyl having 3, 4, 5 or 6 carbon atoms;

or

$R(55)$ is $-\text{CH}_2\text{OH}$;

and

$R(4)$ and $R(5)$ independently of one another are alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, OH, F, Cl, Br, I, CN, $-\text{O}_n-(\text{CH}_2)_o-(\text{CF}_2)_p-\text{CF}_3$;

$n$ is zero or 1;

$o$ is zero, 1 or 2;

$p$ is zero, 1 or 2;

and their pharmaceutically tolerable salts;

(96/F 136)
az) substituted 1-naphthoylguanidines of the formula I

\[
\begin{array}{c}
\text{R}_2 \quad \text{R}_3 \quad \text{R}_4 \\
\text{R}_5 \quad \text{R}_6 \\
\text{R}_7 \quad \text{R}_8 \\
\end{array}
\]

in which:

- \( R_2, R_3, R_4, R_5, R_6, R_7 \) and \( R_8 \) independently of one another are \( H, \text{F}, \text{Cl}, \text{Br}, \text{I}, \text{CN}, \text{NO}_2, \text{CF}_3, \text{C}_2\text{F}_5 \) or \( X,Y,Z \);
- \( X \) is \( \text{O}, \text{S}, \text{NR}(10), \text{CR}(11)\text{R}(12), \text{C}=\text{O}, \text{C}(=\text{O})\text{NR}(10), \text{C}(=\text{O})\text{O}, \text{SO}, \text{SO}_2, \text{SO}_2\text{NR}(10), \text{OC}=\text{O}, \text{NR}(10)\text{C}=\text{O} \) or \( \text{NR}(10)\text{SO}_2 \);
- where the linkage with the naphthalene ring is in each case effected through the atom on the left;
- \( R(10), R(11) \) and \( R(12) \) independently of one another are \( H, \text{alkyl having } 1, 2, 3, 4, 5 \) or \( 6 \) carbon atoms, \( \text{perfluoroalkyl having } 1, 2, 3 \) or \( 4 \) carbon atoms or \( \text{cycloalkyl having } 3, 4, 5, 6 \) or \( 7 \) carbon atoms;
- \( a \) is zero or \( 1 \);
- \( Y \) is alkylene having \( 1, 2, 3, 4, 5, 6, 7 \) or \( 8 \) \( \text{CH}_2 \) groups;
- it being possible for one of these \( \text{CH}_2 \) groups to be replaced by \( \text{O}, \text{S}, \text{NR}(13) \) or \( o-, p- \) or \( m-\text{phenylene} \);
- \( R(13) \) is \( H, \text{alkyl having } 1, 2, 3, 4, 5 \) or \( 6 \) carbon atoms, \( \text{perfluoroalkyl having } 1, 2, 3 \) or \( 4 \) carbon atoms or \( \text{cycloalkyl having } 3, 4, 5 \) or \( 6 \) carbon atoms;
- \( b \) is zero or \( 1 \);
- \( Z \) is \( H, \text{alkyl having } 1, 2, 3, 4, 5, 6 \) or \( 7 \) carbon atoms, \( \text{cycloalkyl having } 3, 4, 5, 6 \) or \( 7 \) carbon atoms, \( \text{C}(=\text{O})\text{R}(15), \text{SO}_2\text{R}(15), \text{etc.} \).
NR(16)R(17) or phenyl, which is not substituted or
substituted by 1-3 substituents selected from the group
consisting of F, Cl, Br, CF₃, methyl, methoxy,
NR(21)R(22);

R(21) and R(22)

independently of one another are H or alkyl
having 1, 2, 3 or 4 carbon atoms or
perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;

R(15) is N=C(NH₂)₂, NR(18)R(19), N(CH₂)ₙNR(18)R(19) or OR(20);

c is 2 or 3;

R(18) and R(19)

independently of one another are H, alkyl having 1, 2,
3, 4, 5, 6, 7 or 8 carbon atoms or perfluoroalkyl having
1, 2, 3 or 4 carbon atoms;

or

R(18) and R(19)

together are 4 or 5 methylene groups,

of which one CH₂ group can be replaced by
oxygen, S, NH, N-CH₃, N-benzyl or

N-(p-chlorophenyl);

R(20) is H, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms,
perfluoroalkyl having 1, 2, 3 or 4 carbon atoms or
cycloalkyl having 3, 4, 5, 6 or 7 carbon atoms;

R(16) and R(17)

independently of one another are H, alkyl having 1, 2, 3, 4, 5,
6, 7 or 8 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4
carbon atoms;

or

R(16) and R(17)

together are 4 or 5 methylene groups, of which one CH₂

group can be replaced by oxygen, S, NH, N-CH₃, N-benzyl or
N-(p-chlorophenyl);
or

Z is a N-containing heterocycle having 1, 2, 3, 4, 5, 6, 7, 8 or 9 carbon atoms,

where the N-containing heterocycle is linked via N or C and is not substituted or substituted by 1-3 substituents selected from the group consisting of F, Cl, Br, CF₃, methyl, methoxy and NR(21)R(22);

but where in the case that R(4) is an alkoxy radical, at least one of the substituents R(2), R(3), R(5), R(6), R(7) and R(8) is not hydrogen;

and their pharmaceutically tolerable salts;

(HOE 96/F 137)

ba) substituted 2-naphthoylguanidines of the formula I

\[
\begin{align*}
\text{R}_1 & \quad \text{R}_6 \\
\text{R}_3 & \quad \text{R}_4 \\
\text{R}_5 & \\
\text{R}_7 & \quad \text{R}_8 \\
\end{align*}
\]

in which:

at least one of the substituents R1, R3, R4, R5, R6, R7 and R8 is XYₐWZ or XY'ₐWZ';

X is O, S, NR(10) or CR(11)R(12);

R(10), R(11) and R(12) independently of one another are H, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, perfluoroalkyl having 1, 2, 3 or 4 carbon atoms or cycloalkyl having 3, 4, 5, 6 or 7 carbon atoms;

Y is alkylene having 1, 2, 3, 4, 5, 6, 7 or 8 CH₂ groups, where one of these CH₂ groups can be replaced by O, S, NR(13) or o-, p- or m-phenylene;

R(13) is H, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;
atoms or cycloalkyl having 3, 4, 5 or 6 carbon atoms;

\[ a \text{ is zero or 1; } \]
\[ W \text{ is CH}_2, \text{SO}_2, \text{S} (=\text{O})(=\text{NH}) \text{ or if } W \text{ does not immediately } \]
follow a hetero atom of the group XY\[\alpha\] - also O or NR(14); \]
\[ R(14) \text{ is H, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, } \]
perfluoroalkyl having 1, 2, 3 or 4 carbon atoms or \]
cycloalkyl having 3, 4, 5 or 6 carbon atoms;

\[ Z \text{ is C}(=\text{O})R(15), \text{SO}_2R(15) \text{ or if } W \text{ is not O or NR(14) - also } \]
\[ \text{NR}(16)R(17); \]
\[ R(15) \text{ is N} = \text{C(NH}_2)_2, \text{NR}(18)R(19), \text{N(CH}_2)_b\text{NR}(18)R(19) \text{ or } \]
OR(20); \]
\[ b \text{ is 2 or 3; } \]
\[ R(18) \text{ and } R(19) \text{ independently of one another are H, alkyl } \]
having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms or \]
perfluoroalkyl having 1, 2, 3 or 4 carbon atoms; \]
or \]
\[ R(18) \text{ and } R(19) \text{ together are 4 or 5 methylene groups, } \]
of which one CH\[2\] group can be replaced \]
by oxygen, S, NH, N-CH\[3\], N-benzyl or \]
N-(p-chlorophenyl); \]
\[ R(20) \text{ is H, alkyl having 1, 2, 3, 4, 5 or 6 carbon } \]
atoms, perfluoroalkyl having 1, 2, 3 or 4 carbon \]
atoms or cycloalkyl having 3, 4, 5, 6 or 7 carbon \]
atoms; \]
\[ R(16) \text{ and } R(17) \text{ independently of one another are H, alkyl having 1, 2, 3, 4, 5, } \]
6, 7 or 8 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4
carbon atoms;

or

R(16) and R(17)

together are 4 or 5 methylene groups,

of which one CH₂ group can be replaced by oxygen, S,
NH, N-CH₃, N-benzyl or N-(p-chlorophenyl);

X' is C=O, C(=O)NR(30), C(=O)O, SO, SO₂, SO₂NR(30), OC=O,
NR(30) C=O or NR(30)SO₂,

where the linkage with the naphthalene ring is in each case
effected through the atom on the left;

R(30) is H, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms,
perfluoroalkyl having 1, 2, 3 or 4 carbon atoms or cycloalkyl
having 3, 4, 5, 6 or 7 carbon atoms;

Z' is C(=O)R(15), SO₂R(15), an N-containing heterocycle having 1, 2,
3, 4, 5, 6, 7, 8 or 9 carbon atoms,

where the N-containing heterocycle is linked via N or C and is
not substituted or substituted by 1-3 substituents selected
from the group consisting of F, Cl, Br, CF₃, methyl, methoxy
and NR(21)R(22);

R(21) and R(22)

independently of one another are H, alkyl having 1, 2,
3 or 4 carbon atoms or perfluoroalkyl having 1, 2, 3 or
4 carbon atoms;

R(15)

is N=C(NH₂)₂, NR(18)R(19), N(CH₃)₂NR(18)R(19) or OR(20);

R(18) and R(19)

independently of one another are H, alkyl having 1, 2,
3, 4, 5, 6, 7 or 8 carbon atoms or perfluoroalkyl having
1, 2, 3 or 4 carbon atoms;

or

R(18) and R(19)

together are 4 or 5 methylene groups,
of which one CH₂ group can be replaced by oxygen, S, NH, N-CH₃, N-benzyl or N-(p-chlorophenyl);

$$b = 2 \text{ or } 3;$$

$$R(20) \text{ is H, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, perfluoroalkyl having 1, 2, 3 or 4 carbon atoms or cycloalkyl having 3, 4, 5, 6 or 7 carbon atoms;}$$

or

$$Z' \text{ - if } W \text{ is not O or NR(14) - is NR(16)R(17);}$$

$$R(16) \text{ and } R(17) \text{ independently of one another are H, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;}$$

or

$$R(16) \text{ and } R(17) \text{ together are 4 or 5 methylene groups, of which one CH₂ group can be replaced by oxygen S, NH, N-CH₃, N-benzyl or N-(p-chlorophenyl);}$$

and in each case the remaining substituents R1, R3, R4, R5, R6, R7 and R8, to which none of the abovementioned definitions has been assigned, independently of one another are H, F, Cl, Br, I, CN, NO₂, CF₃, C₂F₅ or VₚQₗU;

$$V \text{ is O, S, SO, SO₂, NR(60), OC=O, C=O, C(=O)NR(60), C(=O)O or CR(66)R(67);}$$

$$R(60), R(66) \text{ and } R(67) \text{ independently of one another are H, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, perfluoroalkyl having 1, 2, 3 or 4 carbon atoms or cycloalkyl having 3, 4, 5, 6 or 7 carbon atoms;}$$

$$p = \text{zero or 1;}$$

$$Q \text{ is alkylene having 1, 2, 3, 4, 5, 6, 7 or 8 CH₂ groups, where one of these CH₂ groups can be replaced by O,}$$
S, NR(68) or o-, p- or m-phenylene;

R(68)

is H, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, perfluoroalkyl having 1, 2, 3 or 4 carbon atoms or cycloalkyl having 3, 4, 5 or 6 carbon atoms;

q is zero or 1;

U is H, alkyl having 1, 2, 3, 4, 5, 6 or 7 carbon atoms, cycloalkyl having 3, 4, 5, 6 or 7 carbon atoms, C(=O)R(65), SO₂R(65), NR(61)R(62) or phenyl,

which is not substituted or substituted by 1-3 substituents selected from the group consisting of F, Cl, Br, CF₃, methyl, methoxy and NR(63)R(64);

R(63) and R(64) independently of one another are H, alkyl having 1, 2, 3 or 4 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;

R(65) is N=C(NH₂)₂, NR(61)R(62) or OR(60);

R(61) and R(62) independently of one another are H, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;

R(61) and R(62) together are 4 or 5 methylene groups,

of which one CH₂ group can be replaced by oxygen, S, NH, N-CH₃, N-benzyl or N-(p-chlorophenyl);

or

U is an N-containing heterocycle having 1, 2, 3, 4, 5, 6, 7, 8 or 9 carbon atoms,

where the N-containing heterocycle is linked via N or C and is not substituted or substituted by 1-3 substituents selected
from the group consisting of F, Cl, Br, CF₃, methyl, methoxy
and NR(63)R(64);

and at least one of the substituents R₅, R₆, R₇ and R₈ not being
hydrogen;

and their pharmaceutically tolerable salts;

(HOE 96/F 141)

bb) ortho-substituted benzoylguanidines of the formula I

in which:

R(1) is H, F, Cl, Br, I, CN, NO₂, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon
atoms, alkoxy having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, cycloalkyl
having 3, 4, 5, 6, 7 or 8 carbon atoms, cycloalkoxy having 3, 4, 5, 6,
7 or 8 carbon atoms or Xa-(CH₂)ₐ-(CF₂)ₐ-CF₃;

X is oxygen, sulfur or NR(9),
a is zero or 1;
b is zero, 1 or 2;
c is zero, 1, 2 or 3;

R(9) is H, alkyl having 1, 2, 3 or 4 carbon atoms or
-C₆H₁₃-R(6);
d is zero, 1, 2, 3 or 4;

R(6) is cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon
atoms, phenyl, biphenyl or naphthyl,

where the aromatics phenyl, biphenyl
or naphthyl are not substituted or
substituted by 1-3 substituents selected

from the group consisting of F, Cl, CF₃,
methyl, methoxy and NR(7)R(8);
R(7) and R(8)
independently of one another are
H or alkyl having 1, 2, 3 or 4
carbon atoms;

or

5  \( R(1) \) is -SR(10), -OR(10) or -CR(10)R(11)R(12);

\( R(10) \) is -C\(_{1-2}\)cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms in
the cycloalkyl ring,
heteroaryl having 1, 2, 3, 4, 5, 6, 7, 8 or 9 carbon atoms or
phenyl,

10  where heteroaryl and phenyl are unsubstituted or
substituted by 1-3 substituents selected from the group
consisting of F, Cl, CF\(_3\), CH\(_3\) methoxy, hydroxyl,
amino, methylamino and dimethylamino;

\( f \) is zero, 1 or 2;

15  \( R(11) \) and \( R(12) \)
independently of one another are as defined for \( R(10) \) or are
hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

or

R(1) is phenyl, naphthyl, biphenyl or heteroaryl having 1, 2, 3, 4, 5, 6, 7,
8 or 9 carbon atoms, the latter being linked via a carbon or a
nitrogen ring atom,
each of the radicals being unsubstituted or substituted by 1-3
substituents selected from the group consisting of F, Cl, CF\(_3\),
CH\(_3\) methoxy, hydroxyl, amino, methylamino and
dimethylamino,

25  \( k \) is zero, 1, 2, 3 or 4;

or

R(1) is -SR(13), -OR(13), -NHR(13), -NR(13)R(14), -CHR(13)R(15),
-C[R(15)R(16)]OH, -C=CR(18), -C[R(19)]=CHR(18),
-C[R(20)R(21)]_k-(CO)-[CR(22)R(23)]_l-R(24),

30  \( k \) is zero, 1, 2, 3 or 4;

\( l \) is zero, 1, 2, 3 or 4;

\( R(13) \) and \( R(14) \)
are identical or different and are
-(CH$_2$)$_g$-(CHOH)$_h$-(CH$_2$)$_i$-(CHOH)$_k$-R(17) or
-(CH$_2$)$_g$-O-(CH$_2$-CH$_2$O)$_h$-R(24);
R(17) is hydrogen or methyl,

g, h and i

are identical or different and are zero, 1, 2, 3 or 4;
k$k$ is 1, 2, 3 or 4;
R(15) and R(16)
are identical or different and are hydrogen, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, or together with the carbon atom
carrying them are cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon
atoms;

R(18)

is phenyl,

which is unsubstituted or substituted by 1-3
substituents selected from the group consisting of F,
Cl, CF$_3$, methyl, methoxy and NR(25)R(26);
R(25) and R(26)
are H or alkyl having 1, 2, 3 or 4 carbon atoms;
or
R(18) is heteroaryl having 1, 2, 3, 4, 5, 6, 7, 8 or 9 carbon atoms
which is unsubstituted or substituted as for phenyl;
or
R(18) is alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms,
which is unsubstituted or substituted by 1-3 OH;
or
R(18)
is cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms;
R(19), R(20), R(21), R(22) and R(23)
are identical or different and are hydrogen or methyl;
R(24) is H, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, cycloalkyl
having 3, 4, 5, 6, 7 or 8 carbon atoms or $-C_mH_{2m}-R(18)$;

$m$ is 1, 2, 3 or 4;

one of the two substituents $R(2)$ and $R(3)$

is $-O-CO-R(27)$;

$R(27)$ is alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, phenyl, biphenyllyl, naphthyl, pyridyl or quinolyl,

where phenyl, biphenyllyl, naphthyl, pyridyl or quinolyl

are unsubstituted by 1-3 substituents selected from the

group consisting of F, Cl, CF$_3$, methyl, methoxy and NR(7)R(8);

$R(7)$ and $R(8)$

independently of one another are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

one of the substituents $R(2)$ and $R(3)$

always being defined as $R(1)$;

$R(4)$ and $R(5)$

independently of one another are hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms;

alkoxy having 1, 2, 3 or 4 carbon atoms, F, Cl, Br, I, CN or

$-(CH_2)_n-(CF_2)_o-CF_3$;

$n$ is zero or 1;

$o$ is zero or 1;

and their pharmaceutically tolerable salts;

(96/F 154)
bc) benzoylguanidines of the formula I

\[
\begin{array}{c}
\text{R(1)} \\
\text{R(2)} \\
\text{R(3)} \\
\text{R(4)} \\
\text{N} \equiv \text{NH}_2 \\
\text{O} \equiv \text{NH}_2
\end{array}
\]

in which:

R(1) is R(13)-SO\(_m\) or R(14)R(15)N-SO\(_2\); 

m is 1 or 2;

R(13) is alkyl having 1, 2, 3, 5, 6, 7 or 8 carbon atoms, perfluoroalkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, alkenyl having 3, 4, 5, 6, 7 or 8 carbon atoms or -C\(_n\)H\(_{2n}\)-R(16),

n is zero, 1, 2, 3 or 4;

R(16) is cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, phenyl, biphenyl or naphthyl,

where phenyl, biphenyl and naphthyl are not substituted or substituted by 1-3 substituents selected from the group consisting of F, Cl, CF\(_3\), methyl, methoxy and NR(25)R(26);

R(25) and R(26) independently of one another are hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;

R(14) is hydrogen, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, perfluoroalkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, alkenyl having 3, 4, 5, 6, 7 or 8 carbon atoms or -C\(_n\)H\(_{2n}\)-R(27),

n is zero, 1, 2, 3 or 4;

R(27) is cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, phenyl, biphenyl or naphthyl,
where phenyl, biphenyl and naphthyl are not substituted or substituted by 1-3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(28)R(29);

R(28) and R(29) independently of one another are hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;

R(15) is hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;

or

R(14) and R(15) together are 4 or 5 methylene groups, of which one CH₂ group can be replaced by oxygen, S, NH, N-CH₃ or N-benzyl;

one of the substituents R(2) and R(3) is hydrogen;

and the other substituent R(2) and R(3) in each case is -CHR(30)R(31);

R(30)

is -(CH₂)ₙ-(CHOH)ₙ-(CH₂)ₙ-(CHOH)ₙ-R(32) or -(CH₂)ₙ-O-(CH₂-CH₂O)ₙ-R(24);

R(24) and R(32) independently of one another are hydrogen or methyl;

g, h, i are identical or different and are zero, 1, 2, 3 or 4;

k is 1, 2, 3 or 4;

or the other substituent R(2) and R(3) in each case is -C(OH)R(33)R(34);

R(31), R(33) and R(34) are identical or different and are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms
or

\[ R(33) \text{ and } R(34) \]

together are cycloalkyl having 3, 4, 5 or 6 carbon atoms;

5

or

\[ R(33) = \text{-CH}_2\text{OH}; \]

\[ R(4) \text{ is alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, F, Cl, Br, I, CN, -(CH}_2)_n-(CF}_2)_o-CF}_3; \]

\[ n \text{ is zero or 1;} \]

\[ o \text{ is zero, 1 or 2;} \]

and their pharmaceutically tolerable salts;

(HOE 96/F 202)

bd) indanylidineacetylguanidines of formula I

\[ \text{in which} \]

\[ R1, R2, R3, R4, R5 \text{ and } R6 \]

independently of one another are H, C\text{_1-C}_10-alkyl; haloalkyl having 1-6 carbon atoms, O-C\text{_1-C}_10-alkyl, haloalkoxy having 1-6 carbon atoms, F, Cl, Br, I, aryl, substituted aryl, heteroaryl, substituted heteroaryl, OH, O-lower alkyl, O-aryl, O-lower alkylaryl, O-substituted aryl, O-lower alkyl-substituted aryl, O-C(\text{=O})-C\text{_1-C}_4-alkyl, O-C(\text{=O})-NH-C\text{_1-C}_4-alkyl, O-C(\text{=O})-N(C\text{_1-C}_4-alkyl), NO\text{_2}, CN, CF\text{}_3, \text{NH}_2, \text{NH-C(=O)}-C\text{_1-C}_4-alkyl, \text{NH-C(=O)-NH}_2, \text{COOH, C(=O)-O-C\text{_1-C}_4-alkyl, C(=O)-NH}_2, C(=O)-NH-C\text{_1-C}_4-alkyl, C(=O)-N(C\text{_1-C}_4-alkyl), C\text{_1-C}_4-COOH, C\text{_1-C}_4-alkyl-C(\text{=O})-O-C\text{_1-C}_4-alkyl, SO\text{_3}H, SO\text{_2}-alkyl, SO\text{_2}-alkylaryl, SO\text{_2}-N-(alkyl), SO\text{_2}-N(alkyl)(alkylaryl), C(=O)-R\text{\text{11}, C\text{_1-C}_10-alkyl-C(\text{=O})-R\text{\text{11, C\text{_2-C}_10-alkenyl-C(=O)-R\text{\text{11,}}} \]
C₂-C₁₀-alkynyl-C(=O)-R₁₁, NH-C(=O)-C₁-C₁₀-alkyl-C(=O)-R₁₁ or O-C₁-C₁₁-alkyl-C(=O)-R₁₁;
R₁₁ is C₁-C₄-alkyl, C₁-C₄-alkynyl, aryl, substituted aryl, NH₂, NH-C₁-C₄-alkyl, N-(C₁-C₄-alkyl)₂, SO₃H, SO₂-alkyl,
SO₂-alkylaryl, SO₂-N-(alkyl)₂ or SO₂-N(alkyl)(alkylaryl);
X is O, S or NH;
R₇, R₈, R₉ and R₁₀ independently of one another are H, alkyl, cycloalkyl, aryl,
alkylaryl,

or

R₈ and R₉ together are part of a 5-, 6- or 7-membered heterocyclic ring;
or their pharmaceutically tolerable salts;

(HOE96/F 226)

be)

phenyl-substituted alkenylcarboxylic acid guanidines of the formula I

in which:
T is

R(A) is hydrogen, F, Cl, Br, I, CN, OH, OR(6), (C₁-C₄)-alkyl,

R(B) is (CH₂)₆C₆F₂₅⁺, (C₃-C₅)-cycloalkyl or NR(7)R(8)
r is zero or 1;

a is zero, 1, 2, 3 or 4;

b is 1, 2, 3 or 4;

R(6) is (C₁-C₄)-alkyl, (C₁-C₄)-perfluoroalkyl, (C₃-C₆)-alkenyl,
(C₃-C₆)-cycloalkyl, phenyl or benzyl,

where the phenyl ring is not substituted or substituted
by 1-3 substituents selected from the group consisting
of F, Cl, CF₃, methyl, methoxy and NR(9)R(10);

R(9) and R(10)

are H, (C₁-C₄)-alkyl or (C₁-C₄)-perfluoroalkyl;

R(7) and R(8)

independently of one another are defined as R(6);

or

R(7) and R(8)

together are 4 or 5 methylene groups, of which one
CH₂ group can be replaced by oxygen, sulfur, NH,
N-CH₃ or N-benzyl;

R(B), R(C) and R(D)

independently are as defined for R(A);

x is zero, 1 or 2;

y is zero, 1 or 2;

R(F) is hydrogen, F, Cl, Br, I, CN, OR(12), (C₁-C₈)-alkyl, Oₚ(CH₂)ₚC₆F₂g+1,
(C₃-C₆)-cycloalkyl or (C₁-C₉)-heteroaryl;

p is zero or 1;

f is zero, 1, 2, 3 or 4;

g is 1, 2, 3, 4, 5, 6, 7 or 8;

R(12) is (C₁-C₆)-alkyl, (C₁-C₄)-perfluoroalkyl, (C₃-C₆)-alkenyl,
(C₃-C₆)-cycloalkyl, phenyl or benzyl,

where the phenyl ring is not substituted or substituted
by 1-3 substituents selected from the group consisting
of F, Cl, CF₃, methyl, methoxy and NR(13)R(14);

R(13) and R(14)
are H, \((C_1-C_4)\)-alkyl or \((C_1-C_6)\)-perfluoroalkyl;

\(R(E)\) independently is as defined for \(R(F)\);

\(R(1)\) independently is as defined for \(T\);

or

\(R(1)\) is hydrogen, \(-O_k C_m H_{2m+1}\), \(-O_n (CH_2)_p C_q F_{2q+1}\), F, Cl, Br, I, CN,
\(-(C=O)-N=C(NH_2)_2\), \(-SO_2 R(17)\), \(-SO_2 NR(31) R(32)\), \(-O_4(CH_2)_6 C_8 H_5\),
\(-O_{2u}-(C_1-C_9)\)-heteroaryl or \(-S_{2u}-(C_1-C_9)\)-heteroaryl;

\(k\) is zero or 1;

\(m\) is zero, 1, 2, 3, 4, 5, 6, 7 or 8;

\(n\) is zero or 1;

\(p\) is zero, 1, 2, 3 or 4;

\(q\) is 1, 2, 3, 4, 5, 6, 7 or 8;

\(r\) is zero, 1, 2;

\(r2\) is zero, 1, 2;

\(R(31)\) and \(R(32)\) independently of one another are hydrogen, \((C_1-C_6)\)-alkyl or
\((C_1-C_6)\)-perfluoroalkyl;

or

\(R(31)\) and \(R(32)\) together are 4 or 5 methylene groups, of which one \(CH_2\) group can be replaced by oxygen, S, NH, N-CH₃ or N-benzyl;

\(R(17)\) is \((C_1-C_9)\)-alkyl;

\(u\) is zero or 1;

\(u2\) is zero or 1;

\(v\) is zero, 1, 2, 3 or 4;

where the phenyl ring is not substituted or substituted by 1-3 substituents selected from the group consisting of F, Cl, CF₃,
methyl, methoxy, \(-(CH_3)_w NR(21) R(22)\), \(NR(18) R(19)\) and
\((C_1-C_9)\)-heteroaryl;

\(R(18)\), \(R(19)\), \(R(21)\) and \(R(22)\)
independently of one another are (C₁-C₄)-alkyl or (C₁-C₄)-perfluoroalkyl;

\[ w \]  is 1, 2, 3 or 4;

where the heterocycle of the (C₁-C₆)-heteroaryl is unsubstituted or substituted by 1-3 substituents selected from the group consisting of F, Cl, CF₃, methyl or methoxy;

\[ R(2), R(3), R(4) \text{ and } R(5) \]

independently of one another are as defined for \( R(1) \),

or

\[ R(1) \text{ and } R(2) \text{ or } R(2) \text{ and } R(3) \]

in each case together are -CH-CH=CH-CH-,

which is unsubstituted or substituted by 1-3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy, \(-\left(CH₂\right)ₘ₂NR(2₄)R(2₅)\) and \( NR(2₆)R(2₇) \);

\[ R(2₄), R(2₅), R(2₆) \text{ and } R(2₇) \]

are H, (C₁-C₄)-alkyl or (C₁-C₄)-perfluoroalkyl;

\[ w₂ \]  is 1, 2, 3 or 4;

the radical T being present in the molecule at least twice, but at most three times;

and their pharmaceutically tolerable salts;

(HOE 97/F 082)

bf) benzoylguanidines of the formula I

\[
\text{R(1)} \quad \text{R(2)} \quad \text{R(3)} \quad \text{N} - \text{NH}_₂ \quad \text{R(4)} \\
\text{R(2)} \quad \text{R(3)} \quad \text{N} = \text{C} \quad \text{NH}_₂
\]

in which:

\[ R(1) \text{ is } CF₃; \]

one of the substituents \( R(2) \) and \( R(3) \)
is hydrogen;

and the other substituent $R(2)$ and $R(3)$ in each case

is $-\text{C(OH)(CH}_3\text{-CH}_2\text{OH}$, $-\text{CH(CH}_3\text{-CH}_2\text{OH}$ or $-\text{C(OH)(CH}_3\text{)}_2$;

$R(4)$ is methyl, methoxy, Cl or CF$_3$;

and their pharmaceutically tolerable salts;

(DE 195 02 895, DE 44 30 212, EP 667 341, DE 44 04 183, EP 708 088,
EP 726 254, US 4 251 545, DE 35 02 629, WO 84/00875, Kumamoto et

II. Also suitable are compounds of the formula

$\begin{array}{c}
\text{R(3)} \\
\text{R(2)} \\
\text{Z} \\
\text{N} \\
\text{W} \\
\text{Y} \\
\text{R(1)} \\
\text{R(4)} \\
\end{array}$

in which:

$W$, $Y$ and $Z$ are a nitrogen atom or a carbon atom substituted by $R(2)$ or $R(3)$ or

$R(4)$;

$R(1)$ is hydrogen, A, Hal, $-\text{CF}_3$, $-\text{CH}_2\text{F}$, $-\text{CHF}_2$, $-\text{CH}_2\text{CF}_3$, $-\text{C}_2\text{F}_5$, $-\text{CN}$,

$-\text{NO}_2$, -ethynyl, or an $X$-$R'$;

$A$ is alkyl having 1 to 6 carbon atoms;

$\text{Hal}$ is F, Cl, Br or I;

$X$ is oxygen, S or NR$^\text{\textquoteright\textprime}$;

$R''$ is hydrogen, A or a cyclic methylene chain having 3 to

7 carbon atoms;

$R'$ is H, A, HO-A-, HOOC-A-, (C$_3$-C$_7$)-cycloalkyl, (C$_6$-C$_8$)-
cycloalkylalkyl, CF$_3$, CH$_2$F, CHF$_2$, CH$_2$-CF$_3$, Ph, -CH$_2$-Ph or

Het;

$\text{Ph}$ is phenyl, naphthyl or biphenyl which is unsubstituted
or mono-, di- or trisubstituted by A, OA, NR'R'', Hal, CF₃;
Het is a mono- or binuclear saturated, unsaturated or aromatic heterocycle having 1 to 4 nitrogen, oxygen and/or sulfur atoms,
which is unsubstituted or mono-, di- or trisubstituted by Hal, CF₃, A, OH, OA, -X-R', -CN, -NO₂, and/or carbonyl oxygen,
where Het is bonded via N or an alkylene chain CₘH₂ₘ where m = zero to 6;
or R' and R''
together are alkylene having 4 - 5 carbon atoms, in which one CH₂ group can also be replaced by oxygen, S, NH, N-A, N-Ph and N-CH₂-Ph;
R(2) and R(3) independently of one another are hydrogen, Hal, A, HO-A-, X-R', -C(=N-OH)-A, A-O-CO-(C₁-C₄)-alkyl-, CN, NO₂, COOH, halogen-substituted A, in particular CF₃, CH₂F, CHF₂, C₂F₅, CH₂CF₃, or S(O)ₙR''';
R''' is A, Ph or -Het;
n is zero, 1 or 2;
or R(2) and R(3)
are independently of one another are SO₂NR'R'', Ph or -O-Ph, -O-CH₂-Ph, -CO-A, -CHO, -COOA, -CSNR'R'', CONR'R'';
-CH=CH-COOH, -CH=CH-COOA, indenyl, indanyl, decahydronaphthyl, cyclopentenyl, dihydrothienyl, dihydrofuryl, heterobicyclyl, alkylthienyl, halothienyl, haloalkylthienyl, acylthienyl, halofuryl, haloalkylfurly or pyrrolyl;
R(2) and R(3) independently of one another are R(5)-O-;

R(5) is hydrogen, A, (C_{1}-C_{6})-alkenyl or (C_{3}-C_{7})-cycloalkyl;

R(4) is Ph, Het, -O-Het; CF_{3}, S(O)_{n}R'', -SO_{2}NR'R'', alk;

or

two of the substituents R(1) to R(4) together are a group -O-CR(6)R(7)-CO-NR(8)-,

or

where R(2) has the meaning indicated;

R(6), R(7), R(8) and R(9) independently of one another are H or A;

or

R(8) is (C_{5}-C_{7})-cycloalkyl;

or

R(9) is cyano;

alk is straight-chain or branched (C_{1}-C_{8})-alkyl or (C_{3}-C_{6})-cycloalkyl,

which is unsubstituted or mono-, di- or trisubstituted by A;

or

alk is an ethenyl or ethynyl radical which is substituted by H, A, Ph or Het.
III. Compounds of the formula

\[
\begin{array}{c}
\text{Z} - \text{N} - \text{Y} \\
\text{X} - \text{N} - \text{NH}_2 \\
\end{array}
\]

in which:

10 X is H, Hal, (Hal)$_3$C-, (C$_1$-C$_6$)-alkyl, (C$_3$-C$_6$)-cycloalkyl, substituted phenyl, (C$_1$-C$_6$)-alkyl-S- or (C$_1$-C$_6$)-alkyl-SO$_2$-;

Y is NH$_2$ or substituted amino;

or

X and Z together are a -(CH$_2$)$_4$- or a 1,3-butadienylene chain;

or

Z is H, Hal, OH, HS, (C$_1$-C$_6$)-alkyl, (C$_3$-C$_6$)-cycloalkyl, substituted phenyl;

or

Z is an amino group -NR(1)R(2);

R(1) is H, straight- or branched-chain, optionally substituted (C$_1$-C$_6$)-alkyl,

which can be interrupted by oxygen;

or

R(1) is (C$_3$-C$_8$)-alkenyl, (C$_3$-C$_6$)-alkynyl, (C$_3$-C$_7$)-cycloalkyl or OH-substituted phenyl or OH-substituted phenyl-(C$_1$-C$_4$)-alkyl or OH-substituted (C$_3$-C$_7$)-cycloalkyl;

R(2) is 1-morpholino, hydrogen or a straight or branched (C$_1$-C$_6$)-alkyl chain,

which can be interrupted by oxygen or an amino group,

which straight or branched (C$_1$-C$_6$)-alkyl chain is
unsubstituted or substituted by
  a substituted or unsubstituted mono- or polynuclear
  heterocycle which contains nitrogen, oxygen or sulfur
  atoms;

or

which alkyl chain is substituted by phenyl,
  optionally mono- or polysubstituted by (C₁-C₄)-alkoxy,
  optionally substituted by OH, alkylamino, alkyl or
  phenyl;

or

by an aminocarbonyl group
or
by hydroxyl or (C₁-C₄)-alkoxy groups,

or

R(2) is phenyl,
  unsubstituted or substituted by alkyl, alkoxy, an amino
  group, which as substituents carries:
    H, a mono- or polynuclear heterocycle which
    contains nitrogen, oxygen or sulfur atoms,
    which is unsubstituted or substituted by
    H, Hal or (C₁-C₄)-alkyl;
  a phenyl radical,
  unsubstituted or substituted by a
  substituent selected from the group
  consisting of (C₁-C₄)-alkyl, (C₁-C₄)-
  alkoxy, Hal and OH;

or

R(2) is 1-piperidino,
  unsubstituted or substituted in the 4-position by an
  acyl radical of an aliphatic, alicyclic, aromatic or
  heteroaromatic carboxylic acid, (C₁-C₄)-alkyl, which for
  its part can be substituted by OH or (C₁-C₄)-alkoxy or a
(C₁-C₄)-alkoxy-substituted phenyl radical;

or

\( R(2) \) is amidino,

which is unsubstituted or substituted by phenyl,

which is unsubstituted or substituted by Hal or alkyl;

or

\( R(2) \) is an acyl radical of an aliphatic, alicyclic, aromatic or heteroaromatic carboxylic acid,

or

\( R(2) \) is a (C₁-C₄)-alkyl chain, which can be substituted by a phenyl radical carrying OH, alkoxy or alkyl radicals,

or

\( R(1) \) and \( R(2) \) together with the nitrogen atom to which they are bonded, are a piperazine ring,

which is unsubstituted or via a (C₁-C₆)-methylene chain carries a mono- or polynuclear heterocycle,

which contains nitrogen, oxygen or sulfur,

Hal is F, Cl, Br or I.


IV. Likewise suitable are indoloylguanidine derivatives of the formula

\[
[R(1)]_{5}\\ \begin{array}{c}
\text{N} \\
\text{R(2)} \\
\text{O} \\
\text{NH} \\
\text{NH}_{2}
\end{array}
\]

in which

\( R(2) \) is hydrogen, unsubstituted or substituted (C₁-C₆)-alkyl, (C₅-C₇)-cycloalkyl, OH, (C₁-C₆)-alkyl-O-, an aromatic radical or a group -CH₂-R(20);

\( R(20) \) is (C₂-C₆)-alkenyl or (C₂-C₆)-alkynyl;

\( R(1) \) is 1 to 5 identical or different substituents, which are:
hydrogen, unsubstituted or substituted \((C_1-C_8)\)-alkyl, \((C_2-C_6)\)-alkenyl, \((C_2-C_6)\)-alkynyl, \((C_3-C_7)\)-cycloalkyl, halogen, \(-\text{NO}_2\), \((C_2-C_6)\)-alkanoyl, arylalkanoyl having up to 10 carbon atoms, aroyl having up to 11 carbon atoms, \(-\text{COOH}\), \((C_2-C_6)\)-alkoxycarbonyl, an aromatic group or one of the following mentioned groups: \(-\text{OR}(3), -\text{NR}(6)\text{R}(7)\) or \(-\text{S(O)}_n\text{R}(40)\);

\(R(3)\) is hydrogen, \((C_1-C_8)\)-alkyl, substituted \((C_1-C_8)\)-alkyl, \((C_3-C_7)\)-cycloalkyl, an aromatic radical or a group \(-\text{CH}_2\text{-R}(30)\)

\(R(30)\) is alkenyl or alkynyl;

\(R(6)\) and \(R(7)\) independently of one another are hydrogen, unsubstituted or substituted \((C_1-C_8)\)-alkyl, \((C_3-C_7)\)-cycloalkyl, \((C_2-C_6)\)-alkanoyl, an arylalkanoyl group having up to 10 carbon atoms, an aroyl group having up to 11 carbon atoms, an aromatic group or

\(-\text{CH}_2\text{-R}(60)\);

\(R(60)\) is \((C_2-C_6)\)-alkenyl or \((C_2-C_6)\)-alkynyl;

or

\(R(6)\) and \(R(7)\) together with the nitrogen atom are a 5 - 7-membered cyclic amine, which can additionally contain further heteroatoms in the ring;

\(n\) is zero, 1 or 2;

\(R(40)\) is unsubstituted or substituted \((C_1-C_8)\)-alkyl, or an aromatic group, or a group \(-\text{A-CH}_n\text{-N-R'}\)

\(A\) is oxygen, \(-\text{S(O)}_n\text{-}\) or \(-\text{N(R50)}\text{-}\);

\(R(50)\) is hydrogen or \((C_1-C_8)\)-alkyl;

\(R'\) is hydrogen, unsubstituted or substituted \((C_1-C_8)\)-alkyl, in which the ring represents a saturated 3 - 8-membered heterocycle having a nitrogen atom,
said substituted alkyl carries one or more groups selected from the group consisting of halogen, \(-\text{OH}\), \((C_1-C_8)\)-alkoxy, \(-\text{CN}\), \(-\text{COOH}\),
(C_{2}-C_{6})-alkoxycarbonyl, (C_{2}-C_{6})-alkanoyl, arylalkanoyl having up to 10 carbon atoms, aroyl having up to 11 carbon atoms, an aromatic group, -CONR(4)R(5),
R(4) and R(5)

5 identically or differently are hydrogen or (C_{1}-C_{8})-alkyl;
or
R(4) and R(5)

are connected to one another and together form a 5 - 7-membered cyclic amine which can additionally contain

10 further heteroatoms in the ring,
or said substituted alkyl carries a group

in which:

E is a nitrogen atom or a CH group;

15 R'' is hydrogen, (C_{1}-C_{8})-alkyl which is unsubstituted or
substituted by OH, (C_{1}-C_{6})-alkoxy, -CN, -COOH, (C_{2}-C_{6})-alkoxycarbonyl, (C_{2}-C_{6})-alkanoyl, aralkanoyl having up to 10 carbon atoms, aroyl having up to 11 carbon atoms, an aromatic group, -NR(6)R(7), -CONR(4)R(5);

R(4) and R(5)

20 independently of one another are hydrogen or (C_{1}-C_{8})-alkyl;

where the cyclic system of the formula

is a 3 - 8-membered saturated aliphatic or heterocyclic ring system

25 having a nitrogen atom,

and where the aromatic groups mentioned are an aryl radical having up to 10 carbon atoms, a 5- or 6-membered heteroaryl radical having

30 1 - 4 nitrogen atoms, a 5- or 6-membered heteroaryl group containing 1 or 2 nitrogen atoms and a heteroatom which is oxygen or sulfur, or furyl,

and where the aryl radicals mentioned can be unsubstituted or substituted
by unsubstituted (C₁-C₆)-alkyl or substituted (C₁-C₆)-alkyl, halogen, -NO₂, (C₂-C₆)-alkoxycarbonyl, COOH, -OR(3), NR(6)R(7), -CONR(4)R(5), 3O₂NR(6)R(7) or S(O)ₙR(4),

where R(1) and the guanidinocarbonyl radical can be in any desired position of the 5- or 6-membered ring of the indole system, and the appropriate pharmaceutically tolerable salts;

(WO 95 04052)

V. Additionally suitable are heterocyclic guanidine derivatives of the formula

in which:

- X is -O-, -S-, -NH-, -N⁺(C₁-C₄)-alkyl- or -N(phenyl)-;
- R(1), R(2) and R(3)
  are hydrogen, halogen, (C₁-C₄)-alkyl, (C₁-C₄)-alkyl-O-, phenyl, benzyl;

- or
two of the substituents R(1), R(2) and R(3)
  together with one side of the benzo system are a 4 - 6-membered carbcyclic ring;

- R(4) and R(5)
  independently of one another are hydrogen, (C₁-C₁₂)-alkyl, benzhydryl, aralkyl,
  which is unsubstituted or substituted by one or more substituents from the groups halogen, (C₁-C₆)-alkyl, (C₁-C₆)-alkyl-O- or -CF₃, -(CH₂)ₘ-CH₂-T,
  m is zero to 3;
  T is -CO-O-T(1);
T(I) is hydrogen or \((C_1-C_4)\)-alkyl;

\(Cy\) is a benzo-fused unsaturated or dihydro-5-membered ring heterocycle

\[
\begin{array}{c}
\text{a pyrazole or imidazole ring of the formula} \\
\text{or}
\end{array}
\]

\(a\) naphthyl radical or a dihydro- or tetrahydronaphthyl radical

\[
\begin{array}{c}
\text{a 2-, 3- or 4-pyridyl radical}
\end{array}
\]

\(Z\) is N- or CH;

a thienyl radical

\(R(6)\) is hydrogen, halogen, hydroxyl, \((C_1-C_{10})\)-alkyl, \((C_1-C_{10})\)-alkyl-O-, phenoxy, \((C_1-C_{10})\)-alkyloxymethyloxy- or \(-(O)_nS-R(9)\);

\(R(9)\) is \((C_1-C_{10})\)-alkyl, thienyl, pyridyl, thiazolyl, thiadiazolyl, imidazolyl, pyrazolyl or phenyl,

each of which is unsubstituted or mono- or disubstituted by halogen, \((C_1-C_4)\)-alkyl or \((C_1-C_4)\)-alkyl-O-;

\(R(7)\) and \(R(8)\)

is hydrogen, halogen, hydroxyl, \((C_1-C_{10})\)-alkyl,

\((C_1-C_{10})\)-alkyl-O-, phenyl, phenoxy or

\((C_1-C_{10})\)-alkyloxymethyloxy;

or

\(Cy\) is phenyl,
which is unsubstituted or mono- or disubstituted by halogen,
(C_1-C_4)-alkyl or (C_1-C_4)-alkyl-O-;

or

Cy \text{ is } -\text{Gr-Am};

Gr \text{ is } -R(13)-R(12)-(\text{CH}_2)_q-C[W]\{W(1)\}-(\text{CH}_2)_q-; R(13)R(14)- or
-R(15)-;

R(12) \text{ is a single bond, } -\text{O}-, -(\text{O})_n\text{S}-, -\text{CO}- \text{ or } -\text{CONH}-;

R(13) \text{ is a single bond, phenyl, thiencyl, pyridyl, thiazolyl,}
thiadiazolyl, imidazolyl or pyrazolyl;

R(14) \text{ is a single bond or SO}_2-;

R(15) \text{ is (C}_2-C_{10})\text{-alkenyl- or (C}_2-C_{10})\text{-alkynyl};

W \text{ and W}(1)

\text{ independently of one another are hydrogen, (C}_1-C_4)-\text{alkyl;}

or

W \text{ and W}(1)

\text{ cyclically connected to one another are a (C}_3-C_8)-\text{hydrocarbon ring;}

q \text{ and } q'

\text{ are zero to 9;}

Am \text{ is } -\text{NR}(10)R(11);

R(10) \text{ is hydrogen, (C}_1-C_4)-\text{alkyl or benzyl,}

R(11) \text{ is (C}_1-C_4)-\text{alkyl, phenyl or benzyl;}

or

R(10) \text{ and R}(11)

\text{ together are a (C}_3-C_{10})\text{-alkylene group,}

\text{ which is unsubstituted or substituted by } -\text{COOH,}

(C_1-C_5)-\text{alkoxycarbonyl, (C}_2-C_4)\text{-hydroxyl-}

\text{alkylene or benzyl;}

or

Am \text{ is pyrrolyl, pyridyl, pyrazolyl, morpholinyl, dihydropyridyl,}
tetrahydropyridyl, quinuclidinyl, imidazolyl,
3-azabicyclo[3.2.1]octyl,

which is unsubstituted or substituted by (C₁-C₄)-alkyl,

or

Am is azabicyclo[3.2.2]nonyl;

or

Am is a piperazine group of the formula

\[
\begin{array}{c}
\text{N} \\
\text{R(16)} \\
\text{N}
\end{array}
\]

R(16) is hydrogen, (C₁-C₄)-alkyl, (C₃-C₆)-cycloalkyl, phenyl, tolyl, methoxyphenyl, halophenyl, diphenylmethylene, benzyl or pyridyl;

or

Am is an azido group -(O)t-(CH₂)q-C[W][W(1)]-(CH₂)q'-N₃;

t is zero or 1;

where W and W(1) have the previously indicated meaning;

and the optical enantiomers and the pharmacologically tolerable salts;

VI. Furthermore suitable are the guanidine compounds as described in EP-743 301 (DE 195 17 848), EP 758 644 (DE 195 29 612), EP 760 365 (DE 195 31 138)

where R1=R2 is H, halo, alkyl, CN, NO₂, perfluoroalkyl, SO₃CF₃;

R3 = CH=CH₂, CH₂-CH=CH₂, CH₂-CH₂-CH=CH₂, cycloalkenyl, cycloalkenylalkyl; R4 = alkyl, (substituted) phenyl,


Examples of classes of active compounds having cardiovascular activity
which can be combined advantageously with NHE inhibitors therapeutically are beta-receptor blockers, calcium antagonists, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, loop diuretics, thiazide diuretics, potassium-sparing diuretics, aldosterone antagonists, such as are employed, for example, in lowering of the blood pressure, and also cardiac glycosides or other agents increasing the contractile force in the treatment of cardiac insufficiency and of congestive heart failures, and also antiarrhythmics of the classes I - IV, nitrates, $K_{ATP}$ openers, $K_{ATP}$ blockers, inhibitors of the veratridine-activatable sodium channel, etc. For example, the following are thus suitable: the beta-blockers propanolol, atenolol, metoprolol; the calcium antagonists diltiazem hydrochloride, verapamil hydrochloride, nifedipine; the ACE inhibitors captopril, enalapril; the angiotensin receptor antagonist losartan; the loop diuretics furosemide, piretanide, torasemide; the thiazide diuretics hydrochlorothiazide, metolazone, indapamide; the potassium-sparing diuretics amiloride, triamterene, spironolactone; the cardiac glycosides digoxin, digitoxin, strophanthin; the antiarrhythmics amiodarone, sotalol, bretylium, flecainide; the nitrate glycerol trinitrate; the $K^+(ATP)$ openers cromakalim, lemakalim, nocorandil, pinacidil, minoxidil; the inhibitors of the veratridine-activatable Na$^+$ channel.

An example of such a particularly advantageous combination component with NHE inhibitors are blockers of the non-inactivating sodium channel (veratridine-activatable sodium channel). When the two classes of active compounds are therapeutically administered as a combination, they surprisingly show the abovementioned synergistic effects in the treatment of symptoms resulting from ischemic conditions and reperfusion events. The combinations of an NHE inhibitor with a blocker of the non-inactivating sodium channel (veratridine-activatable sodium channel) are thus outstandingly suitable for infarct and reinfarct prophylaxis and infarct treatment and also for the treatment of angina pectoris and the inhibition of ischemically induced cardiac arrhythmias, tachycardia and the formation
and maintenance of ventricular fibrillation, the combinations of an NHE inhibitor with a blocker of the non-inactivating sodium channel also preventively inhibiting or greatly decreasing the pathophysiological processes in the formation of ischemically induced damage. Because of their enhanced protective actions against pathological hypoxic and ischemic situations, the combinations according to the invention of an NHE inhibitor with a blocker of the non-inactivating sodium channel can be used, as a result of enhanced inhibition of the Na⁺ influx into the cell, as pharmaceuticals for the treatment of all acute or chronic damage induced by ischemia or diseases induced primarily or secondarily thereby. This relates to their use as pharmaceuticals for surgical interventions, e.g. in organ transplantation, where the combinations of an NHE inhibitor with a blocker of the non-inactivating sodium channel can be used both for the protection of the organs in the donor before and during removal, for the protection of removed organs, for example, also during storage thereof in physiological bath fluids, and also during transfer to the recipient's body. The combinations of an NHE inhibitor with a blocker of the non-inactivating sodium channel are likewise valuable, protectively acting pharmaceuticals when carrying out angioplastic surgical interventions, for example on the heart, and also on peripheral vessels. In accordance with their protective action against ischemically induced damage, the combinations of an NHE inhibitor with a blocker of the non-inactivating sodium channel are also suitable as pharmaceuticals for the treatment of ischemias of the nervous system, in particular of the central nervous system, where they are suitable for the treatment of stroke or of cerebral edema. Moreover, the combinations according to the invention of an NHE inhibitor with a blocker of the non-inactivating sodium channel are also suitable for the treatment of forms of shock, such as, for example, of allergic, cardiogenic, hypovolemic and bacterial shock.

Thus, for example, it has surprisingly been found that the combination of the NHE inhibitor cariporide (HOE 642)
described, for example, in US patent US 5 591 754, with the inhibitor of the non-inactivating sodium channel (veratridine-activatable sodium channel) R56865 [N-[1-[4-(4-fluorophenoxy)butyl]-4-piperidinyl]-N-methyl-2-benzothiazolamine (see Verdonck F, Bielen F, Ver Donck L: Preferential block of the veratridine-induced, noninactivating Na⁺ current by R56865 in single cardiac Purkinje cells. Eur J Pharmacol 1991; 203; 371-378)] in a model of experimental cardiac infarct in rats showed an activity which is considerably greater than additive activity. The reduction of the size of the infarct which was obtained using the combination of cariporide and R56865 exceeded the maximum effect of the individual substances in this model by far. The study was carried out as described below.

Preparation of the animals
Male rats having a body weight of 280 to 410 g were classed into four groups and anaesthetized. The thorax was opened close to the sternum, a silk thread (Ethicon®; 1.0 metric, 5-0) was placed around left coronary artery and the two loose ends of the thread were pulled through a small plastic tube.

For administration of substance, a catheter was placed into the left jugular vein. The systemic blood pressure was recorded in the left carotid artery using a pressure recorder (Combitrans®, B. Braun Melsungen AG) and the ECG was registered using subcutaneous electrodes. After digital conversion, the data were registered in a computer and the ECG was evaluated in accordance with the guidelines of the Lambeth Convention (6. Walker MJA, Curtis MJ, Hearse DJ, Campbell RWF, Janse MJ, Yellon DM, Cobbe SM, Cokes SJ, Harness JB, Harron DWG, Higgins SJ, Julian DG,
Protocol of the experiment

Hoe 642 was dissolved in doubly distilled water and R56865 in tartaric acid (0.6%), dilution was carried out using doubly distilled water, and 4% of mannitol were added. After the preparation of the animals, the substances were administered intravenously on their own or in combination. The control animals were only given the solvent. The volume of the injection was 1 ml per kg of body weight. Five minutes later, the silk thread was constricted by moving the plastic tube forward, and the coronary artery was closed for one hour. The plastic tube was fixed by a clamp. After reopening of the coronary artery, the tissue was reperfused for two hours.

Determination of the size of the infarct

The coronary artery which had been tied off was closed again, and ink was injected into the left ventricle of heart via the apex of the heart to mark the heart tissue which had been supplied normally with blood. The animals were sacrificed, the hearts were removed and the left ventricle of heart was prepared and cut into slices vertically to the axis of the heart. The slices were washed in sodium chloride solution and subsequently incubated in triphenyltetrazolium chloride at 37°C for 5-7 minutes to stain the tissue that was still live. The slices were subsequently weighed and measured planimetrically (Imaging Res. Inc. Brock University, St. Catherines, Ontario, Canada, Phoenix Technologies, Matrox Electronic Systems OS/2). Determined were: firstly, the size of the tissue which had been supplied normally with blood, secondly, the area which had not been supplied with blood after constriction of the loop (risk area), and thirdly the size of the area in which the cells had died (size of infarct).

The statistical evaluation of the differences between the individual groups
was carried out using Student's t-test.

Results

Administration of the substances did not effect blood flow in the tissue which was supplied normally with blood. Consequently, there was no change in the size of the risk area of, on average, 59.3% of the left ventricle. In the control group, necrosis of the tissue occurred owing to the one-hour blockade of perfusion and reperfusion. In the control group, the size of infarct was 63.4 ± 4.3% (n = 8) of the risk area. Administration of 10 mg/kg of body weight of Hoe 642 reduced the size of infarct to 33.2 ± 3.7% (n = 7), and administration of 3 mg/kg of body weight of R56865 reduced the size of infarct to 38.9 ± 3.1% (n = 8). Using the combination of the two substances in the dosage in question, however, it was possible to reduce the infarct to 10.5 ± 2.6% (n = 10) of the risk area.

All figures given are mean ± S.E.M.

"comprises/comprising" when used in this specification is taken to specify the presence of stated features, integers, steps or components but does not preclude the presence or addition of one or more other features, integers, steps, components or groups thereof.
THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A pharmaceutical combination preparation which comprises an inhibitor of the Na⁺/H⁺ exchanger and a substance having cardiovascular activity.

2. A pharmaceutical combination preparation which comprises an inhibitor of the Na⁺/H⁺ exchanger and a substance having cardiovascular activity, the inhibitor of the Na⁺/H⁺ exchanger being selected from the following compounds:

   guanidine derivatives, as described in Edward J. Cragoe, Jr., "DIURETICS, Chemistry, Pharmacology and Medicine", J. WILEY & Sons (1983), 303-341, and additionally compounds of the following formulae:

   I

   a) benzoylguanidines of the formula I

   ![Chemical Structure]

   in which:

   R(1) or R(2)

   is R(6)-S(O)ₙ- or R(7)R(8)N-O₂S-;

   and the other substituent R(1) or R(2) in each case

   is H, F, Cl, Br, (C₁-C₄)-alkyl, (C₁-C₄)-alkoxy or phenoxy, which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of fluorine, chorine, methyl and methoxy;

   or the other substituent R(1) or R(2) in each case

   is R(6)-S(O)ₙ or R(7)R(8)N-;

   n is zero, 1 or 2;

   R(6) is (C₁-C₆)-alkyl, (C₅-C₇)-cycloalkyl, cyclopentylmethyl,
cyclohexylmethyl or phenyl,
which is unsubstituted or substituted by 1 - 3
substituents selected from the group consisting of
fluorine, chlorine, methyl and methoxy;

R(7) and R(8)
identically or differently are H or (C₆H₅)-alkyl;
or

R(7) is phenyl-(CH₂)m;
m is 1 - 4;
or

R(7) is phenyl,
which is unsubstituted or substituted by 1 - 2
substituents selected from the group consisting of
fluorine, chlorine, methyl and methoxy;
or

R(7) and R(8)
together are a straight-chain or branched (C₄-C₇)-chain,
where the chain can additionally be interrupted by O, S or
NR(9);
or

R(9) is H or methyl;
or

R(7) and R(8)
together with the nitrogen atom to which they are bonded, are
a dihydroindole, tetrahydroquinoline or tetrahydroisoquinoline
system;

R(3), R(4) and R(5)
independently of one another are H or (C₃-C₅)-alkyl;
or

R(3) and R(4)
together are a (C₃-C₅)-alkylene chain;
or

R(4) and R(5)
together are a \((C_4-C_7)\)-alkylene chain; and their pharmaceutically tolerable salts;

b) benzoylguanidines of the formula I

\[
\begin{align*}
R(1) & \quad \text{is } R(4)\text{-SO}_m \text{ or } R(5)R(6)\text{-SO}_2^-; \\
m & \quad \text{is zero, 1 or 2;} \\
R(4) \text{ and } R(5) & \quad \text{are } C_1-C_9\text{-alkyl, } C_3-C_6\text{-alkenyl or } -C_n\text{H}_{2n-}\text{-R(7);} \\
n & \quad \text{is zero, 1, 2, 3 or 4;} \\
R(7) & \quad \text{is } C_5-C_7\text{-cycloalkyl or phenyl,} \\
\text{which is unsubstituted or substituted by 1 - 3} \\
\text{substituents selected from the group consisting} \\
of \text{F, Cl, CF}_3, \text{methyl, methoxy and } \text{NR(8)R(9);} \\
R(8) \text{ and } R(9) & \quad \text{are } H \text{ or } C_1-C_4\text{-alkyl;} \\
or \\
R(5) & \quad \text{is } H; \\
R(6) & \quad \text{is } H \text{ or } C_1-C_4\text{-alkyl,} \\
or \\
R(5) \text{ and } R(6) & \quad \text{together are } 4 \text{ or } 5 \text{ methylene groups, of which one } \text{CH}_2 \\
\text{group can be replaced by an } O, S, \text{NH, } N-\text{CH}_3 \text{ or N-benzyl;} \\
R(2) & \quad \text{is hydrogen, } F, \text{Cl, Br, } (C_1-C_4)\text{-alkyl-}, \text{O-}\text{(CH}_2)_m\text{C}_p\text{F}_{2p+1} \text{ or } -X-R(10); \\
m & \quad \text{is zero or 1;} \\
p & \quad \text{is 1, 2 or 3;}
\end{align*}
\]
$X$ is O, S or NR(11);

R(10) is H, C$_1$-C$_6$-alkyl, C$_5$-C$_7$-cycloalkyl, cyclohexylmethyl,
cyclopentylmethyl or -C$_n$H$_{2n}$-R(12);

n is zero, 1, 2, 3 or 4;

R(12) is phenyl,

which is unsubstituted or substituted by 1 - 3
substituents selected from the group consisting
of F, Cl, CF$_3$, methyl, methoxy und NR(8)R(9);

R(8) and R(9)

are H or C$_1$-C$_4$-alkyl;

R(11) is hydrogen or C$_1$-C$_3$-alkyl;

or

R(10) and R(11)

together are 4 or 5 methylene groups, of which one

CH$_2$ group can be replaced by O, S, NH, N-CH$_3$ or

N-benzyl;

R(3) is defined as R(1), or is C$_1$-C$_6$-alkyl, nitro, cyano, trifluoromethyl, F,

Cl, Br, I or -X-R(10);

R(10) is H, C$_1$-C$_6$-alkyl, C$_5$-C$_7$-cycloalkyl, cyclohexylmethyl,
cyclopentylmethyl or -C$_n$H$_{2n}$-R(12);

n is zero to 4;

R(12) is phenyl,

which is unsubstituted or substituted by 1 - 3
substituents selected from the group consisting of F,

Cl, CF$_3$, methyl, methoxy und NR(8)R(9);

R(8) and R(9)

are H or C$_1$-C$_4$-alkyl;

R(11) is C$_1$-C$_3$-alkyl;

or

R(10) and R(11)

together are 4 or 5 methylene groups, of which one
CH₂ group can be replaced by O, S, NH, N-CH₃ or N-benzyl;
and their pharmaceutically tolerable salts;

c) ortho-substituted benzoylguanidines of the formula I

\[
\begin{align*}
R(1) & \quad R(2) \\
R(3) & \quad R(4) \\
& \quad R(5)\\
& \quad N \quad NH₂
\end{align*}
\]

in which:

- \( R(1) \) is F, Cl, Br, I, C₁₋₆-alkyl or -X-R(6);
- \( X \) is O, S, NR(7) or Y-ZO;
- \( Y \) is O or NR(7);
- \( Z \) is C or SO;
- \( R(6) \) is H, C₁₋₆-alkyl, C₅₋₇-cycloalkyl, cyclohexylmethyl, cyclopentylmethyl, \(-(CH₂)ₘC₆Fₙ₊₁\) or \(-C₆H₂n-R(8)\);
- \( m \) is zero or 1;
- \( p \) is 1 - 3;
- \( n \) is zero to 4;
- \( R(8) \) is phenyl,

which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of the groups F, Cl, CF₃, methyl, methoxy and NR(9)R(10);

- R(9) and R(10) are H or C₁₋₄-alkyl;
- R(7) is H or C₁₋₃-alkyl;

or
R(6) and R(7) together are 4 or 5 methylene groups, of which one CH$_2$ group can be replaced by O, S, NH, N-CH$_3$ or N-benzyl;

R(3) is H or -X-R(6);

5 X is O, S, NR(7) or Y-ZO;

R(7) is H or C$_1$-C$_3$-alkyl;

Y is O or NR(7);

where Y is bonded to the phenyl radical of the formula I,

10 Z is C or SO;

R(6) is H, C$_1$-C$_4$-alkyl, C$_5$-C$_7$-cycalkyl, cyclohexylmethyl, cyclopentylmethyl, -(CH$_2$)$_m$C$_p$F$_{2p+1}$ or -C$_n$H$_{2n}$-R(8);

m is zero or 1;

p is 1 - 3;

15 n is zero to 4;

R(8) is phenyl, which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF$_3$, methyl, methoxy and NR(9)R(10);

20 R(9) and R(10) are H or C$_1$-C$_4$-alkyl;

or

R(6) and R(7) together are 4 or 5 methylene groups, of which one CH$_2$ group can be replaced by O, S, NH, N-CH$_3$ or N-benzyl;

R(2) and R(4) identically or differently are R(11)-SO$_q$- or R(12)R(13)N-SO$_2$-;

q is zero - 2;

R(11) is C$_1$-C$_4$-alkyl, which is unsubstituted or carries phenyl as a substituent, where phenyl is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF$_3$, ...
methyl, methoxy and \( NR(9)R(10) \);

\( R(9) \) and \( R(10) \)
are H or \( C_1-C_4 \)-alkyl;

\( R(12) \) and \( R(13) \)
are defined as \( R(6) \) and \( R(7) \);
or one of the two radicals \( R(2) \) or \( R(4) \)
is hydrogen or is defined as \( R(1) \);
\( R(5) \) is H, methyl, F, Cl or methoxy,
and their pharmaceutically tolerable salts;

\[ \text{d) benzoylguanidines of the formula I} \]

\[
\begin{array}{c}
\text{R(1)} \\
\text{N NH}_2 \\
\text{NH} \\
\text{R(2)} \\
\text{O} \\
\text{NH}_2 \\
\end{array}
\]

in which:
\( R(1) \) or \( R(2) \)
is an amino group \(-NR(3)R(4)\);

\( R(3) \) and \( R(4) \)
identically or differently are H, \( C_1-C_6 \)-alkyl or \( C_3-C_7 \)-cycloalkyl;
or
\( R(3) \) is phenyl-(\( CH_2 \)\( p \))\;
\( p \) is 0, 1, 2, 3 or 4;
or
\( R(3) \) is phenyl,
where the phenyl in each case is unsubstituted or carries one to two
substituents selected from the group consisting of fluorine, chlorine,
methyl and methoxy;
or
\( R(3) \) and \( R(4) \)
together can be a straight-chain or branched
C₄-C₇-methylene chain, where one -CH₂- member of the methylene chain can be replaced by oxygen, S or NR(5); R(5) is H or lower alkyl; the other substituent R(1) or R(2) in each case is H, F, Cl, C₁-C₄-alkyl, C₁-C₄-alkoxy, CF₃, C₁₋F₂₋CH₂, benzyl or phenoxy, where the respective phenyl radical is unsubstituted or carries one to two substituents selected from the group consisting of methyl, methoxy, fluorine and chlorine; m is 1, 2 or 3; and their pharmaceutically tolerable salts;

e) benzoylguanidines of the formula I

\[
\begin{align*}
\text{R}(1) & \quad \text{R}(2) \\
\text{R}(3) & \\
\text{N} & \\
\text{NH₂} & \\
\text{O} & \\
\text{NH₂} &
\end{align*}
\]

in which:
R(1) is R(4)-SOₘ or R(5)R(6)N-SO₂⁻;
 R(4) and R(5) are C₁-C₆-alkyl, C₃-C₆-alkenyl or -CₙH₂₋₋₋₋R(7);
 n is zero, 1, 2, 3 or 4;
R(7) is C₅-C₇-cycloalkyl or phenyl, which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(8)R(9);
R(8) and R(9) are H or C₁-C₄-alkyl; or
R(5) is H;
R(6) is H or C_{1}-C_{4}-alkyl;
or
R(5) and R(6) together are 4 or 5 methylene groups, of which one CH\_2 group can be replaced by an O, S, NH, N-CH\_3 or N-benzyl;
R(2) is hydrogen, straight-chain or branched (C_{5}-C_{9})-alkyl,
-CR(13)=CHR(12) or -C≡CR(12);
R(12) is phenyl,
which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF\_3, methyl, methoxy and NR(14)R(15);
R(14) and R(15) are H or (C\_1-C\_4)-alkyl;
or
R(12) is (C\_1-C\_9)-heteroaryl,
which is unsubstituted or substituted as phenyl,
or
R(12) is (C\_1-C\_9)-alkyl,
which is unsubstituted or substituted by 1 - 3 OH,
or
R(12) is (C\_3-C\_8)-cycloalkyl;
R(13) is hydrogen or methyl,
or
R(12) is (C\_3-C\_8)-cycloalkyl, (C\_3-C\_8)-cycloalkyl-(C\_1-C\_4)-alkyl, phenyl, C\_6H\_5-(C\_1-C\_4)-alkyl, naphtyl, biphenyl, 1,1-diphenyl-(C\_1-C\_4)-alkyl, cyclopentadienyl, pyridyl, pyrrolyl, furanyl, thienyl, thiazolyt, oxazolyl, indenyl, quinolyl, indolyl, benzofurany, benzothienyl, benzothiazolyl, benzoazolyl, imidazolyl, pyrazolyl, triazolyl, tetrazolyl, isoxazolyl, isothiazolyl, pyrazinyl, pyrimidiny, pyridazinyl, indazolyl, isoquinolyl, phthalazinyl, quinoxaliny, quinazoliny or cinnoliny;
R(3) is defined as R(2);
and where the aromatic substituents R(2) and R(3) are unsubstituted or
substituted by 1 - 3 substituents from the groups F, Cl, CF₃, (C₁₋₄)-alkyl or
-alkoxy, or NR(10)R(11) with R(10) and R(11) being H or (C₁₋₄)-alkyl;
and their pharmaceutically tolerable salts;

f) benzoylguanidines of the formula I

\[
R(1) \quad \text{C} = \text{C} \quad \text{C} \quad \text{NH} \quad \text{C} \quad \text{C} \quad \text{C} \quad \text{N} = \text{C} \quad \text{NH}_2
\]

in which:
R(1) or R(2)
is R(3)-S(O)ₙ- or
\[
R(4) \quad \text{N} - \text{O}_2 \text{S} - \\
R(5)
\]
the other substituent R(1) or R(2) in each case
is H, OH, F, Cl, Br, I, C₁₋₄-alkyl, C₁₋₄-alkoxy, benzyloxy or
phenoxy,
which is unsubstituted or carries one to three substituents
selected from the group consisting of fluorine, chlorine,
methyl, methoxy, hydroxyl and benzyloxy,
R(3)-S(O)ₙ-, NR(4)R(5) or 3,4-dehydroperipnidine
R(3) is C₁₋₆-alkyl, C₅₋₇-cycloalkyl, cyclopentylmethyl,
cyclohexylmethyl or phenyl,
which is unsubstituted or substituted by one to three
substituents selected from the group consisting of
fluorine, chlorine, methyl and methoxy;
R(4) and R(5)
identically or differently, are H or C₁-C₆-alkyl;

or

R(4) is phenyl-(CH₂)ₘ⁻;

ₘ is 1, 2, 3 or 4;

or

R(4) is phenyl,

which is unsubstituted or carries one to two

substituents selected from the group consisting of

fluorine, chlorine, methyl and methoxy;

or

R(4) and R(5)

together are a straight-chain or branched C₄-C₇-chain, where the
chain can additionally be interrupted by O, S or NR(6),

R(6) is H or methyl;

or

R(4) and R(5)

together with the nitrogen atom to which they are bonded, are

a dihydroindole, tetrahydroquinoline or tetrahydroisoquinoline

system;

n is zero, 1 or 2;

and their pharmaceutically tolerable salts;

g) isoquinolines of the formula I

in which:

R(1) is hydrogen, alkyl, cycloalkyl, arylalkyl, alkenyl, substituted

aminoalkyl or an aryl or heteroaryl ring;

where the rings are unsubstituted or substituted by 1 - 3
groups selected from the group consisting of halogen, nitro, amino, mono(lower alkyl)amino, di(lower alkyl)amino, lower alkyl, lower alkoxy, benzyloxy, phenoxy, hydroxyl, trifluoromethyl,

5  \( R(2) \) is hydrogen, halogen, alkyl or aryl;
which is unsubstituted or substituted by 1 - 3 groups selected from the group consisting of halogen, nitro, amino, mono(lower alkyl)amino, di(lower alkyl)amino, lower alkyl, lower alkoxy, benzyloxy, phenoxy, hydroxyl,

10  \( G \) is

\[
\begin{align*}
\text{R(3)} & \\
\text{R(4)} & \\
\text{R(5)} & \\
\text{R(6)} & \\
\end{align*}
\]

15  \( X(2), X(3) \) and \( X(4) \)

independently of one another are hydrogen, halogen, nitro, amino, alkyl, sulfonamide, mono(lower alkyl)amino, di(lower alkyl)amino, lower alkyl, benzyloxy, hydroxyl;

20  \( X(1) \) is hydrogen, oxygen, sulfur or NR(7);

\( R(7) \) is hydrogen, alkyl, cycloalkyl, arylalkyl, alkenyl, substituted aminoalkyl or an aryl or a heteroaryl ring;

which rings are unsubstituted or substituted by 1 - 3 groups selected from the group consisting of halogen, nitro, amino, mono(lower alkyl)amino, di(lower alkyl)amino, lower alkyl, lower alkoxy, benzyloxy, phenoxy, hydroxyl and trifluoromethyl;

in which substituents each alkyl chain or alkenyl chain can be interrupted by oxygen, sulfur or NR(8);

25  \( R(8) \) is hydrogen, alkyl, cycloalkyl, arylalkyl, alkenyl, substituted aminoalkyl or an aryl or heteroaryl ring,

which rings are unsubstituted or substituted by
1 - 3 groups selected from the group consisting of halogen, nitro, amino, mono(lower alkyl)amino, di(lower alkyl)amino, lower alkyl, lower alkoxy, benzyloxy, phenoxy, hydroxyl and trifluoromethyl;

and their pharmaceutically acceptable salts;

h) compounds of the formula I

\[
\begin{align*}
\text{R(1)} & \quad \text{is hydrogen, F, Cl, Br, I, -NO}_2, -\text{C}=\text{N}, -\text{CF}_3, \text{R(4)}-\text{SO}_m \text{ or } R(5)R(6)\text{N-SO}_m^2; \\
m & \quad \text{is zero, 1 or 2}; \\
\text{R(4)} \text{ and } \text{R(5)} \\
& \quad \text{are } (\text{C}_1-\text{C}_8)-\text{alkyl}, (\text{C}_3-\text{C}_6)-\text{alkenyl}, -\text{C}_n\text{H}_{2n}-\text{R(7)} \text{ or } \text{CF}_3; \\
n & \quad \text{is zero, 1, 2, 3 or 4}; \\
\text{R(7)} & \quad \text{is } (\text{C}_3-\text{C}_7)-\text{cycloalkyl} \text{ or phenyl,}
\end{align*}
\]

which is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(8)R(9); R(8) and R(9)

\[
\begin{align*}
& \quad \text{are } \text{H} \text{ or } \text{C}_1-\text{C}_4-\text{alkyl}; \\
& \quad \text{or} \\
\text{R(5)} & \quad \text{is } \text{H}; \\
\text{R(6)} & \quad \text{is } \text{H} \text{ or } (\text{C}_1-\text{C}_4)-\text{alkyl};
\end{align*}
\]
or

R(5) and R(6)

together are 4 or 5 methylene groups, of which one CH$_2$
group can be replaced by oxygen, S, NH, N-CH$_3$ or N-benzyl;

5  R(2) is -SR(10), -OR(10), -NHR(10), -NR(10)R(11), -CHR(10)R(12),
    -[CR(12)R(13)OR(13')]$_n$ -{C-[CH$_2$-OR(13')]$_m$R(12)R(13)} or
    -[CR(18)R(17)]$_p$-(CO)-[CR(19)R(20)]$_q$-R(14);
R(10), R(11)
    identically or differently

10  are -[CHR(16)]$_r$-(CH$_2$)$_p$-(CHOH)$_q$-(CH$_2$)$_r$-(CHOH)$_s$-R(21) or
    -(CH$_2$)$_p$-O-(CH$_2$-CH$_2$O)$_q$-R(21),
R(21) is hydrogen, methyl,
p, q, r identically or differently
    are zero, 1, 2, 3 or 4;

15  s is zero or 1;
    t is 1, 2, 3 or 4;
R(12) and R(13)
    identically or differently are hydrogen, (C$_1$-C$_6$)-alkyl or,
together with the carbon atom carrying them, are a

20  (C$_3$-C$_6$)-cycloalkyl,
R(13') is hydrogen or (C$_1$-C$_4$)-alkyl;
R(14) is H, (C$_1$-C$_6$)-alkyl, (C$_3$-C$_6$)-cycloalkyl or -C$_3$H$_{2a}$-R(15);
a is zero, 1, 2, 3 or 4;
R(15) is phenyl,

25  which is unsubstituted or substituted by 1 - 3
substituents selected from the group consisting
of F, Cl, CF$_3$, methyl, methoxy and NR(8)R(9);
R(8) and R(9)
    are H or (C$_1$-C$_4$)-alkyl;

30  or
R(15) is (C$_1$-C$_6$)-heteroaryl,
    which is unsubstituted or substituted as phenyl,
or
R(15) is \((C_1-C_6)\)-alkyl,
which is unsubstituted or substituted by 1 - 3
OH;

\[ \begin{align*}
R(16), R(17), R(18), R(19) \text{ and } R(20) \\
\text{are hydrogen or } (C_1-C_3)\)-alkyl;
\end{align*} \]

R(3) is defined as R(1),
or
R(3) is \((C_1-C_6)\)-alkyl or \(-X-R(22)\);

\[ \begin{align*}
X & \text{ is oxygen, } S \text{ or } NR(16); \\
R(16) & \text{ is } H \text{ or } (C_1-C_3)\)-alkyl; \\
or \\
R(22) \text{ and } R(16) & \text{ together are 4 or 5 methylene groups, of which one}
\end{align*} \]

CH\(_2\) group can be replaced by oxygen, S, NH, N-CH\(_3\)
or N-benzyl;

R(22) is defined as R(14);
and their pharmaceutically tolerable salts;

\[ \text{i) benzoylguanidines of the formula I} \]

\[ \begin{align*}
\text{in which:}
R(1) & \text{ is hydrogen, } F, Cl, Br, I, -NO\textsubscript{2}, -C=\text{N}, R(16)-C_pH_{2p-O_q}, R(4)-SO_m \text{ or } R(5)R(6)N-SO_2^-;
\end{align*} \]

\[ \begin{align*}
m & \text{ is zero, 1 or 2;} \\
p & \text{ is zero or 1;} \\
q & \text{ is zero, 1, 2 or 3;} \\\n\end{align*} \]
R(16) is C_{r}F_{2r+1};

r \text{ is } 1, 2 \text{ or } 3;

R(4) \text{ and } R(5)

\text{are } (C_{1}-C_{6})\text{-alkyl, } (C_{3}-C_{8})\text{-alkenyl, } -C_{n}H_{2n}-R(7) \text{ or } CF_{3};

n \text{ is zero, } 1, 2, 3 \text{ or } 4;

R(7) \text{ is } (C_{5}-C_{7})\text{-cycloalkyl or phenyl,}

\text{which is not substituted or is substituted by } 1 \text{ - } 3
\text{substituents selected from the group consisting of } F, \text{ Cl, } CF_{3}, \text{ methyl, methoxy and } NR(8)R(9);

R(8) \text{ and } R(9)

\text{are } H \text{ or } C_{1}-C_{4}\text{-alkyl;}

or

R(5) \text{ is } H;

R(6) \text{ is } H \text{ or } (C_{1}-C_{4})\text{-alkyl;}

or

R(5) \text{ and } R(6)

together are 4 or 5 methylene groups, of which one CH_{2}
group can be replaced by oxygen, S, NH, N-CH_{3} \text{ or N-benzyl,}

R(2) \text{ is } (C_{1}-C_{6})\text{-heteroaryl,}

\text{which is linked via C or N and which is unsubstituted or}
\text{substituted by } 1 \text{ - } 3 \text{substituents selected from the group}
\text{consisting of } F, \text{ Cl, } CF_{3}, \text{ CH}_{3}, \text{ methoxy, hydroxyl, amino,}
methylamino and dimethylamino; 

or

R(2) \text{ is } -SR(10), -OR(10), -NR(10)R(11), -CR(10)R(11)R(12);

R(10) \text{ is } -C_{a}H_{2a-}(C_{1}-C_{9})\text{-heteroaryl,}

\text{which is unsubstituted or substituted by } 1 \text{ - } 3
\text{substituents selected from the group consisting of } F,
\text{ Cl, } CF_{3}, \text{ CH}_{3}, \text{ methoxy, hydroxyl, amino, methylamino}
\text{and dimethylamino;}

a \text{ is zero, } 1 \text{ or } 2;

R(11) \text{ and } R(12)
independently of one another are defined as $R(10)$ or are hydrogen or $(C_1-C_4)$-alkyl;

$R(3)$ is defined as $R(1)$, or is $(C_1-C_6)$-alkyl or $-X-R(13)$;

$X$ is oxygen, S, or NR(14);

$R(14)$ is H or $(C_1-C_6)$-alkyl;

$R(13)$ is H, $(C_1-C_6)$-alkyl, $(C_3-C_6)$-cycloalkyl or $-C_6H_{2n}$-$R(15)$;

$b$ is zero, 1, 2, 3 or 4;

or

$R(13)$ and $R(14)$ together are 4 or 5 methylene groups, of which one $CH_2$ group can be replaced by oxygen, S, NH, N-CH$_3$ or N-benzyl;

$R(15)$ is phenyl, which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, $CF_3$, methyl, methoxy and NR(8)R(9);

$R(8)$ and $R(9)$ are H or $(C_1-C_6)$-alkyl;

and their pharmaceutically tolerable salts;

k) benzoylguanidines of the formula I

\[
\begin{align*}
\text{I} & \\
R(1) & \\
R(2) & \\
R(3) & \\
R(4) & \\
R(5) & \\
R(6) & \\
\end{align*}
\]

in which:

one of the substituents $R(1)$, $R(2)$, $R(3)$ or $R(4)$ is an amino group $\text{N}^\text{\textbullet}^\text{\textbullet}$

$C_nH_{2n}$-$R(6)$
R(5) is hydrogen or C(1-6)-alkyl;
n is zero, 1, 2, 3 or 4;
R(6) is H or C(1-4)-alkyl;
in which one CH₂ group can be replaced by 1 sulfur atom or a group

5
NR(7);
R(7) is hydrogen, methyl or ethyl;
or
R(6) is C(3-9)-cycloalkyl or phenyl,
which is unsubstituted or carries 1, 2 or 3 substituents

10
selected from the group consisting of F, Cl, Br, methyl,
methoxy, -NR(8)R(9);
R(8) and R(9)
are H, methyl or ethyl;
or
R(5) and R(6)
together with the nitrogen atom are a 5-, 6- or 7-membered
ring, in which 1 carbon atom can be replaced by oxygen, S or
NR(10);
R(10) is H, C(1-3)-alkyl or benzyl;

20
and the other substituents R(1), R(2), R(3), R(4) in each case are:
hydrogen, F, Cl, Br, I, CN, CF₃, NO₂, CF₃-O-, CₘF₂ₘ₊₁-CH₂-O- or
R(11)-CₙH₂ₙ-Xₓp⁻;
m is 1, 2 or 3;
q is zero, 1, 2, 3 or 4;
p is zero or 1;
X is oxygen or NR(12);
R(12) is H or C(1-3)-alkyl;
R(11) is hydrogen, C(1-6)-alkyl, C(3-9)-cycloalkyl or phenyl,
which is unsubstituted or substituted by 1, 2 or 3

30
substituents selected from the group consisting of F,
Cl, CH₃, CH₃-O- and NR(13)R(14);
R(13), R(14)
are H, methyl or ethyl;
and their pharmaceutically tolerable salts;

l) benzoylguanidines of the formula I

\[
\begin{align*}
&\text{R(1)} = \text{R(4)R(5)N-C(X)-;} \\
&\text{R(2)} = \text{H, F, Cl, Br, I, (C}_1\text{-C}_8\text{-alkyl, 1-alkenyl or 1-alkynyl, (C}_3\text{-C}_8\text{-cycloalkyl, (C}_3\text{-C}_8\text{-cycloalkyl-(C}_1\text{-C}_4\text{-alkyl), phenyl, (C}_6\text{H}_5-(C}_1\text{-C}_4\text{-alkyl, naphthyl, biphenyl, 1,1-diphenyl-(C}_1\text{-C}_4\text{-alkyl, cyclopentadienyl, pyridyl, thiopyridyl, pyrrolyl, furanyl, thienyl, thiazolyl, oxazolyl, indenyl, quinolyl, indolyl, benzofuranyl, benzothienyl, benzothiazolyl, benzoxazolyl or -W-R(8);} \\
&W = \text{oxygen, S or NR(9)}; \\
&R(8) = \text{H, (C}_1\text{-C}_8\text{-alkyl, (C}_5\text{-C}_7\text{-cycloalkyl, cyclohexylmethyl};}
\end{align*}
\]

in which

\[
\begin{align*}
&\text{R(1)} = \text{R(4)R(5)N-C(X)-;} \\
&\text{R(2)} = \text{H, F, Cl, Br, I, (C}_1\text{-C}_8\text{-alkyl, 1-alkenyl or 1-alkynyl, (C}_3\text{-C}_8\text{-cycloalkyl, (C}_3\text{-C}_8\text{-cycloalkyl-(C}_1\text{-C}_4\text{-alkyl), phenyl, (C}_6\text{H}_5-(C}_1\text{-C}_4\text{-alkyl, naphthyl, biphenyl, 1,1-diphenyl-(C}_1\text{-C}_4\text{-alkyl, cyclopentadienyl, pyridyl, thiopyridyl, pyrrolyl, furanyl, thienyl, thiazolyl, oxazolyl, indenyl, quinolyl, indolyl, benzofuranyl, benzothienyl, benzothiazolyl, benzoxazolyl or -W-R(8);} \\
&W = \text{oxygen, S or NR(9)}; \\
&R(8) = \text{H, (C}_1\text{-C}_8\text{-alkyl, (C}_5\text{-C}_7\text{-cycloalkyl, cyclohexylmethyl};}
\end{align*}
\]

1) benzoylguanidines of the formula I

\[
\begin{align*}
&\text{R(1)} = \text{H, methyl or ethyl;} \\
&\text{and their pharmaceutically tolerable salts;} \\
&\text{in which} \\
&\text{R(1)} = \text{R(4)R(5)N-C(X)-;} \\
&\text{X = oxygen, S or N-R(6);} \\
&\text{R(4) and R(5)} \\
&\text{identically or differently, are H, (C}_1\text{-C}_8\text{-alkyl, (C}_3\text{-C}_8\text{-alkenyl or -C}_n\text{H}_{2n}\text{-R(7);} \\
&\text{n is zero, 1, 2, 3 or 4;} \\
&\text{R(7) = (C}_5\text{-C}_7\text{-cycloalkyl or phenyl,} \\
&\text{which is unsubstituted or substituted by 1 - 3} \\
&\text{substituents selected from the group consisting} \\
&\text{of F, Cl, CF}_3\text{, methoxy and (C}_1\text{-C}_4\text{-alkyl;} \\
&\text{or} \\
&\text{R(4) and R(5)} \\
&\text{together are 4 or 5 methylene groups, of which one CH}_2\text{ group can be replaced by oxygen, S, NH, N-CH}_3\text{ or N-benzyl;} \\
&\text{R(6) is defined as R(4) or is amidine;} \\
&\text{R(2)} = \text{H, F, Cl, Br, I, (C}_1\text{-C}_8\text{-alkyl, 1-alkenyl or 1-alkynyl,} \\
&(\text{C}_3\text{-C}_8\text{-cycloalkyl, (C}_3\text{-C}_8\text{-cycloalkyl-(C}_1\text{-C}_4\text{-alkyl, phenyl,} \\
&\text{C}_6\text{H}_5-(\text{C}_1\text{-C}_4\text{-alkyl, naphthyl, biphenyl, 1,1-diphenyl-(C}_1\text{-C}_4\text{-alkyl,} \\
&\text{cyclopentadienyl, pyridyl, thiopyridyl, pyrrolyl, furanyl, thienyl,} \\
&\text{thiazolyl, oxazolyl, indenyl, quinolyl, indolyl, benzofuranyl,} \\
&\text{benzothienyl, benzothiazolyl, benzoxazolyl or -W-R(8);} \\
&W = \text{oxygen, S or NR(9)}; \\
&R(8) = \text{H, (C}_1\text{-C}_8\text{-alkyl, (C}_5\text{-C}_7\text{-cycloalkyl, cyclohexylmethyl};}
\end{align*}
\]
cyclopentylmethyl, -(CH₂)mC₆F₂p+₁ or -C₉H₂₃-R(10);
m is zero or 1;
p is 1, 2 or 3;
q is zero, 1, 2, 3 or 4;
R(10) is phenyl, which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(11)R(12);
R(11) and R(12) are H or (C₁-C₄)-alkyl;

R(9) is H or (C₁-C₃)-alkyl;
or
R(8) and R(9) together are 4 or 5 methylene groups, of which one CH₂ group can be replaced by oxygen, S, NH, N-CH₃ or N-benzyl;
R(3) is H, F, Cl, Br, I, (C₁-C₆)-alkyl or -W-R(8) as defined for R(2), and their pharmaceutically acceptable salts;

m) benzoylguanidines of the formula I

in which:

R(1), R(2), R(3) are hydrogen, F, Cl, Br, I or (C₁-C₁₂)-alkyl;
one of the substituents R(1), R(2) or R(3)
is \(N_3, \text{CN, OH or (C}_1^{-10}\text{-alkyloxy, if at least one of the remaining}
\text{substituents R(1), R(2) or R(3) is a sufficiently lipophilic alkyl radical}
\text{having 3 to 12 carbon atoms;}}

\text{or}

5 \text{ one of the substituents R(1), R(2) and R(3) is R(4)-C}_n\text{H}_{2n}\text{-O}_m\text{;}
\text{m is zero or 1;}
\text{n is zero, 1, 2 or 3;}
\text{R(4) is C}_p\text{F}_{2p+1};
\text{p is 1, 2 or 3, if n is zero or 1;}
\text{or}
\text{R(4) is (C}_3^{-12}\text{-cycloalkyl, phenyl, pyridyl, quinolyl or isoquinolyl,}
\text{where the aromatic and heteroaromatic ring systems are}
\text{unsubstituted or substituted by a substituent selected from}
\text{the group consisting of F, CI, CF}_3\text{, methyl, methoxy and}
\text{NR(5)R(6);}
\text{R(5) and R(6) are hydrogen or (C}_1^{-6}\text{-alkyl;}
\text{or one of the substituents R(1), R(2) and R(3) is -C=CR(5) or -C[R(6)] = CR(5);}
\text{R(5) is phenyl,}
\text{which is unsubstituted or substituted by 1 - 3}
\text{substituents selected from the group consisting of F,}
\text{Cl, CF}_3\text{, methyl, methoxy, hydroxyl, amino,}
\text{methylamino and dimethylamino,}
\text{(C}_1^{-9}\text{-heteroaryl,}
\text{which is unsubstituted or substituted as phenyl,}
\text{or}
\text{R(5) is (C}_1^{-6}\text{-alkyl,}
\text{which is unsubstituted or substituted by 1 - 3 OH;}
\text{or}
\text{R(5) is (C}_3^{-6}\text{-cycloalkyl,}
R(6) is hydrogen or methyl;
and their pharmacologically acceptable salts;

o) benzoylguanidines of the formula I

\[
\begin{align*}
\text{R(1)} & \quad \text{R(2)} \\
\text{R(3)} & \quad \text{R(4)} \\
\text{R(5)} & \quad \text{R(6)} \\
\text{R(7)} & \quad \text{R(8)} \\
\end{align*}
\]

in which:

\[ 
\begin{align*}
\text{R(1)} & \quad \text{is hydrogen, F, Cl, Br, I, } -\text{NO}_2, -\text{C}≡\text{N}, X_\alpha-(\text{CH}_2)_\beta-(\text{CF}_2)_\gamma-\text{CF}_3, \\
\text{R(5)} & \quad \text{SO}_m, \text{R(6)}-\text{CO- or } \text{R(6)}\text{R(7)}-\text{SO}_2, \text{where} \\
\text{X} & \quad \text{is oxygen, S or } \text{NR(14)}; \\
\text{m} & \quad \text{is zero, 1 or 2}; \\
\text{o} & \quad \text{is zero or 1}; \\
\text{p} & \quad \text{is zero, 1 or 2}; \\
\text{q} & \quad \text{is zero, 1, 2, 3, 4, 5 or 6}; \\
\text{R(5) and R(6)} & \quad \text{are } (\text{C}_1-\text{C}_8)-\text{alkyl, } (\text{C}_3-\text{C}_6)-\text{alkenyl, } -\text{C}_n\text{H}_{2n+1}-\text{R}(8) \text{ or } \text{CF}_3; \\
\text{n} & \quad \text{is zero, 1, 2, 3 or 4}; \\
\text{R(8)} & \quad \text{is } (\text{C}_3-\text{C}_7)-\text{cycloalkyl or phenyl}, \\
\text{which is not substituted or is substituted by 1 - 3} \\
\text{substituents selected from the group consisting} \\
\text{of F, Cl, CF}_3, \text{methyl, methoxy and } \text{NR(9)R(10)}; \\
\text{R(9) and R(10)} & \quad \text{are H or } \text{C}_1-\text{C}_4-\text{alkyl}; \\
or & \quad \\
\text{R(6)} & \quad \text{is H;} \\
\text{R(7)} & \quad \text{is H or } (\text{C}_1-\text{C}_4)-\text{alkyl};
\end{align*}
\]
R(6) and R(7) together are 4 or 5 methylene groups, of which one CH$_2$ group can be replaced by oxygen, S, NH, N-CH$_3$ or N-benzyl;

$$R(2) \text{ is } -Y-(C)_{h}-(CHOH)_{i}-(CH_{2})_{j}-(CHOH)_{k}-R(11)$$

or

$$-Y-(C)_{h}-(CHOH)_{i}-(CH_{2})_{j}-(CHOH)_{k}-R(11)$$

or

$$-Y-(C)_{h}-(CHOH)_{i}-(CH_{2})_{j}-(CHOH)_{k}-R(11)$$

Y is oxygen, -S- or -NR(12)-;

R(11) and R(12) are hydrogen or (C$_1$-C$_3$)-alkyl;

h is zero or 1;

i, j and k independently are zero, 1, 2, 3 or 4;

but where h, i and k are not simultaneously zero, R(3) is defined as R(1), or is (C$_1$-C$_6$)-alkyl or -X-R(13);

X is oxygen, S or NR(14);

R(14) is H or (C$_1$-C$_3$)-alkyl;

R(13) is H, (C$_1$-C$_6$)-alkyl, (C$_3$-C$_6$)-cycloalkyl or -C$_6$H$_{2b}$-R(15);

b is zero, 1, 2, 3 or 4;

or

R(13) and R(14) together are 4 or 5 methylene groups, where one CH$_2$ group can be replaced by oxygen, S, NH, N-CH$_3$ or
N-benzyl;
R(15) is phenyl,
which is unsubstituted or substituted by 1 - 3
substituents selected from the group consisting
of F, Cl, CF₃, methyl, methoxy and NR(9)R(10);
R(9) and R(10)
are H or (C₁-C₄)-alkyl;
R(4) is hydrogen, -OR(16) or -NR(16)R(17);
R(16) and R(17)
independently are hydrogen or (C₁-C₃)-alkyl;
and their pharmaceutically tolerable salts;
p) benzoylguanidines of the formula I

\[
\begin{align*}
R(1) & \quad N \quad R(4) \\
R(2) & \quad R(5) \\
R(3) & \quad R(4) \\
& \quad NH₂ \\
& \quad NH₂ \\
\end{align*}
\]

in which:
R(1) is R(6)-CO or R(7)R(8)N-CO;
R(6) is (C₁-C₈)-alkyl, (C₁-C₈)-perfluoroalkyl, (C₃-C₈)-alkenyl or
-CₙH₂ₙ-R(9);
n is zero, 1, 2, 3 or 4;
R(9) is (C₃-C₈)-cycloalkyl, phenyl, biphenyl or naphthyl,
where the aromatics are not substituted or are
substituted by 1 - 3 substituents selected from
the group consisting of F, Cl, CF₃, methyl,
methoxy and NR(10)R(11);
R(10) and R(11)
are H, (C₁-C₄)-alkyl or (C₁-C₄)-perfluoro-
alkyl;
R(7) is H, (C₁-C₈)-alkyl, (C₁-C₈)-perfluoroalkyl, (C₃-C₈)-alkenyl or
-CₙH₂ₙ-R(12);
n is zero, 1, 2, 3 or 4;
R(12) is (C₃-C₈)-cycloalkyl, phenyl, biphenyl or naphthyl, where the aromatics are not substituted or are substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(13)R(14);
R(13) and R(14) are H, (C₁-C₄)-alkyl or (C₁-C₄)-perfluoroalkyl;
R(8) is H, (C₁-C₄)-alkyl or (C₁-C₄)-perfluoroalkyl;
or R(7) and R(8) together are 4 or 5 methylene groups, of which one CH₂ group can be replaced by oxygen, S, NH, N-CH₃ or N-benzyl;
R(2) is defined as R(1), or is H, F, Cl, Br, I, CN, NO₂, (C₁-C₈)-alkyl, (C₁-C₈)-perfluoroalkyl, (C₃-C₈)-alkenyl or -CₙH₂ₙR(15);
n is zero 1, 2, 3, 4;
R(15) is (C₃-C₈)-cycloalkyl, phenyl, biphenyl or naphthyl, where the aromatics are not substituted or are substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(16)R(17);
R(16) and R(17) are H, (C₁-C₄)-alkyl or (C₁-C₄)-perfluoroalkyl;
or R(2) is (C₁-C₈)-heteroaryl, which is linked via C or N and which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino and dimethylamino;
or

R(2) is SR(18), -OR(18), -NR(18)R(19), -CR(18)R(19)R(20);

R(18) is -C₅Hₓₐ-(C₁-C₉)-heteroaryl,

which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino and dimethylamino;

a is zero, 1 or 2;

R(19) and R(20) independently of one another are defined as R(18) or are hydrogen, (C₁-C₄)-alkyl or (C₁-C₄)-perfluoroalkyl;

or

R(2) is R(21)-SOₘ or R(22)R(23)N-SO₂⁻;

m is 1 or 2;

R(21) is (C₁-C₆)-alkyl, (C₁-C₆)-perfluoroalkyl, (C₃-C₆)-alkenyl, -CₙH₂n⁻

R(24),

n is zero, 1, 2, 3 or 4;

R(24) is (C₃-C₆)-cycloalkyl, phenyl, biphenylyl or naphthyl,

where the aromatics are not substituted or are substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(27)R(28);

R(27) and R(28) are H, (C₁-C₄)-alkyl or (C₁-C₄)-perfluoroalkyl;

R(22) is H, (C₁-C₆)-alkyl, (C₁-C₆)-perfluoroalkyl, (C₂-C₆)-alkenyl, -CₙH₂n⁻R(29);

n is zero, 1, 2, 3 or 4;

R(29) is (C₃-C₆)-cycloalkyl, phenyl, biphenylyl or naphthyl,

where the aromatics are not substituted or are substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl,
methoxy and NR(30)R(31); 
R(30) and R(31) 
are H, (C<sub>1</sub>-C<sub>4</sub>)-alkyl or (C<sub>1</sub>-C<sub>4</sub>)-perfluoroalkyl; 

R(23) is H, (C<sub>1</sub>-C<sub>4</sub>)-alkyl or (C<sub>1</sub>-C<sub>4</sub>)-perfluoroalkyl; 
or 
R(22) and R(23) together are 4 or 5 methylene groups, of which one CH<sub>2</sub> group can be replaced by oxygen, S, NH, N-CH<sub>3</sub> or N-benzyl; 
or 
R(2) is R(33)X-; 
X is oxygen, S, NR(34), (D=O)A-, NR(34)C=MN(*)R(35)-; 
M is oxygen or S; 
A is oxygen or NR(34); 
D is C or SO; 
R(33) is (C<sub>1</sub>-C<sub>6</sub>)-alkyl, (C<sub>3</sub>-C<sub>6</sub>)-alkenyl, (CH<sub>2</sub>)<sub>b</sub>C<sub>d</sub>F<sub>2d+1</sub>, -C<sub>n</sub>H<sub>2n</sub>-R(36), 
b is zero or 1; 
d is 1, 2, 3, 4, 5, 6 or 7; 
n is zero, 1, 2, 3 or 4; 
R(36) is (C<sub>3</sub>-C<sub>8</sub>)-cycloalkyl, phenyl, biphenylyl or naphthyl, where the aromatics are not substituted or are substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF<sub>3</sub>, methyl, methoxy and NR(37)R(38); 
R(37) and R(38) are H, (C<sub>1</sub>-C<sub>4</sub>)-alkyl or (C<sub>1</sub>-C<sub>4</sub>)-perfluoroalkyl; 
R(34) is H, (C<sub>1</sub>-C<sub>4</sub>)-alkyl or (C<sub>1</sub>-C<sub>4</sub>)-perfluoroalkyl; 
R(35) is defined as R(33); 
or 
R(33) and R(34) together are 4 or 5 methylene groups, of which one
CH$_2$ group can be replaced by oxygen, S, NH, N-CH$_3$

or N-benzyl;

where A and N$^{(4)}$ are bonded to the phenyl nucleus of the
benzoylguanidine parent structure;

R(2) is -SR(40), -OR(40), -NHR(40), -NR(40)R(41), -CHR(40)R(42),

-C[R(42)R(43)OH], -C=CR(45), -CR(46)=CHR(45),

-[CR(47)R(48)]$_v$-(CO)-[CR49]R(50)$_v$-R(44);

R(40), R(41)

identically or differently are -(CH$_2$)$_p$-(CHOH)$_q$-(CH$_2$)$_r$-(CHOH)$_t$

R(51) or -(CH$_2$)$_p$-O-(CH$_2$-CH$_2$O)$_q$-R(51);

R(51) is hydrogen or methyl;

u is 1, 2, 3 or 4;

v is zero, 1, 2, 3 or 4;

p, q, r

identically or differently are zero, 1, 2, 3 or 4;

R(42) and R(43)

identically or differently are hydrogen or (C$_1$-C$_6$)-alkyl;

R(42) and R(43)

together with the carbon atom carrying them form a (C$_3$-C$_8$)-cycloalkyl;

R(44) is H, (C$_1$-C$_6$)-alkyl, (C$_3$-C$_8$)-cycloalkyl or -C$_6$H$_{2e}$-R(45);

e is zero, 1, 2, 3 or 4;

R(45) is phenyl,

which is unsubstituted or substituted by 1 - 3

substituents from the group consisting of F, Cl, CF$_3$,
methyl, methoxy and NR(52)R(53) where

R(52) and R(53) are H or (C$_1$-C$_4$)-alkyl, or

R(45) is (C$_1$-C$_9$)-heteroaryl,

which is unsubstituted or substituted as phenyl;
or

R(45) is (C₁-C₆)-alkyl,

which is unsubstituted or substituted by 1 - 3 OH;

R(46), R(47), R(48), R(49) and R(50)

are hydrogen or methyl;

or

R(2) is R(55)-NH-SO₂⁻;

R(55) is R(56)R(57)N-(C=Y)-;

Y is oxygen, S or N-R(58);

R(56) and R(57)

identically or differently are H, (C₁-C₆)-alkyl, (C₃-C₆)-

alkenyl or -C₇H₂fR(59);

f is zero, 1, 2, 3 or 4;

R(59) is (C₅-C₇)-cycloalkyl or phenyl,

which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methoxy and

(C₁-C₄)-alkyl;

or

R(56) and R(57)

together are 4 or 5 methylene groups, of which one CH₂ group can be replaced by oxygen, S, NH, N-CH₃

or N-benzyl;

R(58) is defined as R(56) or is amidine;

R(3), R(4) and R(5)

independently of one another are defined as R(1) or R(2);

and their pharmaceutically tolerable salts;

q) benzoylguanidines of the formula I
in which:

10  \( R(1) \) is hydrogen, F, Cl, Br, I, -NO₂, -C≡N, -X₅₋₋(CH₂)ₖ₋₋(CF₂)ₖ₋₋CF₃,
    \( R(5) \)-SO₃⁻, \( R(6) \)-CO⁻, \( R(6) \)\( R(7) \)-N-\( CO₋ \) or \( R(6) \)\( R(7) \)-N-SO₂⁻;
    \( X \) is oxygen, -S- or NR(14);
    \( m \) is zero, 1 or 2;
    \( o \) is zero or 1;

15  \( p \) is zero, 1 or 2;
    \( q \) is zero, 1, 2, 3, 4, 5 or 6;

20  \( R(5) \) and \( R(6) \)
    are (C₁-C₈)-alkyl, (C₃-C₆)-alkenyl, -CₙH₂₋₋R(8) or CF₃;
    \( n \) is zero, 1, 2, 3 or 4;

25  \( R(8) \) is (C₃-C₇)-cycloalkyl, phenyl,
    which is not substituted or is substituted by 1 to
    3 substituents selected from the group
    consisting of F, Cl, CF₃, methyl, methoxy and
    NR(9)R(10);

25  \( R(9) \) and \( R(10) \)
    are H or (C₁-C₄)-alkyl;
    or

30  \( R(6) \) is hydrogen;
    \( R(7) \) is hydrogen or (C₁-C₄)-alkyl;
    or

30  \( R(6) \) and \( R(7) \)
    together are 4 or 5 methylene groups, of which one CH₂
group can be replaced by oxygen, S, NH, N-CH₃ or N-benzyl;

R(2) is

\[
\begin{align*}
- & Y - \text{R}(11) \quad \text{or} \quad - Y - \text{R}(11) \\
\end{align*}
\]

R(11) is \((C₁-C₉)\)-heteroaryl,
which is linked via C or N and which is unsubstituted
or substituted by 1 to 3 substituents selected from the
group consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl,
amino, methylamino, dimethylamino and benzyl;

\(Y\) is oxygen, S- or NR(12);
R(12) is H or \((C₁-C₄)\)-alkyl;

10 R(3) is defined as R(1); or
R(3) is \((C₁-C₉)\)-alkyl or -X-R(13);

\(X\) is oxygen, S- or NR(14);
R(14) is H or \((C₁-C₉)\)-alkyl;

15 R(13) is H, \((C₁-C₉)\)-alkyl, \((C₃-C₉)\)-cycloalkyl or \(-C₆H₂b\)-R(15);
b is zero, 1, 2, 3 or 4;
or
R(13) and R(14)
together are 4 or 5 methylene groups, of which one
20 CH₂ group can be replaced by oxygen, S, NH, N-CH₃
or N-benzyl;
R(15) is phenyl,
which is unsubstituted or substituted by 1 - 3
substituents selected from the group consisting
25 of F, Cl, CF₃, methyl, methoxy and NR(9)R(10);
R(9) and R(10)
are H or \((C₁-C₄)\)-alkyl;

R(4) is hydrogen, -OR(16), -NR(16)R(17) or \(C_iF_{2n+1}\);
R(16) and R(17)
independently are hydrogen or (C₁-C₆)-alkyl;

r is 1, 2, 3 or 4;

and their pharmaceutically tolerable salts;

5 r) benzo-fused 5-membered ring heterocycles of the formula I

\[
\begin{align*}
\text{R(1) A} & \quad \text{B} \\
\text{R(5)} & \quad \text{Y} \\
\text{R(4)} & \\
\end{align*}
\]

in which:

\begin{align*}
X & \quad \text{is N or CR(6);} \\
Y & \quad \text{is oxygen, S or NR(7);} \\
A, B & \quad \text{together are a bond or} \\
& \quad \text{or} \\
& \quad \text{A, B are both hydrogen, if X is simultaneously CR(6) and Y is NR(7);} \\
& \quad \text{one of the substituents R(1) to R(6) is a -CO-N=C(NH₂₂ group;} \\
& \quad \text{the other substituents R(1) to R(6) in each case} \\
& \quad \text{are hydrogen, F, Cl, Br, I or (C₁-C₆)-alkyl;} \\
& \quad \text{up to two of the other substituents R(1) to R(6)} \\
& \quad \text{are CN, NO₂, N₃, (C₁-C₄)-alkyloxy or CF₃;} \\
& \quad \text{up to one of the other substituents} \\
& \quad \text{is R(8)-CₙH₂ₙ-Z;} \\
& \quad \text{n is zero to 10;} \\
& \quad \text{where the alkylene chain -CₙH₂ₙ- is straight-chain or branched} \\
& \quad \text{and where one carbon atom can be replaced by an oxygen or} \\
& \quad \text{sulfur atom or by a nitrogen atom;} \\
& \quad \text{R(8) is hydrogen, (C₂-C₆)-alkenyl or (C₃-C₁₀)-cycloalkyl,} \\
& \quad \text{which is unsubstituted or substituted by 1 to 4 methyl} \\
& \quad \text{groups or an OH group, or can contain an ethylene}
\end{align*}
group -CH=CH-, and in which one methylene group can be replaced by an oxygen or sulfur atom or by a nitrogen atom;

or

5  R(8) is phenyl,

which is unsubstituted or substituted by 1 to 3 substituents selected from the group consisting of F, Cl, Br, I, CF₃, CH₂-S(O)ₙ-, or R(9)-Wₙ;

s is zero, 1 or 2;

10  R(9) is H, methyl, ethyl, W is oxygen or NR(10);

R(10) is H or methyl;

y is zero or 1;

or

15  R(8) is CₙF₂m₊₁;

m is 1 to 3;

or

R(8) is 1- or 2-naphthyl, pyridyl, quinolyl or isoquinolyl;

Z is -CO-, -CH₂- or -[CR(11)(OH)]ₙ;

q is 1, 2 or 3;

20  R(11) is H or methyl;

or

Z is oxygen or -NR(12)-;

R(12) is H or methyl;

25  or

Z is -S(O)ₙ-;

s is zero, 1 or 2;

or

Z is -SO₂-NR(13)-;

30  R(13) is H or (C₁-C₄)-alkyl;

R(7) is hydrogen, (C₁-C₁₀)-alkyl, (C₂-C₁₀)-alkenyl or R(8)-CₙH₂ₙ-;

and their pharmaceutically tolerable salts;
s) benzoylguanidines of the formula I

\[ \text{Formula I} \]

in which:

R(1), R(3) or R(4)

is \(-\text{NR}(6) \text{C=X} \text{NR}(7)\text{R}(8);\)

\(X\) is oxygen or S;

R(6) is hydrogen, \((\text{C}_1-\text{C}_6)\)-alkyl, \((\text{C}_1-\text{C}_6)\)-perfluoroalkyl,

\((\text{C}_3-\text{C}_6)\)-alkenyl or \(-\text{C}_n\text{H}_{2n}\text{-R}(9);\)

\(n\) is zero, 1, 2, 3 or 4;

R(9) is \((\text{C}_3-\text{C}_6)\)-cycloalkyl, phenyl, biphenylyl or naphthyl,

where the aromatics are not substituted or are substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and

NR(10)R(11);

R(10) and R(11) are H, \((\text{C}_1-\text{C}_4)\)-alkyl or \((\text{C}_1-\text{C}_4)\)-perfluoroalkyl;

R(7) is hydrogen, \((\text{C}_1-\text{C}_6)\)-alkyl, \((\text{C}_1-\text{C}_6)\)-perfluoroalkyl,

\((\text{C}_3-\text{C}_6)\)-alkenyl or \(-\text{C}_o\text{H}_{2o}\text{-R}(12);\)

\(o\) is zero, 1, 2, 3 or 4;

R(12) is \((\text{C}_3-\text{C}_6)\)-cycloalkyl, phenyl, biphenylyl or naphthyl,

where the aromatics are not substituted or are substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and
NR(13)R(14);
R(13) and R(14)
are H, (C\textsubscript{1}-C\textsubscript{4})-alkyl or (C\textsubscript{1}-C\textsubscript{4})-
perfluoroalkyl;

R(8) is defined as R(7);
or
R(7) and R(8)
together are 4 or 5 methylene groups, of which one
CH\textsubscript{2} group can be replaced by oxygen, S, NH, N-CH\textsubscript{3}

or N-benzyl;

the remaining substituents R(2), R(3), R(4), R(5) or R(1), R(2), R(4), R(5)
or R(1), R(2), R(3), R(5) in each case
independently of one another are hydrogen, F, Cl, Br, I, -O\textsubscript{ta}(C\textsubscript{1}-C\textsubscript{6})-
alkyl, -O\textsubscript{tb}(C\textsubscript{3}-C\textsubscript{9})-alkenyl,

-O\textsubscript{tb}(CH\textsubscript{2})\textsubscript{b}C_{d}F_{2d+1}, -O\textsubscript{tb}C_{p}H_{2p}R(18),
or up to 2 groups CN, NO\textsubscript{2}, NR(16)R(17),

b is zero or 1;
d is 1, 2, 3, 4, 5, 6 or 7;
ta is zero or 1;
tb is zero or 1;
tc is zero or 1;
td is zero or 1;
p is zero, 1, 2, 3 or 4;

R(18) is (C\textsubscript{3}-C\textsubscript{8})-cycloalkyl, phenyl, biphenyl or naphthyl,
where the aromatics are not substituted or are
substituted by 1 - 3 substituents selected from the
group consisting of F, Cl, CF\textsubscript{3}, methyl, methoxy and
NR(19)R(20);
R(19) and R(20)
are hydrogen or (C\textsubscript{1}-C\textsubscript{4})-alkyl or (C\textsubscript{1}-C\textsubscript{4})-
perfluoroalkyl;

R(16) is hydrogen, (C\textsubscript{1}-C\textsubscript{8})-alkyl, (C\textsubscript{1}-C\textsubscript{8})-perfluoroalkyl, (C\textsubscript{3}-C\textsubscript{9})-
alkenyl, \(-C\text{C}_qH_{2q}\)-R(21),

q is zero, 1, 2, 3 or 4;

R(21) is \((C_3-C_6)\)-cycloalkyl, phenyl, biphenylyl or naphthyl,

where the aromatics are not substituted or are

substituted by 1 - 3 substituents from the group

F, Cl, CF₃, methyl, methoxy or NR(22)R(23),

R(22) and R(23) are hydrogen, \((C_1-C_4)\)-alkyl or

\((C_1-C_4)\)-perfluoroalkyl;

R(17) is hydrogen, \((C_1-C_6)\)-alkyl, \((C_1-C_6)\)-perfluoroalkyl, \((C_3-C_6)\)-

alkenyl, \(-C\text{H}_{2r}\)-R(24);

r is zero, 1, 2, 3 or 4;

R(24) is \((C_3-C_6)\)-cycloalkyl, phenyl, biphenylyl or naphthyl,

where the aromatics are not substituted or are

substituted by 1 - 3 substituents selected from

the group consisting of F, Cl, CF₃, methyl,

methoxy and NR(25)R(26);

R(25) and R(26)

are hydrogen, \((C_1-C_4)\)-alkyl or \((C_1-C_4)\)-

perfluoroalkyl;

or

R(16) and R(17)

together are 4 or 5 methylene groups, of which one CH₂

group can be replaced by oxygen, S, NH, N-CH₃ or N-benzyl;

and their pharmaceutically tolerable salts;

t) diacyl-substituted guanidines of the formula \(\text{I}\)

\[
\begin{array}{c}
\text{X(1) } \quad \text{NH} \quad \text{NH} \quad \text{X(2)} \\
\text{0} \quad \text{NH} \quad 0
\end{array}
\]

in which:

X(1) and X(2) are
R(1 01)
R(1 02)
C(R(A)R(B))
R(1 03)
R(1 04)
R(1 05)

T1 is zero, 1, 2, 3 or 4;
R(A) and R(B) independently of one another are hydrogen, F, Cl, Br, I, CN,
OR(106), (C_1-C_8)-alkyl, (C_3-C_8)-cycloalkyl, O_{z_k}(CH_{2})_{z_l}C_{z_m}F_{2z_m+1},
NR(107)R(108), phenyl or benzyl,

where the aromatics are not substituted or are substituted by 1-3 substituents selected from the group consisting of F, Cl, CF_3, methyl, methoxy and NR(109)R(110);

R(109) and R(110) are hydrogen, (C_1-C_4)-alkyl or (C_1-C_4)-perfluoroalkyl;

z_l is zero, 1, 2, 3 or 4;
z_k is zero or 1;
z_m is 1, 2, 3, 4, 5, 6, 7 or 8;

R(106) is hydrogen, (C_1-C_8)-alkyl, (C_1-C_8)-perfluoroalkyl, (C_3-C_8)-alkenyl, (C_3-C_8)-cycloalkyl, phenyl or benzyl,

where the aromatics are not substituted or are substituted by 1-3 substituents selected from the group consisting of F, Cl, CF_3, methyl, methoxy and NR(111)R(112);

R(111) and R(112) are hydrogen, (C_1-C_4)-alkyl or (C_1-C_4)-perfluoroalkyl;

R(107) and R(108) independently of one another are defined as R(106), or
R(107) and R(108) together are 4 or 5 methylene groups, of which one CH₂ group can be replaced by oxygen, S, NH, N-CH₃ or N-benzyl;

or

X(1) and X(2) are

![Structure diagram]

T2a and T2b independently of one another are zero, 1 or 2;

where the double bond can have the (E)- or (Z)-configuration;

or

X(1) and X(2) are

![Structure diagram]

T3 is zero, 1 or 2;

U, YY and Z independently of one another are C or N,

where U, YY, Z can carry the following number of substituents:

<table>
<thead>
<tr>
<th>U, YY or Z</th>
<th>Bonded in the ring to a double bond</th>
<th>Number of permitted substituents</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>yes</td>
<td>1</td>
</tr>
<tr>
<td>C</td>
<td>no</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>N</td>
<td>yes</td>
<td>0</td>
</tr>
<tr>
<td>N</td>
<td>no</td>
<td>1</td>
</tr>
</tbody>
</table>

R(D) is hydrogen, (C₁-C₆)-alkyl or (C₁-C₆)-perfluoroalkyl, R(U₁), R(U₂), R(Y₁), R(Y₂), R(Z₁), R(Z₂) independently of one another are hydrogen, F, Cl, Br, I, CN, OR(114), (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl, Oₙₖₐ₁(CH₂)ₙ₁ₘ₁ₐ₁ₙ₁₊₁₁, NR(115)R(116), phenyl or benzyl, where the aromatics are not substituted or are substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy, NR(117)R(118), R(117) and R(118) are hydrogen, (C₁-C₄)-alkyl or (C₁-C₄)-perfluoroalkyl, zka is zero or 1; zla is zero, 1, 2, 3 or 4; zma is 1, 2, 3, 4, 5, 6, 7 or 8; R(114) is hydrogen, (C₁-C₆)-alkyl, (C₁-C₆)-perfluoroalkyl, (C₃-C₆)-alkenyl, (C₃-C₆)-cycloalkyl, phenyl or benzyl, where the aromatics are not substituted or are substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(119)R(120); R(119) and R(120) are hydrogen, (C₁-C₄)-alkyl or (C₁-C₄)-perfluoroalkyl; R(115) and R(116) independently of one another are defined as R(114); or R(115) and R(116) together are 4 or 5 methylene groups, of which one CH₂ group can be replaced by oxygen, S, NH, N-CH₃ or N-benzyl;
but where the constitution of U is nitrogen (N), YY is nitrogen (N) and Z is carbon (C) is excluded,

\[ R(101), R(102), R(103), R(104) \text{ and } R(105) \]

independently of one another are hydrogen, F, Cl, Br, I, -C≡N,

\[ X_{\text{zaa}}(\text{CH}_2)_{\text{zpax}}(\text{C}_{\text{zqa}} \text{F}_{\text{zqa+1}}), R(110a)-\text{SO}_{\text{zbm}}, R(110b)R(110c)N-\text{CO}, \]
\[ R(111a)\text{-CO- or } R(112a)R(113a)N-\text{SO}_{2}^- \]

where the perfluoroalkyl group is straight-chain or branched,

\[ X \]

is oxygen, S or NR(114a);

\[ R(114a) \]

\[ z_{\text{zaa}} \]

is H or (C\(_1\)-C\(_3\))-alkyl;

\[ z_{\text{zbm}} \]

is zero or 1;

\[ z_{\text{zpax}} \]

is zero, 1 or 2;

\[ z_{\text{zqa}} \]

is zero, 1, 2, 3 or 4;

\[ z_{\text{zqa}} \]

is 1, 2, 3, 4, 5, 6, 7 or 8;

\[ R(110a), R(110b), R(111a) \text{ and } R(112a) \]

independently of one another are (C\(_1\)-C\(_6\))-alkyl,

(C\(_3\)-C\(_6\))-alkenyl, -C\(_{2n}\)H\(_{2n}\)-R(115a) or (C\(_1\)-C\(_8\))-perfluoroalkyl;

\[ z_{n} \]

is zero, 1, 2, 3 or 4;

\[ R(115a) \]

is (C\(_3\)-C\(_8\))-cycloalkyl, phenyl, biphenyl or naphthyl,

where the aromatics are not substituted or are substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF\(_3\), methyl, methoxy and NR(116a)R(117a);

\[ R(116a) \text{ and } R(117a) \]

are hydrogen, (C\(_1\)-C\(_4\))-perfluoroalkyl or (C\(_1\)-C\(_4\))-alkyl;

or

\[ R(110b), R(111a) \text{ and } R(112a) \]

are hydrogen;

\[ R(110c) \text{ and } R(113a) \]

independently are hydrogen, (C\(_1\)-C\(_4\))-perfluoroalkyl or
(C<sub>1</sub>-C<sub>4</sub>)-alkyl;

or

R(110b) and R(110c) and R(112a) and R(113a)

together are 4 or 5 methylene groups, of which one CH<sub>2</sub>
group can be replaced by oxygen, sulfur, NH, N-CH<sub>3</sub> or
N-benzyl;

or

R(101), R(102), R(103), R(104), R(105)

independently of one another are (C<sub>1</sub>-C<sub>8</sub>)-alkyl, -(C<sub>2</sub>zalH<sub>2zal</sub>)R(118a) or
(C<sub>3</sub>-C<sub>6</sub>)-alkenyl,
zal is zero, 1, 2, 3 or 4;

R(118a)

is (C<sub>3</sub>-C<sub>8</sub>)-cycloalkyl, phenyl, biphenyl or naphthyl,
where the aromatics are not substituted or are
substituted by 1 - 3 substituents from the group
consisting of F, Cl, CF<sub>3</sub>, methyl, methoxy or
NR(119a)R(119b);

R(119a) and R(119b)

are hydrogen, (C<sub>1</sub>-C<sub>4</sub>)-alkyl or (C<sub>1</sub>-C<sub>8</sub>)
perfluoroalkyl;

or

R(101), R(102), R(103), R(104), R(105)

independently of one another are (C<sub>1</sub>-C<sub>8</sub>)-heteroaryl,
which is linked via C or N and which is unsubstituted or
substituted by 1 - 3 substituents from the group consisting of
F, Cl, CF<sub>3</sub>, CH<sub>3</sub>, methoxy, hydroxyl, amino, methylamino and
dimethylamino;

or

R(101), R(102), R(103), R(104), R(105)

independently of one another are -C=C-R(193);

R(193)

is phenyl which is not substituted or is substituted by 1 - 3
substituents from the group consisting of F, Cl, CF₃, methyl, methoxy or NR(194)R(195);
R(194) and R(195)
are hydrogen or CH₃;

5  or
R(101), R(102), R(103), R(104), R(105)
independently of one another are
-Y-para-C₆H₄-(CO)ₜ_(zh) -(CHOH)ₜ_(zi) -(CH₂)ₜ_(zj) -(CHOH)ₜ_(zk) -R(123),
-Y-meta-C₆H₄-(CO)ᵦ_(zad) -(CHOH)ᵦ_(zae) -(CH₂)ᵦ_(zaf) -(CHOH)ᵦ_(zag) -R(124)
10  or
-Y-ortho-C₆H₄-(CO)ᵦ_(zah) -(CHOH)ᵦ_(zae) -(CH₂)ᵦ_(zaf) -(CHOH)ᵦ_(zag) -R(125);
Y is oxygen, -S- or -NR(122d)-;
zh, zad, zah
  independently are zero or 1;
zi, zj, zk, zae, zaf, zag, zao, zap and zak
  independently are zero, 1, 2, 3 or 4;
but where in each case
zh, zi and zk are not simultaneously zero,
  zad, zae and zag are not simultaneously zero, and
zh, zao and zak are not simultaneously zero,
R(123), R(124) R(125) and R(122d)
independently are hydrogen or (C₁-C₃)-alkyl;

25  or
R(101), R(102), R(103), R(104) and R(105)
independently of one another are SR(129), -OR(130),
-NR(131)R(132) or -CR(133)R(134)R(135);
R(129), R(130), R(131) and R(133)
independently are -Cₚₗ₋ₙ₋ₚ₋ₚ₋ₙ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ₋ₚ_-...
zab is zero, 1 or 2;

R(132), R(134) and R(135) independently of one another are defined as R(129) or are hydrogen, (C₁-C₄)-alkyl or (C₁-C₄)-perfluoroalkyl;

or

R(101), R(102), R(103), R(104) and R(105) independently of one another are -W-para-(C₆H₄)-R(196), -W-meta-(C₆H₄)-R(197) or -W-ortho-(C₆H₄)-R(198);

R(196), R(197) and R(198) independently are (C₁-C₈)-heteroaryl, which is linked via C or N and which is unsubstituted or substituted by 1 to 3 substituents from the group consisting of F, Cl, CF₃, CH₃ methoxy, hydroxyl, amino, methylamino, dimethylamino and benzyl;

W is oxygen, S or NR(136)-;

R(136) is hydrogen or (C₁-C₄)-alkyl;

or

R(101), R(102), R(103), R(104) and R(105) independently of one another are R(146)X(1a)-;

X(1a) is oxygen, S, NR(147), (D=O)A-, NR(148)C=MN(*)R(149)-;

M is oxygen or sulfur;

A is oxygen or NR(150);

D is C or SO;

R(146) is (C₁-C₈)-alkyl, (C₃-C₈)-alkenyl, (CH₂)zbzCzdzFzdz₊₁ or -CₓₖH₂ₓₖ₋₁-R(151);

zbz is zero or 1;

zdz is 1, 2, 3, 4, 5, 6 or 7;

zxa is zero, 1, 2, 3 or 4;

R(151)
is \((C_3 - C_8)\)-cycloalkyl, phenyl, biphenylyl or naphthyl, where the aromatics are not substituted or are substituted by 1 - 3 substituents from the group consisting of F, Cl, CF₃, methyl, methoxy and

\[ NR(152)R(153); \]
\[ R(152) \text{ and } R(153) \]

are hydrogen, \((C_1 - C_4)\)-alkyl or \((C_1 - C_4)\)-perfluoroalkyl;

\[ R(147), R(148) \text{ and } R(150) \]

independently are hydrogen, \((C_1 - C_4)\)-alkyl, \((C_1 - C_4)\)-perfluoroalkyl;

\[ R(149) \text{ is defined as } R(146), \]

or

\[ R(146) \text{ and } R(147), \text{ or } R(146) \text{ and } R(148) \]

together are 4 or 5 methylene groups, of which one CH₂ group can be replaced by oxygen, sulfur, NH, N-CH₃ or N-benzyl;

where \(A\) and \(N^{(\*k)}\) are bonded to the phenyl nucleus of the alkanoyl parent structure;

\[ R(146), R(147), R(148) \text{ and } R(150) \]

independently of one another are \(-\text{SR}(164), -\text{OR}(165), -\text{NHR}(166), -\text{NR}(167)\text{R}(168), -\text{CHR}(169)\text{R}(170), -\text{CR}(154)\text{R}(155)\text{OH}, -\text{C}=\text{CR}(156), -\text{CR}(158)\text{CR}(157)\text{OH}, -\text{CR}(159)\text{R}(160)\text{R}(161)\text{R}(162)\text{R}(163)\text{R}(164), R(165), R(166), R(167), R(169) \]

equally or differently are \(-(\text{CH}_2)_z\text{R}(171)\) or \(-(\text{CH}_2)_{za}\text{O}(\text{CH}_2)_{za}^2\text{R}(172)\);

\[ R(171) \text{ and } R(172) \]

are hydrogen or methyl;

\(z-u\) is 1, 2, 3 or 4;

\(z-v\) is zero, 1, 2, 3 or 4;
zy, zz, zaa, zab, zac

identically or differently are zero, 1, 2, 3 or 4;

zt is 1, 2, 3 or 4;

R(168), R(170), R(154), R(155)

identically or differently are hydrogen or (C_1-C_6)-alkyl,

or

R(169) and R(170), or R(154) and R(155)

together with the carbon atom carrying them are a (C_5-C_9)-
cycloalkyl;

R(163)

is hydrogen, (C_1-C_6)-alkyl, (C_3-C_9)-cycloalkyl or

-C_{zeb}H_{2zeb}-R(173);

zeb is zero, 1, 2, 3 or 4;

R(156), R(157) and R(173)

independently are phenyl which is unsubstituted or is

substituted by 1 - 3 substituents from the group

consisting of F, Cl, CF_3, methyl, methoxy and

NR(174)R(175);

R(174) and R(175)

are hydrogen or (C_1-C_4)-alkyl;

or

R(156), R(157) and R(173)

independently are (C_1-C_9)-heteroaryl,

which is unsubstituted or substituted as phenyl;

R(158), R(159), R(160), R(161) and R(162)

are hydrogen or methyl,

or

R(101), R(102), R(103), R(104), R(105)

independently of one another are R(176)-NH-SO_2^-;

R(176)

is R(177)R(178)N-(C=Y')-;

Y' is oxygen, S or N-R(179);
R(177) and R(178) identically or differently are hydrogen, (C₁-C₆)-alkyl, (C₃-C₆)-alkenyl or -C₀₂₅H₂₅₋₂₋₅-R(180);

zfa is zero, 1, 2, 3 or 4;

5 R(180)

is (C₅-C₇)-cycloalkyl or phenyl, which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methoxy or (C₁-C₄)-alkyl;

or

R(177) and R(178) together are 4 or 5 methylene groups, of which one CH₂ group can be replaced by oxygen, sulfur, NH, N-CH₃ or N-benzyl;

15 R(179)

is defined as R(177) or is amidine,

or

20 R(101), R(102), R(103), R(104), R(105) independently of one another are NR(184a)R(185), OR(184b), SR(184c) or -Cₓ₋ₓHₓ₋ₓ-R(184d);

znx is zero, 1, 2, 3 or 4;

25 R(184d)

is (C₃-C₇)-cycloalkyl or phenyl, which is not substituted or substituted by 1 - 3 substituents from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(116k)R(117k);

R(116k) and R(117k)

are hydrogen or C₁-C₄-alkyl;

30 R(184a), R(184b), R(184c), R(185)

independently of one another are hydrogen, (C₁-C₆)-alkyl,
(C₁-C₈)-perfluoroalkyl or (CH₂)ₙ₋₉⁻abies -R(184g);
zao is zero, 1, 2, 3 or 4;
R(184g)
is (C₃-C₇)-cycloalkyl or phenyl,
which is not substituted or substituted by 1-3 substituents from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(184u)R(184v);
R(184u) and R(184v) are hydrogen or C₁-C₄-alkyl;
or
R(184a) and R(185) together are 4 or 5 methylene groups, of which one CH₂ group can be replaced by oxygen, sulfur, NH, N-CH₃ or N-benzyl;
and their pharmaceutically tolerable salts;
u) benzoylguanidines of the formula I

\[
\begin{array}{c}
\text{\textbf{R(1)}} \\
\text{\textbf{R(2)}} \\
\text{\textbf{R(3)}} \\
\text{\textbf{R(4)}} \\
\end{array}
\]

\[
\begin{array}{c}
\text{\textbf{NH₂}} \\
\text{\textbf{NH₂}} \\
\end{array}
\]

in which:
R(1) is H, F, Cl, Br, I, CN, NO₂, (C₁-C₈)-alkyl, (C₃-C₇)-cycloalkyl or \(X_a\)-(CH₂)ₙ⁻(CF₂)ₙ⁻CF₃;
X is oxygen, S or NR(5);
a is zero or 1;
b is zero, 1 or 2;
c is zero, 1, 2 or 3;
R(5) is H, (C₁-C₄)-alkyl or \(-C₆H₁₃\)R(6);
$d$ is zero, 1, 2, 3 or 4;

$R(6)$ is $(C_3-C_9)$-cycloalkyl, phenyl, biphenylyl or naphthyl,

where the aromatics are not substituted or are substituted by 1 to 3 substituents selected from the group consisting of F, Cl, CF$_3$, methyl, methoxy and NR(7)R(8);

$R(7)$ and R(8)

independently are H or (C$_1$-C$_4$)-alkyl;

or

$R(1)$ is -SR(10), -OR(10) or -CR(10)R(11)R(12);

$R(10)$ is $C_{12r}$-(C$_3$-C$_9$)-cycloalkyl, -(C$_1$-C$_9$)-heteroaryl or phenyl,

where the aromatic systems are unsubstituted or substituted by one to 3 substituents selected from the group consisting of F, Cl, CF$_3$, CH$_3$, methoxy, hydroxyl, amino, methylamino and dimethylamino;

$f$ is zero, 1 or 2;

$R(10)$ and R(12)

independently of one another are defined as R(10) or are hydrogen or (C$_1$-C$_4$)-alkyl;

or

$R(1)$ is phenyl, naphthyl, biphenylyl or (C$_1$-C$_9$)-heteroaryl, the latter linked via C or N,

and which are unsubstituted or substituted by 1 to 3 substituents selected from the group consisting of F, Cl, CF$_3$, CH$_3$, methoxy, hydroxyl, amino, methylamino and dimethylamino;

or

$R(1)$ is -SR(13), -OR(13), -NHR(13), -NR(13)R(14), -CHR(13)R(15), -C[R(15)R(16)]OH, -C=CR(18), -C[R(19)]=CR(18), -[CR(20)R(21)]_k-(CO)-[CR(22)R(23)R(24)];
R(13) and R(14) identically or differently are -(CH₂)ₓ-(CHOH)ₙ-(CH₂)ᵧ-(CHOH)ᵢ-
R(17),
R(17) is hydrogen or methyl;
5 -(CH₂)ₓ-O-(CH₂-CH₂O)ₙ-R(24),
g, h, i identically or differently are zero, 1, 2, 3 or 4;
j is 1, 2, 3 or 4;
R(15) and R(16) identically or differently are hydrogen, (C₃-C₆)-alkyl or
together with the carbon atom carrying them are a (C₃-C₆)-
cycloalkyl;
R(18) is phenyl,
which is unsubstituted or substituted by 1 to 3
15 substituents selected from the group consisting of F,
Cl, CF₃, methyl, methoxy and NR(25)R(26);
R(25) and R(26)
are H or (C₁-C₄)-alkyl;
or
20 R(18) is (C₃-C₆)-heteroaryl,
which is unsubstituted or substituted as phenyl;
or
R(18) is (C₁-C₆)-alkyl,
which is unsubstituted or substituted by 1 to 3 OH;
25 or
R(18) is (C₃-C₆)-cycloalkyl;
R(19), R(20), R(21), R(22) and R(23)
are hydrogen or methyl;
k is zero, 1, 2, 3 or 4;
30 l is zero, 1, 2, 3 or 4;
R(24) is H, (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl or -CₘH₂ₙ₋ᵢ-R(18);
m is 1, 2, 3 or 4;
R(2) and R(3)

independently of one another are defined as R(1);

R(4) is (C₁₋₃)-alkyl, F, Cl, Br, I, CN or -(CH₂)ₙ-(CF₂)ₖ-CF₃;

n is zero or 1;

o is zero, 1 or 2;

and their pharmaceutically tolerable salts;

v) acylguanidines of the formula I

\[
\begin{array}{c}
R(1) \\
R(2)
\end{array}
\]

in which:

X is carbonyl, sulfonyl,

R(1) is H, (C₁₋₃)-alkyl,

unsubstituted or substituted by hydroxyl,

(C₃₋₆)-cycloalkyl, phenyl,

which is unsubstituted or substituted by 1 - 3 substituents from the group F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino,

methylamino or dimethylamino,

R(2) is H, (C₁₋₄)-alkyl,

and their pharmaceutically tolerable salts;

w) phenyl-substituted alkycarboxylic acid guanidides, carrying perfluoroalkyl groups, of the formula I

\[
\begin{array}{c}
R(1) \\
R(2) \\
R(3) \\
R(4) \\
R(5) \\
R(A) \\
R(B)
\end{array}
\]

and their pharmaceutically tolerable salts;
in which:

- R(A) is hydrogen, F, Cl, Br, I, CN, OR(6), (C₁-C₉)-alkyl, (C₃-C₆)-cycloalkyl, O₁(CH₂)ₐC₆F₂b₊₁ or NR(7)R(8);
- r is zero or 1;
- a is zero, 1, 2, 3 or 4;
- b is 1, 2, 3, 4, 5, 6, 7 or 8;
- R(6) is hydrogen, (C₁-C₉)-alkyl, (C₃-C₆)-alkenyl, (C₃-C₆)-cycloalkyl, phenyl or benzyl,

where the aromatics are not substituted or are substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and OR(9)R(10);

- R(9) and R(10) are H, (C₁-C₄)-alkyl or (C₁-C₄)-perfluoroalkyl;

R(7) and R(8) independently of one another are defined as R(6);

- R(B) independently is defined as R(A);
- X is 1, 2 or 3;
- R(1) is hydrogen, (C₁-C₉)-alkyl, (C₃-C₆)-cycloalkyl, -O₁(CH₂)ₐC₆F₂b₊₁, F, Cl, Br, I or CN;
- t is zero or 1;
- d is zero, 1, 2, 3 or 4;
- e is 1, 2, 3, 4, 5, 6, 7 or 8;

R(2), R(3), R(4) and R(5) independently of one another are defined as R(1);

but with the condition that at least one of the substituents R(1), R(2), R(3), R(4), R(5), R(A) and R(B) is an -O₁(CH₂)ₐC₆F₂b₊₁ or an O₁(CH₂)ₐC₆F₂b₊₁ group, and their pharmaceutically tolerable salts;
x) heteroarylguanidines of the formula I

\[
\begin{array}{c}
\text{R(3)} \\
\text{HA} \\
\text{R(1)} \\
\text{R(2)} \\
\text{R(4)} \\
\end{array}
\]

in which:

HA\( \) is SO\(_m\), O or NR(5);

\( m \) is zero, 1 or 2;

R(5)\( \) is hydrogen, \( (C_1-C_6)\)-alkyl or \( -C_\text{am}H_{2\text{am}}R(81); \)

\( \text{am} \) is zero, 1 or 2;

R(81)\( \) is \( (C_3-C_8)\)-cycloalkyl or phenyl, which is not substituted or is substituted by 1-3 substituents selected from the group consisting of F, Cl, CF\(_3\), methyl, methoxy and NR(82)R(83);

R(82) and R(83) is H or CH\(_3\);

or

R(81)\( \) is \( (C_1-C_9)\)-heteroaryl, which is linked via C or N and which is unsubstituted or substituted by 1-3 substituents selected from the group consisting of F, Cl, CF\(_3\), CH\(_3\), methoxy, hydroxyl, amino, methylamino and dimethylamino;

one of the two substituents R(1) and R(2)

is -CO-N=C(NH\(_2\))\(_2\);

and the other in each case

is hydrogen, F, Cl, Br, I, \( (C_1-C_3)\)-alkyl, \(-OR(6), \) \( C_1F_{2r+1}, \) -CO-N=C(NH\(_2\))\(_2\) or \(-NR(6)R(7); \)

R(6) and R(7)

independently are hydrogen or \( (C_1-C_3)\)-alkyl;

\( r \) is 1, 2, 3 or 4;

R(3) and R(4)
independently of one another are hydrogen, F, Cl, Br, I, -C=, X-
(CH2)ₚ-(C₆H₂R(8)-SO₃m, R(9)R(10)N-CO, R(11)-CO- or
R(12)R(13)N-SO₂⁻,

where the perfluoroalkyl group is straight-chain or branched,

5  X  is oxygen, S or NR(14);
R(14)  is H or (C₃-C₅)-alkyl;

bm  is zero, 1 or 2;
p  is zero, 1 or 2;
q  is zero, 1, 2, 3, 4, 5 or 6;

10  R(8), R(9), R(11) and R(12)

independently are (C₁-C₇)-alkyl, (C₃-C₅)-alkenyl, -CₙH₂ₙ₁-R(15),

CF₅,

n  is zero, 1, 2, 3 or 4;

15  R(15)  is (C₃-C₇)-cycloalkyl or phenyl;

which is not substituted or is substituted by 1 - 3
substituents selected from the group consisting
of F, Cl, CF₃, methyl, methoxy or NR(16)R(17);
R(16) and R(17)

are H or C₅-C₇-alkyl;

20  or
R(9), R(11) and R(12)

are H;

R(10) and R(13)

independently are H or (C₁-C₄)-alkyl;

25  or
R(9) and R(10), and R(12) and R(13)

together are 4 or 5 methylene groups, of which one CH₂
group can be replaced by oxygen, S, NH, N-CH₃ or N-benzyl,
or

30  R(3) and R(4)

independently of one another are (C₁-C₅)-alkyl or -CₐH₂ₐ₉R(18);

ₐ  is zero, 1 or 2;
R(18) is (C₃-C₈)-cycloalkyl or phenyl;
which is not substituted or is substituted by 1 - 3
substituents selected from the group consisting of F,
Cl, CF₃, methyl, methoxy and NR(19)R(20);

R(19) and R(20)
are H or CH₃;
or
R(3) and R(4)
individually of one another are (C₅-C₆)-heteroaryl,
which is linked via C or N and which is unsubstituted or
substituted by 1 - 3 substituents selected from the group
consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino,
methylamino and dimethylamino;
or
R(3) and R(4)
individually of one another are
\[
\begin{align*}
- \text{Y} & - (\text{C})_{\text{h}} - (\text{CHOH})_{\text{i}} - (\text{CH}_2)_{\text{j}} - (\text{CHOH})_{\text{k}} - \text{R(23)} \\
\text{or} & \\
- \text{Y} & - (\text{C})_{\text{ad}} - (\text{CHOH})_{\text{ae}} - (\text{CH}_2)_{\text{af}} - (\text{CHOH})_{\text{ag}} - \text{R(24)} \\
\text{or} & \\
- \text{Y} & - (\text{C})_{\text{ch}} - (\text{CHOH})_{\text{co}} - (\text{CH}_2)_{\text{cp}} - (\text{CHOH})_{\text{cq}} - \text{R(25)}
\end{align*}
\]

Y is oxygen, -S- or -NR(22)-;
h, ad, ah independently are zero or 1;
i, j, k, ae, af, ag, ao, ap and ak independently are zero, 1, 2, 3, 4,
but where in each case
h, i and k are not simultaneously zero,
ad, ae and ag are not simultaneously zero,
ah, ao and ak are not simultaneously zero,

R(23), R(24) R(25) and R(22)

independently are hydrogen or (C₁-C₉)-alkyl;

or

5 R(3) and R(4)

independently of one another are hydrogen, F, Cl, Br, I, CN, (C₁-C₉)-
alkyl, (C₁-C₉)-perfluoroalkyl, (C₃-C₈)-alkenyl or -C₉H₂₉R(26);

g is zero, 1, 2, 3 or 4;

R(26) is (C₅-C₈)-cycloalkyl, phenyl, biphenyl or naphthyl,

where the aromatics are not substituted or are

substituted by 1 - 3 substituents selected from the

group consisting of F, Cl, CF₃, methyl, methoxy and

NR(27)R(28);

R(27) and R(28)

are H, (C₁-C₄)-alkyl or (C₁-C₄)-perfluoroalkyl;

or

R(3) and R(4)

independently of one another are SR(29), -OR(30), -NR(31)R(32) or

-CR(33)R(34)R(35);

R(29), R(30), R(31) and R(33)

independently are -C₉H₂₉-(C₁-C₉)-heteroaryl,

which is unsubstituted or substituted by 1 - 3

substituents selected from the group consisting of F,

Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino

and dimethylamino;

a is zero, 1 or 2;

R(32), R(34) and R(35)

independently of one another are defined as R(29) or are

hydrogen, (C₁-C₄)-alkyl or (C₁-C₄)-perfluoroalkyl;

or

R(3) and R(4)

independently of one another are
R(96), R(97) and R(98) independently are \((C_1-C_9)\)-heteroaryl, which is linked via C or N and which is unsubstituted or substituted by 1 to 3 substituents selected from the group consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino, dimethylamino or benzyl;

W is oxygen, S or \(NR(36)\)-;

R(36) is H or \((C_1-C_4)\)-alkyl;

or

R(3) and R(4) independently of one another are \(R(37)\)-SO\(_{cm}\) or \(R(38)R(39)N\)-SO\(_2\)-; \(cm\) is 1 or 2;

R(37) is \((C_1-C_9)\)-alkyl, \((C_1-C_9)\)-perfluoroalkyl, \((C_3-C_9)\)-alkenyl or \(-C_8H_{2s}R(40)\); s is zero, 1, 2, 3 or 4;

R(40) is \((C_3-C_9)\)-cycloalkyl, phenyl, biphenylyl or naphthyl, where the aromatics are not substituted or are substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl,

R(41) and R(42) are H, \((C_1-C_4)\)-alkyl or \((C_1-C_4)\)-perfluoroalkyl;

R(38) is H, \((C_1-C_9)\)-alkyl, \((C_1-C_9)\)-perfluoroalkyl, \((C_3-C_9)\)-alkenyl or \(-C_wH_{2w}R(43)\); w is zero, 1, 2, 3 or 4;

R(43) is \((C_3-C_9)\)-cycloalkyl, phenyl, biphenylyl or naphthyl, where the aromatics are not substituted or are substituted by 1 - 3 substituents selected from
the group consisting of F, Cl, CF₃, methyl, methoxy and NR(44)R(45); 
R(44) and R(45) are H, (C₁-C₄)-alkyl or (C₁-C₄)-perfluoroalkyl;

R(39) is H, (C₁-C₄)-alkyl or (C₁-C₄)-perfluoroalkyl; or
R(38) and R(39) together are 4 or 5 methylene groups, of which one
  group can be replaced by oxygen, S, NH, N-CH₃ or N-benzyl; or
R(3) and R(4) independently of one another are R(46)X(1)-;
X(1) is oxygen, S, NR(47), (D=O)A-, NR(48)C=MN(*)R(49)-,
m is oxygen or S;
A is oxygen or NR(50); 
D is C or SO;
R(46) is (C₁-C₈)-alkyl, (C₃-C₈)-alkenyl, (CH₂)ₙC₆F₂d₊₁ or -CₓH₂x-R(51);
b is zero or 1;
d is 1, 2, 3, 4, 5, 6 or 7;
x is zero, 1, 2, 3 or 4;
R(51) is (C₃-C₈)-cycloalkyl, phenyl, biphenylyl or naphthyl,
  where the aromatics are not substituted or are substituted by 1 - 3 substituents selected from
the group consisting of F, Cl, CF₃, methyl, methoxy and NR(52)R(53); 
R(52) and R(53) are H, (C₁-C₄)-alkyl or (C₁-C₄)-perfluoroalkyl;

R(47), R(48) and R(50) independently are hydrogen, (C₁-C₄)-alkyl or (C₁-C₄)-perfluoroalkyl;
R(49) is defined as R(46);

or

R(46) and R(47), or R(46) and R(48)

together are 4 or 5 methylone groups, of which one

CH₂ group can be replaced by oxygen, S, NH, N-CH₃,
or N-benzyl,

where A and N(*) are bonded to the phenyl nucleus of the

benzoylguanidine parent structure;

or

R(3) and R(4)

independently of one another are -SR(64), -OR(65), -NHR(66),
-NR(67)R(68), -CHR(69)R(70), -C(OH)R(54)R(55), -C=CR(56),
-CR(58)CHR(57), -[CR(59)R(60)]_u-(CO)-[CR(61)R(62)]_v-R(63);

R(64), R(65), R(66), R(67) and R(69)

identically or differently are

(CH₂)yz-(CHOH)za-(CH₂)ab-
(CH₂OH)R(71) or -(CH₂)ab-O-(CH₂-C₂H₂O)ac-R(72),

R(71) and R(72)

are hydrogen or methyl;

u is 1, 2, 3 or 4;

v is zero, 1, 2, 3 or 4;

y, z, aa

identically or differently are zero, 1, 2, 3 or 4;

t is 1, 2, 3 or 4;

R(68), R(70), R(54) and R(55)

identically or differently are hydrogen, (C₁-C₆)-alkyl;

or

R(69) and R(70), or R(54) and R(55)

together with the carbon atom carrying them are a (C₃-C₈)-
cycloalkyl;

R(63)

is H, (C₁-C₆)-alkyl, (C₃-C₈)-cycloalkyl or -C₆H₂e-R(73);

e is zero, 1, 2, 3 or 4;
R(56), R(57) and R(73)
indipendently are phonyl,
which are unsubstituted or substituted by 1 - 3
substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(74)R(75);
R(74) and R(75)
are H or (C₁-C₄)-alkyl;
or
R(56), R(57) and R(73)
independently are (C₁-C₆)-heteroaryl,
which is unsubstituted or substituted as phenyl;
R(58), R(59), R(60), R(61) and R(62)
are hydrogen or methyl;
or
R(3) and R(4)
indipendently of one another are R(76)-NH-SO₂⁻;
R(76) is R(77)R(78)N-(C=Y')⁻;
Y' is oxygen, S or N-R(79);
R(77) and R(78)
identically or differently are H, (C₁-C₈)-alkyl, (C₃-C₈)-alkenyl, -
C₁H₂f-R(80);
f is zero, 1, 2, 3 or 4;
R(80) is (C₅-C₇)-cycloalkyl or phenyl,
which is unsubstituted or substituted by 1 - 3
substituents selected from the group consisting
of F, Cl, CF₃, methoxy and (C₁-C₄)-alkyl;
or
R(77) and R(78)
together are 4 or 5 methylene groups, of which one CH₂
is defined as R(77) or is amidine;
or
R(3) and R(4)

independently of one another are NR(84)R(85);
R(84) and R(85)

independently of one another are H, (C1-C4)-alkyl, or together
are 4 or 5 methylene groups,
of which one CH2 group can be replaced by oxygen, S, NH, N-CH3 or N-benzyl; or of which one or two CH2 groups can be replaced by CH-CdH2dm+1,
and their pharmaceutically tolerable salts;

y) bicyclic heteroaroylguanidines of the formula I

\[
\begin{align*}
R(1) & \quad \text{and } R(2) \\
R(3) & \quad \text{in which:} \\
T, U, V, W, X, Y \text{ and } Z & \quad \text{independently of one another are nitrogen or carbon;} \\
& \quad \text{but with the restriction} \\
& \quad \text{that } X \text{ and } Z \text{ are not simultaneously nitrogen,} \\
& \quad \text{and that } T, U, V, W, X, Y \text{ and } Z \text{ carry no substituents if they are} \\
& \quad \text{nitrogen,} \\
& \quad \text{and that no more than four of them are simultaneously nitrogen,} \\
R(1) \text{ and } R(2) & \quad \text{independently of one another are hydrogen, F, Cl, Br, I, (C1-C3)-} \\
& \quad \text{alkyl, (C1-C3)-perfluoroalkyl, OR(8), NR(8)R(9) or C(=O)N=C(NH2)2;} \\
R(8) \text{ and } R(9) & \quad \text{independently of one another are hydrogen or (C1-C3)-alkyl,}
\end{align*}
\]
or

$$R(8) \text{ and } R(9)$$

together are 4 or 5 methylene groups, of which one CH$_2$

group can be replaced by oxygen, S, NH, N-CH$_3$ or N-benzyl;

$$R(3), R(4), R(5), R(6) \text{ and } R(7)$$

independently of one another are hydrogen, F, Cl, Br, I, -C=O, X$_k$-

$$(CH_2)_p(C_2F_2q+1), R(10a)-SO_{bm}, R(10b)R(10c)N-CO, R(11)-CO- \text{ or}$$

$$R(12)R(13)N-SO_2^-,$$

where the perfluoroalkyl group is straight-chain or branched;

$$X$$

is oxygen, S or NR(14);

$$R(14)$$

is H or (C$_1$-C$_3$)-alkyl;

$$bm$$

is zero, 1 or 2;

$$p$$

is zero, 1 or 2;

$$k$$

is zero or 1;

$$q$$

1, 2, 3, 4, 5 or 6;

$$R(10a), R(10b), R(11) \text{ and } R(12)$$

independently of one another are (C$_1$-C$_8$)-alkyl,

$$(C_3-C_6)\text{-alkenyl}, -C_nH_{2n}-R(15) \text{ or } (1, \ldots, 8)\text{-perfluoroalkyl;}$$

$$n$$

is zero, 1, 2, 3 or 4;

$$R(15)$$

is (C$_3$-C$_7$)-cycloalkyl or phenyl, which is not substituted

or is substituted by 1 - 3 substituents selected from the

group consisting of F, Cl, CF$_3$, methyl, methoxy and

NR(16)R(17);

$$R(16)$$

and $$R(17)$$

are H or C$_1$-C$_4$-alkyl;

or

$$R(10b), R(11) \text{ and } R(12)$$

are hydrogen;

$$R(10c)$$

and $$R(13)$$

independently are hydrogen or (C$_1$-C$_4$)-alkyl;

or

$$R(10b)$$

and $$R(10c)$$

and $$R(12)$$

and $$R(13)$$
together are 4 or 5 methylene groups, of which one CH₂
group can be replaced by oxygen, sulfur, NH, N-CH₃ or
N-benzyl;

or

5. \( R(3), R(4), R(5), R(6) \) and \( R(7) \)
   independently of one another are \((C₅-C₆)\)-alkyl, \(-C₆H₂R(18)\) or \((C₃-C₅)\)-alkenyl;
   \( a₁ \) is zero, 1 or 2;
   \( R(18) \) is \((C₃-C₆)\)-cycloalkyl, phenyl, biphenyl or naphthyl, where
   the aromatics are not substituted or are substituted by 1 - 3
   substituents selected from the group consisting of F, Cl, CF₃,
   methyl, methoxy and \( NR(19a)R(19b) \);
   \( R(19a) \) and \( R(19b) \)
   are hydrogen, \((C₄-C₆)\)-alkyl or \((C₅-C₈)\)-perfluoroalkyl;

or

R(3), \( R(4), R(5), R(6) \) and \( R(7) \)
   independently of one another are \((C₅-C₆)\)-heteroaryl, which is linked
   via C or N and which is unsubstituted or substituted by 1 - 3
   substituents from the group consisting of F, Cl, CF₃, CH₃, methoxy,
   hydroxyl, amino, methylamino or dimethylamino;
R(3), R(4), R(5), R(6) and R(7) independently of one another are

\[ -Y-(C)^{h}-(CHOH)^{i}-(CH_{2})^{j}-(CHOH)^{k}-R(23) \]

or

\[ -(C)^{ad}-(CHOH)^{ae}-(CH_{2})^{af}-(CHOH)^{ag}-R(24) \]

or

\[ -(C)^{ah}-(CHOH)^{ao}-(CH_{2})^{ap}-(CHOH)^{ak}-R(25) \]

5  \( Y \) is oxygen, -S- or -NR(22)-;

h, ad, ah

independently of one another are zero or 1;

i, j, k, ae, af, ag, ao, ap and ak

independently of one another are zero, 1, 2, 3 or 4;

but where in each case

h, i and k are not simultaneously zero,

ad, ae and ag are not simultaneously zero, and

ah, ao and ak are not simultaneously zero,

R(23), R(24) R(25) and R(22)

15 independently of one another are hydrogen or (C\textsubscript{1}-C\textsubscript{3})-alkyl;

or

R(3), R(4), R(5), R(6) and R(7)

independently of one another are SR(29), -OR(30), -NR(31)R(32) or -CR(33)R(34)R(35);

20 R(29), R(30), R(31) and R(33)

independently of one another are -C\textsubscript{a}H\textsubscript{2a}-(C\textsubscript{1}-C\textsubscript{a})-heteroaryl, which is
unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino and dimethylamino;

\[ a \] is zero, 1 or 2;

R(32), R(34) and R(35)

independently of one another are defined as R(29) or are hydrogen, (C₁-C₄)-alkyl or (C₁-C₄)-perfluoroalkyl;

or

R(3), R(4), R(5), R(6) and R(7)

independently of one another are

\[
\begin{align*}
W & \quad R(96) & \quad R(97) & \quad R(98) \\
\end{align*}
\]

R(96), R(97) and R(98)

independently of one another are (C₁-C₃)-heteroaryl, which is linked via C or N and which is unsubstituted or substituted by 1 to 3 substituents from the group consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino, dimethylamino or benzyl;

W is oxygen, S or NR(36)-;

R(36) is H or (C₁-C₄)-alkyl;

or

R(3), R(4), R(5), R(6) and R(7)

independently of one another are R(46)X(1)-;

X(1) is oxygen, S, NR(47), (D=O)A- or NR(48)C=MN(*)R(49)-;

M is oxygen or sulfur;

A is oxygen or NR(50);

D is C or SO;

R(46) is (C₁-C₈)-alkyl, (C₃-C₈)-alkenyl, (CH₂)ₐC₀F₂d+₁ or -CₓH₂ₓ-R(51);

\[ b \] is zero or 1;

\[ d \] is 1, 2, 3, 4, 5, 6 or 7;
x is zero, 1, 2, 3 or 4;

R(51) is (C$_{3}$-C$_{6}$)-cycloalkyl, phenyl, biphenylyl or naphthyl, where the aromatics are not substituted or are substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF$_{3}$, methyl, methoxy and NR(52)R(53);

R(52) and R(53) are hydrogen, (C$_{1}$-C$_{4}$)-alkyl or (C$_{1}$-C$_{4}$)-perfluoroalkyl;

R(47), R(48) and R(50) independently are hydrogen, (C$_{1}$-C$_{4}$)-alkyl or (C$_{1}$-C$_{4}$)-perfluoroalkyl;

R(49) is defined as R(46);

or

R(46) and R(47), or R(46) and R(48) together are 4 or 5 methylene groups, of which one CH$_{2}$ groups can be replaced by oxygen, sulfur, NH, N-CH$_{3}$ or N-benzyl;

where A and N$^{(*)}$ are bonded to the phenyl nucleus of the heteroaroylguanidine parent structure;

or

R(3), R(4), R(5), R(6) and R(7) independently of one another are -SR(64), -OR(65), -NHR(66), -NR(67)R(68), -CHR(69)R(70) or -CR(54)R(55)OH, -C=CR(56), -CR(58)=CR(57) or -[CR(59)R(60)]$_{u}$-CO-[CR(61)R(62)]$_{v}$-R(63);

R(64), R(65), R(66), R(67) and R(69) identically or differently are

-(CH$_{2}$)$_{y}$-(CHOH)$_{z}$-(CH$_{2}$)$_{as}$-(CHOH)$_{t}$-R(71) or

-(CH$_{2}$)$_{ab}$-O-(CH$_{2}$-CH$_{2}$O)$_{ac}$-R(72);

R(71) and R(72) independently of one another are hydrogen or methyl;

u is 1, 2, 3 or 4;

v is zero, 1, 2, 3 or 4;
y, z, a identically or differently are zero, 1, 2, 3 or 4;

\( t \) is 1, 2, 3 or 4;

\( R(68), R(70), R(54) \) and \( R(55) \)

5 identically or differently are hydrogen or \((C_1-C_6)\)-alkyl;

or

\( R(69) \) and \( R(70) \), or \( R(54) \) and \( R(55) \)

together with the carbon atom carrying them are \((C_3-C_6)\)-cycloalkyl;

\( R(63) \)

is hydrogen, \((C_1-C_6)\)-alkyl, \((C_3-C_6)\)-cycloalkyl or \(-C_6H_{120}^*\) \( R(73) \);

\( e \) is zero, 1, 2, 3 or 4;

\( R(56), R(57) \) and \( R(73) \) independently

are phenyl, which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of \( F \), \( Cl \), \( CF_3 \), methyl, methoxy and \( NR(74)R(75) \);

\( R(74) \) and \( R(75) \)

are hydrogen or \((C_1-C_6)\)-alkyl;

or

\( R(56), R(57) \) and \( R(73) \) independently

are \((C_1-C_6)\)-heteroaryl, which is unsubstituted or substituted as phenyl;

\( R(58), R(59), R(60), R(61) \) and \( R(62) \)

are hydrogen or methyl;

\( R(3), R(4), R(5), R(6) \) and \( R(7) \)

independently of one another are \( R(76)-NH-SO_2^- \);

\( R(76) \) is \( R(77)R(78)N-(C=Y')^- \);

\( Y' \) is oxygen, \( S \) or \( N-R(79) \);

\( R(77) \) and \( R(78) \)

identically or differently are hydrogen, \((C_1-C_6)\)-alkyl, \((C_3-C_6)\)-alkenyl or \(-C_6H_{20}^*\) \( R(80) \);
f is zero, 1, 2, 3 or 4;

R(80) is (C₅₋C₇)-cycloalkyl or phenyl, which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methoxy and (C₆₋C₈)-alkyl;

or

R(77) and R(78) together are 4 or 5 methylene groups, of which one CH₂ group can be replaced by oxygen, sulfur, NH, N-CH₃ or N-benzyl;

R(79) is defined as R(77) or is amidine;

or

R(3), R(4), R(5), R(6) and R(7) independently of one another are NR(84a)R(85), OR(84b), SR(84c)
or

-CₙH₂n-R(84d);

n is zero, 1, 2, 3 or 4;

R(84d) is (C₅₋C₇)-cycloalkyl or phenyl, which is not substituted or is substituted by 1 - 3 substituents from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(16)R(17);

R(16) and R(17) are hydrogen or C₁₋C₈-alkyl;

R(84a), R(84b), R(84c) and R(85) independently of one another are hydrogen, (C₁₋C₉)-alkyl,

(C₁₋C₈)-perfluoroalkyl or (CH₂)ₐ₋ₚ-R(84g);

ax is zero, 1, 2, 3 or 4;

R(84g) is (C₅₋C₇)-cycloalkyl or phenyl, which is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(84u)R(84v);

R(84u) and R(84v)
are hydrogen or C₁-C₄-alkyl; 

or 

R(84a) and R(85) 

together are 4 or 5 methylene groups, of which one CH₂ 

group can be replaced by oxygen, sulfur, NH, N-CH₃ or 

N-benzyl, 

and their pharmaceutically tolerable salts; 

z) benzyloxyguanidines of the formula I 

\[
\begin{align*}
R(1) & \quad R(2) \quad R(3) \\
R(4) & \quad R(5) \\
\end{align*}
\]

in which: 

R(1) is \(R(6)-SO_{m}\);  

m is zero, 1 or 2;  

R(6) is perfluoroalkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, which 

is straight-chain or branched;  

R(2) and R(3) 

independently of one another are hydrogen, F, Cl, Br, I, alkyl having 

1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms 

or phenoxy, 

which is unsubstituted or substituted by 1 - 3 substituents 

selected from the group consisting of F, Cl, methyl and 

methoxy; 

or 

R(2) and R(3) 

independently of one another are pyrrol-1-yl, pyrrol-2-yl or pyrrol-3-yl, 

which is not substituted or is substituted by 1 to 4
substituents selected from the group consisting of F, Cl, Br, I, CN, alkanoyl having 2, 3, 4, 5, 6, 7 or 8 carbon atoms, alkoxyformyl having 2, 3, 4, 5, 6, 7 or 8 carbon atoms, formyl, carboxyl, CF₃, methyl and methoxy;

R(4) and R(5) independently of one another are hydrogen, alkyl having 1, 2 or 3 carbon atoms, F, Cl, Br, I, CN, OR(7), NR(8)R(9) or -(CH₂)ₙ-(CF₂)₀-CF₃;

R(7), R(8) and R(9) independently of one another are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

n is zero or 1;

o is zero, 1 or 2;

and their pharmacologically acceptable salts;

aa) phenyl-substituted alkenylcarboxylic acid guanidides, carrying perfluoroalkyl groups, of the formula I

in which:

R(A) is hydrogen, F, Cl, Br, I, CN, OH, OR(6), (C₁-C₈)-alkyl,

O₃(CH₂)a-C₆-F₂b+1, (C₃-C₈)-cycloalkyl or NR(7)R(8);

r is zero or 1;

a is zero, 1, 2, 3 or 4;
b is 1, 2, 3, 4, 5, 6, 7 or 8;
R(6) is (C₁-C₈)-alkyl, (C₁-C₄)-perfluoroalkyl, (C₃-C₆)-alkenyl, (C₃-C₆)-cycloalkyl, phenyl or benzyl;

where the aromatics are not substituted or are substituted by 1 - 3 substituents from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(9)R(10);
R(9) and R(10)
are H, (C₁-C₄)-alkyl or (C₁-C₄)-perfluoroalkyl;

R(7) and R(8)
are independently of one another defined as R(6);
or
R(7) and R(8)
together are 4 or 5 methylene groups, of which one CH₂

R(B) independently defined as R(A);
x is zero, 1 or 2;
y is zero, 1 or 2;

R(C) is hydrogen, F, Cl, Br, I, CN, OR(12), (C₁-C₈)-alkyl, Oₚ(CH₂)ₗCₜF₉₊ₙ, or (C₃-C₆)-cycloalkyl;
p is zero or 1;
f is zero, 1, 2, 3 or 4;
g is 1, 2, 3, 4, 5, 6, 7 or 8;

R(12)
is (C₁-C₈)-alkyl, (C₁-C₄)-perfluoroalkyl, (C₃-C₆)-alkenyl, (C₃-C₆)-cycloalkyl, phenyl or benzyl;
where the aromatics phenyl or benzyl are not substituted or are substituted by 1 - 3 substituents from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(13)R(14);
R(13) and R(14)
independently of one another are H, (C₁₋₄)-alkyl or (C₁₋₄)-perfluoroalkyl;

R(D) independently is defined as R(C),

R(1) is hydrogen, (C₁₋₄)-alkyl, -O(CH₂)₉C₆F₂e+1, (C₃₋₄)-cycloalkyl, F, Cl,
Br, I or CN;

t is zero or 1;
d is zero, 1, 2, 3 or 4;
e is 1, 2, 3, 4, 5, 6, 7 or 8;
R(2), R(3), R(4) and R(5)

independently of one another are defined as R(1);

but with the condition

that at least one of the substituents R(A), R(B), R(C), R(D), R(1), R(2), R(4) or R(5) is a

O(CH₂)₉C₆F₂e+1, O₂(CH₂)₉C₆F₂e+1 or O₄(CH₂)₉C₆F₂e+1 group and

R(3) is not a O₄(CH₂)₉C₆F₂e+1 group;

and their pharmaceutically tolerable salts;

ab) ortho-amino-substituted benzoylguanidines of the formula I

in which:

R(1) is NR(50)R(6),

R(50) and R(6)

independently of one another are hydrogen, (C₁₋₄)-alkyl or
(C₁₋₄)-perfluoroalkyl;

R(2), R(3), R(4) and R(5)

independently of one another are R(10)-SO₄⁻, R(11)R(12)N-CO⁻,

R(13)-CO⁻ or R(14)R(15)N-SO₄⁻;

a is zero, 1 or 2,

R(10), R(11), R(12), R(13), R(14) and R(15)
independently of one another are (C1-C6)-alkyl, (C1-C6)-perfluoroalkyl, (C2-C6)-alkenyl or -C_{ab}H_{2ab}-R(16);
ab is zero, 1, 2, 3 or 4;
R(16) is (C3-C7)-cycloalkyl, phenyl,
which is not substituted or is substituted by 1 - 3
substituents selected from the group consisting of F, Cl, CF3, methyl, methoxy and NR(17)R(18);
R(17) and R(18)
independently of one another are H, CF3 or
(C1-C4)-alkyl;
or
R(11), R(12), and also R(14) and R(15)
together are 4 or 5 methylene groups, of which one
CH2 group can be replaced by oxygen, S, NH, N-CH3
or N-benzyl;
or
R(11), R(12), R(14) and R(15)
independently of one another are hydrogen;
or
R(2), R(3), R(4) and R(5)
independently of one another are SR(21), -OR(22), -NR(23)R(24) or
-CR(25)R(26)R(27);
R(21), R(22), R(23) and R(25)
independently of one another are -C_bH_{2b}(C1-C6)-heteroaryl,
which is unsubstituted or substituted by 1 - 3 substituents
selected from the group consisting of F, Cl, CF3, CH3,
methoxy, hydroxyl, amino, methylamino and dimethylamino;
b is zero, 1 or 2;
R(24), R(26) and R(27)
independently of one another are hydrogen, (C1-C4)-alkyl or
(C1-C4)-perfluoroalkyl;
R(2), R(3), R(4) and R(5)

independently of one another are hydrogen, F, Cl, Br, I, CN,
-\((Xa)_{dg}^{-}\)C_{da}H_{2da+1}, \((Xb)_{dh}^{-}\)(CH_{2}^{de})C_{de}F_{2de+1}, (C_{3}-C_{6})-alkenyl or
\(-C_{df}^{de}H_{2df}R(30);

\(5\)

\((Xa)\) is O, S or NR(33);

R(33)

is H, (C_{1}-C_{4})-alkyl or (C_{1}-C_{4})-perfluoroalkyl;

dg is zero or 1;

\((Xb)\) is O, S or NR(34);

R(34)

is H, (C_{1}-C_{4})-alkyl or (C_{1}-C_{4})-perfluoroalkyl;

dh is zero or 1;

da is zero, 1, 2, 3, 4, 5, 6, 7, 8;

db is zero, 1, 2, 3, 4;

de is zero, 1, 2, 3, 4, 5, 6, 7;

df is zero, 1, 2, 3, 4;

R(30)

is (C_{3}-C_{6})-cycloalkyl, phenyl, biphenyl or naphthyl, where
the aromatics phenyl, biphenyl or naphthyl are not
substituted or are substituted by 1 - 3 substituents selected
from the group consisting of F, Cl, CF_{3}, methyl, methoxy and
NR(31)R(32);

R(31) and R(32)

are H, (C_{1}-C_{4})-alkyl or (C_{1}-C_{4})-perfluoroalkyl;

or

R(2), R(3), R(4) and R(5)

independently of one another are NR(40)R(41) or -(Xe)-
(CH_{2})^{eb}R(45);

R(40) and R(41)

\(30\)

independently of one another are hydrogen, (C_{1}-C_{4})-alkyl,
(C_{1}-C_{6})-perfluoroalkyl or (CH_{2})^{e}R(42);

e is zero, 1, 2, 3 or 4;
R(42) is \((C_3-C_7)\)-cycloalkyl, phenyl, which is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF\(_3\), methyl, methoxy and NR(43)R(44);

R(43) and R(44) independently of one another are H, CF\(_3\) or \((C_1-C_4)\)-alkyl;

or

R(40) and R(41) together are 4 or 5 methylene groups, of which one CH\(_2\) group can be replaced by oxygen, sulfur, NH, N-CH\(_3\) or N-benzyl;

(Xe) is O, S or NR(47);

R(47) is H, \((C_1-C_4)\)-alkyl or \((C_1-C_4)\)-perfluoroalkyl;

eb is zero, 1, 2, 3 or 4;

R(45) is \((C_3-C_7)\)-cycloalkyl, phenyl, which is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF\(_3\),methyl, methoxy, NR(50)R(51) and - (Xfa)-(CH\(_2\))\(_{ed}\)-(Xfb)R(46);

Xfa is CH\(_2\), O, S or NR(48);

Xfb is O, S or NR(49);

ed is 1, 2, 3 or 4;

R(46) is H, \((C_1-C_4)\)-alkyl or \((C_1-C_4)\)-perfluoroalkyl;

R(48), R(49), R(50) and R(51) independently of one another are H or \((C_1-C_4)\)-alkyl or \((C_1-C_4)\)-perfluoroalkyl;

where R(3) and R(4), however, cannot be hydrogen, and their pharmaceutically tolerable salts;
ac) t-zoarylguanidines of the formula I

in which:

one of the three substituents \( R(1) \), \( R(2) \) and \( R(3) \)

is \((C_1-C_9)\)-heteroaryl-N-oxide,

which is linked to a \( C \) or \( N \) and which is unsubstituted or

substituted by 1 - 3 substituents selected from the group

consisting of \( F \), \( Cl \), \( CF_3 \), \( CH_3 \), methoxy, hydroxyl, amino,

methylamino and \( \alpha \)-methylamino;

or

one of the three substituents \( R(1) \), \( R(2) \) and \( R(3) \)

is \(-SR(10)\), \(-OR(10)\), \(-NR(10)R(11)\) or \(-CR(10)R(11)R(12)\);

\( R(10) \)

is \(-C_\alpha H_{2\alpha}(C_1-C_9)\)-heteroaryl-N-oxide,

which is unsubstituted or substituted by 1 - 3

substituents selected from the group consisting of \( F \),

\( Cl \), \( CF_3 \), \( CH_3 \), methoxy, hydroxyl, amino, methylamino

and dimethylamino;

\( a \)

is zero, 1 or 2;

\( R(11) \) and \( R(12) \)

independently of one another are defined as \( R(10) \),

are hydrogen or \((C_1-C_9)\)-alkyl;

and the other substituents \( R(1) \), \( R(2) \) and \( R(3) \) in each case

independently of one another are \((C_1-C_9)\)-alkyl, \((C_2-C_9)\)-alkenyl or

\(-C_m H_{2m} R(14)\);

\( m \)

is zero, 1 or 2;
R(14) is (C₃-C₈)-cycloalkyl or phenyl, which is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and

NR(15)R(16),

R(15) and R(16) are hydrogen or CH₃;

or

the other substituents R(1), R(2) and R(3) in each case independently of one another are hydrogen, F, Cl, Br, I, -C≡N, X-(CH₂)ₚ-(C₉F₂₀+₁), R(22)-SOᵤ, R(23)R(24)N-CO, R(25)-CO- or R(26)R(27)N-SO₂⁺, where the perfluoroalkyl group is straight-chain or branched;

X is a bond, oxygen, S or NR(28);

u is zero, 1 or 2;

p is zero, 1 or 2;

q is zero, 1, 2, 3, 4, 5 or 6;

R(22), R(23), R(25) and R(26) independently are (C₁-C₆)-alkyl, (C₂-C₆)-alkenyl, -OH₂, -R(29) or CF₃;

n is zero, 1, 2, 3 or 4;

R(28) is hydrogen or (C₁-C₃)-alkyl;

R(29) is (C₃-C₇)-cycloalkyl or phenyl, which is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and

NR(30)R(31);

R(30) and R(31) are hydrogen or C₁-C₄-alkyl,

or

R(23), R(25) and R(26) are also hydrogen;
R(24) and R(27) independently of one another are hydrogen or (C₁-C₄)-alkyl;

or

R(23) and R(24), and also R(26) and R(27) together are 4 or 5 methylene groups, of which one CH₂ group can be replaced by oxygen, S, NH, N-CH₃ or N-benzyl;

or

the other substituents R(1), R(2) and R(3) in each case independently of one another are OR(35) or NR(35)R(36);

R(35) and R(36) independently of one another are hydrogen or (C₁-C₅)-alkyl;

or

R(35) and R(36) together are 4-7 methylene groups, of which one CH₂ group can be replaced by oxygen, S, NH, N-CH₃ or N-benzyl,

R(4) and R(5) independently of one another are hydrogen, (C₁-C₄)-alkyl, F, Cl, -OR(32), -NR(33)R(34) or C₅F₁₊₁;

R(32), R(33) and R(34) independently of one another are hydrogen or (C₁-C₃)-alkyl;

r is 1, 2, 3 or 4;

and their pharmaceutically tolerable salts;

ad) benzoylguanidines of the formula I

in which:
R(1) is hydrogen, F, Cl, Br, I, CN, NO₂, OH, (C₁-C₈)-alkyl, (C₃-C₆)-cycloalkyl, Oₕ(CH₂)ₘ(CF₃)ₙ-CF₃;
    a is zero or 1;
    b is zero, 1 or 2;
    c is zero, 1, 2 or 3;

or

R(1) is R(5)-SOₘ or R(6)R(7)N-SO₂⁻;
    m is zero, 1 or 2;
R(5) and R(6) independently of one another

are (C₁-C₈)-alkyl, (C₃-C₆)-alkenyl, CF₃ or -CₙH₂ₙ-R(8);
    n is zero, 1, 2, 3 or 4;

R(7) is hydrogen or (C₁-C₄)-alkyl;

R(8) is (C₃-C₇)-cycloalkyl or phenyl,
    which is not substituted or is substituted by 1 - 3

substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(9)R(1₀);
R(9) and R(1₀) independently of one another

are hydrogen or (C₁-C₄)-alkyl;

or

R(6) is H;

or R(6) and R(7)

together are 4 or 5 methylene groups, of which one CH₂ group can be replaced by oxygen, S, NH, N-CH₃ or N-benzyl,

or

R(1) is -SR(1₁), -OR(1₁) or -CR(1₁)R(1₂)R(1₃);
R(1₁) is -CₚH₂ₙ-(C₃-C₆)-cycloalkyl, -(C₁-C₉)-heteroaryl or phenyl,
    where the aromatic systems are unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methyamino and dimethylamino;

R(1₂), R(1₃) independently of one another
are defined as R(1) or are hydrogen or (C₁-C₄)-alkyl;

\[ p \] is zero, 1 or 2;

R(1) is phenyl, naphthyl, biphenylyl or (C₁-C₉)-heteroaryl, the latter linked via C or N,
which are unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino and dimethylamino;

R(2) is -CF₂R(14), -CF[R(15)][R(16)], -CF[(CF₂)ₜ-CF₃][R(15)],
-C[[CF₂]ₕ-CF₃]=CR(15)R(16);
R(14) is (C₁-C₄)-alkyl or (C₃-C₆)-cycloalkyl;
R(15) and R(16) independently of one another
are hydrogen or (C₁-C₄)-alkyl;

q is zero, 1 or 2;
r is zero, 1 or 2;
R(3) is defined as R(1);
R(4) is hydrogen, (C₁-C₃)-alkyl, F, Cl, Br, I, CN, -(CH₂)ₖ-(CF₂)ₜ-CF₃;
s is zero or 1;
t is zero, 1 or 2;
and their pharmaceutically tolerable salts;

ae) benzoylguanidines of the formula

\[ \text{I} \]

in which:
one of the three substituents R(1), R(2) and R(3)
is -Y-4-[(CH₂)ₖ-CHR(7)-(C=O)R(8)]-phenyl,
-Y-3-[(CH₂)ₖ-CHR(7)-(C=O)R(8)]-phenyl or
-Y-2-[(CH₂)ₖ-CHR(7)-(C=O)R(8)]-phenyl,
where the phenyl in each case is unsubstituted or substituted
by 1 - 2 substituents from the group F, Cl, -CF₃, methyl,
hydroxyl, methoxy, or -NR(37)R(38);
R(37) and R(38)
independently of one another are hydrogen or -CH₃;
Y is a bond, oxygen, -S- or -NR(9);
R(9) is hydrogen or -(C₁₋₄)-alkyl;
R(7) is -OR(10) or -NR(10)R(11);
R(10) and R(11)
independently of one another are hydrogen, -(C₁₋₃)-alkyl,
-(C₁₋₃)-alkanoyl, -(C₁₋₃)-alkoxycarbonyl,
benzyl, benzyloxycarbonyl;
or
R(10) is trityl;
R(8) is -OR(12) or -NR(12)R(13);
R(12) and R(13)
independently of one another are hydrogen, -(C₁₋₃)-alkyl or benzyl;
k is zero, 1, 2, 3 or 4;
and the other radicals R(1), R(2) and R(3) in each case
independently of one another are -(C₁₋₃)-alkyl, -(C₂₋₃)-alkenyl or
-(CH₂)ₘR(14);
m is zero, 1 or 2;
R(14) is -(C₃₋₆)-cycloalkyl or phenyl,
which is not substituted or is substituted by 1 - 3 substituents
selected from the group consisting of F, Cl, -CF₃, methyl,
methoxy and -NR(15)R(16);
R(15) and R(16)
are hydrogen or -CH₃;
or

the other radicals R(1), R(2) and R(3) in each case

independently of one another are R(18)R(19)N-(C=\text{Y}')-NH-SO_2-;

\text{Y}' is oxygen, -S- or -N-R(20);

R(18) and R(19)

independently of one another are hydrogen, -(C_1-C_6)-alkyl,

-(C_3-C_6)-alkenyl or -(CH_2)_t-R(21);

\text{t is zero, 1, 2, 3 or 4};

R(21) is -(C_5-C_7)-cycloalkyl or phenyl,

which is unsubstituted or substituted by 1 - 3

substituents selected from the groups consisting of F,

Cl, -CF_3, methoxy and -(C_1-C_4)-alkyl;

or

R(18) and R(19)

together are 4 or 5 methylene groups, of which one CH_2

group can be replaced by oxygen, -S-, -NH-, -N-CH_3 or -N-benzyl;

R(20)

is defined as R(18) or is amidine;

or

the other radicals R(1), R(2) and R(3) in each case

independently of one another are hydrogen, F, Cl, Br, I, -C=N,

X-(CH_2)_p-(C_qF_{2q+1}), R(22)-SO_2-, R(23)R(24)N-CO-, R(25)-CO- or

R(26)R(27)N-SO_2-, where the perfluoroalkyl group is straight-chain

or branched;

X is a bond, oxygen, -S- or -NR(28);

\text{u is zero, 1 or 2};

\text{p is zero, 1 or 2};

\text{q is 1, 2, 3, 4, 5 or 6};

R(22), R(23), R(25) and R(26)

independently of one another are -(C_1-C_6)-alkyl,

-(C_3-C_6)-alkenyl, -(CH_2)_n-R(29) or -CF_3;
n is zero, 1, 2, 3 or 4;
R(28) is hydrogen or \(-(\text{C}_1\text{-C}_3)\)-alkyl;
R(29) is \(-(\text{C}_2\text{-C}_7)\)-cycloalkyl or phenyl,
which is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F, Cl, -CF₃, methyl, methoxy and -NR(30)R(31);
R(30) and R(31)
are hydrogen or \(-(\text{C}_1\text{-C}_4)\)-alkyl;
or
10 R(23), R(25) and R(26)
are hydrogen;
R(24) and R(27)
independently of one another are hydrogen or \(-(\text{C}_1\text{-C}_4)\)-alkyl;
or
15 R(23) and R(24), and also R(26) and R(27)
together are 4 or 5 methylene groups, of which one CH₂ group can be replaced by oxygen, -S-, -NH-, -N-CH₃ or -N-benzyl;
or
20 the other radicals R(1), R(2) and R(3) in each case independently of one another are \(-\text{OR}(35)\) or \(-\text{NR}(35)\text{R}(36)\);
R(35) and R(36)
independently of one another are hydrogen or \(-(\text{C}_1\text{-C}_3)\)-alkyl;
or
25 R(35) and R(36)
together are 4 - 7 methylene groups, of which one CH₂ group can be replaced by oxygen, -S-, -NH-, -N-CH₃ or -N-benzyl;
R(4) and R(5)
independently of one another are hydrogen, \(-(\text{C}_1\text{-C}_4)\)-alkyl, F, Cl,
\(-\text{OR}(32), -\text{NR}(33)\text{R}(34)\) or \(-\text{C}_r\text{F}_{2r+1}\);
R(32), R(33) and R(34)
independently of one another are hydrogen or \(-(\text{C}_1\text{-C}_3)\)-alkyl;
r is 1, 2, 3 or 4;
and their pharmaceutically tolerable salts;

af) benzoylguanidines of the formula I

\[
\begin{align*}
\text{R(1)} & \text{ is R(6)-CO or R(7)R(8)N-CO;} \\
\text{R(6)} & \text{ is (C}_{1-6}\text{)-alkyl, (C}_{1-6}\text{)-perfluoroalkyl, (C}_{3-6}\text{)-alkenyl} \\
& \text{or -C}_{n}\text{H}_{2n}\text{-R(9),} \\
n & \text{ is zero, 1, 2, 3 or 4;} \\
\text{R(9)} & \text{ is (C}_{3-6}\text{)-cycloalkyl, phenyl, biphenylyl or} \\
& \text{ naphthyl,} \\
& \text{ where the aromatics are not substituted} \\
& \text{ or are substituted by 1 - 3 substituents} \\
& \text{ selected from the group consisting of F,} \\
& \text{ Cl, CF}_3\text{, methyl, methoxy and} \\
& \text{ NR(10)R(11),} \\
\text{R(10) and R(11)} & \text{ are H, (C}_{1-4}\text{)-alkyl or (C}_{1-4}\text{-)} \\
& \text{ perfluoroalkyl;} \\
\text{R(7)} & \text{ is H, (C}_{1-6}\text{)-alkyl, (C}_{1-6}\text{)-perfluoroalkyl, (C}_{3-6}\text{-)} \\
& \text{ alkenyl or -C}_{n}\text{H}_{2n}\text{-R(12);} \\
n & \text{ is zero, 1, 2, 3 or 4;} \\
\text{R(12)} & \text{ is (C}_{3-6}\text{)-cycloalkyl, phenyl, biphenylyl or} \\
& \text{ naphthyl,} \\
& \text{ where the aromatics are not substituted} \\
& \text{ or are substituted by 1 - 3 substituents}
\end{align*}
\]
selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(13)R(14); R(13) and R(14) are H, (C₁₋₄)-alkyl or (C₁₋₄)-perfluoroalkyl;

- \( R(8) \) is H, (C₁₋₄)-alkyl or (C₁₋₄)-perfluoroalkyl;

or

- R(7) and R(8) together are 4 or 5 methylene groups, of which one CH₂ group can be replaced by oxygen, S, NH, N-OH₃ or N-benzyl;

- \( R(2) \) is defined as H, OH, F, Cl, Br, I, CN, NO₂, (C₁₋₄)-alkyl, (C₁₋₄)-perfluoroalkyl, (C₅₋₈)-alkenyl or -CₙH₂ₙR(15);

- \( n \) is zero, 1, 2, 3 or 4;

- \( R(15) \) is (C₃₋₉)-cycloalkyl, phenyl, biphenyl or naphthyl, where the aromatics are not substituted or are substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(16)R(17);

- \( R(16) \) and \( R(17) \) are H, (C₁₋₄)-alkyl or (C₁₋₄)-perfluoroalkyl;

or

- \( R(2) \) is (C₁₋₄)-heteroaryl, which is linked via C or N and which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino and dimethylamino;

or

- \( R(2) \) is SR(18), -OR(18), -NR(18)R(19) or -CR(18)R(19)R(20);

- \( R(18) \) is CₙH₂ₙ-(C₁₋₄)-heteroaryl, which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino,
dimethylamino; 

a is zero, 1 or 2; 

R(19) and R(20) 

independently of one another are defined as R(18) or 

are hydrogen, (C₁₋₄)-alkyl or (C₁₋₄)-perfluoroalkyl; 

or 

R(2) is R(21)-SO₃⁻ or R(22)R(23)N-SO₂⁻; 

m is 1 or 2; 

R(21) is (C₁₋₆)-alkyl, (C₁₋₆)-perfluoroalkyl, (C₃₋₆)-alkenyl or 

-CₙH₂ₙ-R(24); 

n is zero, 1, 2, 3 or 4; 

R(24) is (C₃₋₆)-cycloalkyl, phenyl, biphenylyl or naphthyl, 

where the aromatics are not substituted or are 

substituted by 1 - 3 substituents selected from 

the group consisting of F, Cl, CF₃, methyl, 

methoxy and NR(27)R(28); 

R(27) and R(28) 

are H, (C₁₋₄)-alkyl or (C₁₋₄)- 

perfluoroalkyl; 

R(22) is H, (C₁₋₆)-alkyl, (C₁₋₆)-perfluoroalkyl, (C₃₋₆)-alkenyl or 

-CₙH₂ₙ-R(29); 

n is zero, 1, 2, 3 or 4; 

R(29) is (C₃₋₆)-cycloalkyl, phenyl, biphenylyl or naphthyl, 

where the aromatics are not substituted 

or are substituted by 1 - 3 substituents 

selected from the group consisting of F, 

Cl, CF₃, methyl, methoxy and 

NR(30)R(31); 

R(30) and R(31) 

are H, (C₁₋₄)-alkyl or (C₁₋₄)- 

perfluoroalkyl; 

R(23) is hydrogen, (C₁₋₄)-alkyl or (C₁₋₄)-perfluoroalkyl;
R(22) and R(23) together are 4 or 5 methylene groups, of which one CH₂ group can be replaced by oxygen, S, NH, N-CH₃ or N-benzyl; or

R(2) is R(33)X⁻;

R(33) is (C₁₋C₈)-alkyl, (C₃₋C₈)-alkenyl, (CH₂)ₙC₆F₂d₁⁺ or -CₙH₂n⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻粲-

R(36) is (C₃₋C₈)-cycloalkyl, phenyl, biphenyl or naphthyl,

where the aromatics are not substituted or are substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(37)R(38);

R(37) and R(38) are H, (C₁₋C₄)-alkyl or (C₁₋C₄)-perfluoroalkyl;

R(34) is hydrogen, (C₁₋C₄)-alkyl or (C₁₋C₄)-perfluoroalkyl;

R(35) is defined as R(33);

or

R(33) and R(34) together are 4 or 5 methylene groups, of which one CH₂ group can be replaced by oxygen, S, NH, N-CH₃ or N-benzyl;

where A and N⁽ⁿ⁾ are bonded to the phenyl nucleus of the
benzoylguanidine parent structure;

or

\[ R(2) \text{ is } -SR(40), -OR(40), -NHR(40), -NR(40)R(41), -CHR(40)R(42), -CR(42)R(43)OH, -C=CR(45), -CR(46)=CR(45) \text{ or} \]

\[ -[CR(47)R(48)]_u-CO-[C(R49)R(50)]_v-R(44); \]

\[ R(40) \text{ and } R(41) \]

independently of one another are \(-(CH_2)_p-(CHOH)_q-(CH_2)_r-(CHOH)_t-R(51)\) or \(-(CH_2)_p-O-(CH_2-CH_2O)_q-R(51)\); \n
\[ R(51) \text{ is hydrogen or methyl;} \]

\[ u \text{ is } 1, 2, 3 \text{ or } 4; \]

\[ v \text{ is zero, } 1, 2, 3 \text{ or } 4; \]

\[ p, q \text{ and } r \]

independently of one another are zero, 1, 2, 3 or 4;

\[ t \text{ is } 1, 2, 3 \text{ or } 4; \]

\[ R(42) \text{ and } R(43) \]

independently of one another are hydrogen or \((C_1-C_6)-alkyl\);

or

\[ R(42) \text{ and } R(43) \]

together with the carbon atom carrying them are a \((C_3-C_8)-cycloalkyl\);

\[ R(44) \text{ is hydrogen, } (C_1-C_6)-alkyl, (C_3-C_8)-cycloalkyl, -C_6H_{25}-R(45); \]

\[ e \text{ is zero, } 1, 2, 3 \text{ or } 4; \]

\[ R(45) \text{ is phenyl,} \]

which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF_3, methyl, methoxy and NR(52)R(53);

\[ R(52) \text{ and } R(53) \]

are H or \((C_1-C_4)-alkyl\);

or

\[ R(45) \text{ is } (C_1-C_6)-heteroaryl, \]

which is unsubstituted or substituted as phenyl;

or
R(45) is (C_{1}-C_{6})-alkyl,
which is unsubstituted or substituted by 1 - 3 OH;
R(46), R(47), R(48), R(49) and R(50)
individually of one another are hydrogen or methyl;

5     or

R(2) is R(55)-NH-SO_{2}^{-};
R(55) is R(56)R(57)N-(C=Y)-;
Y is oxygen, S or N-R(58);
R(56) and R(57)
10    independently of one another are hydrogen, (C_{1}-C_{6})-alkyl,
(C_{3}-C_{6})-alkenyl or -C_{6}H_{2}-R(59);
\( f \) is zero, 1, 2, 3 or 4;
R(59) is (C_{5}-C_{7})-cycloalkyl, phenyl,
which is unsubstituted or substituted by 1 - 3 substituents selected from the
15    group consisting of F, Cl, CF_{3}, methoxy
and (C_{1}-C_{4})-alkyl;
or
R(56) and R(57)
20    together are 4 or 5 methylene groups, of which one CH_{2}
group can be replaced by oxygen, S, NH, N-CH_{3} or N-benzyl;
R(58)
is defined as R(56) or is amidine;
R(3), R(4) and R(5) are independently of one another defined as R(1) or
R(2), but where at least one of the substituents R(2), R(3), R(4) and R(5)
must be OH;
and their pharmaceutically tolerable salts;
ag) benzoylguanidines of the formula \( I \)

\[
\begin{align*}
\text{R(2)} & \quad \text{R(5)} \\
\text{R(3)} & \quad \text{N} \quad \text{NH}_2 \\
\text{R(4)} & \quad \text{O} \quad \text{NH}_2
\end{align*}
\]

in which:

one of the three substituents \( \text{R(1)}, \text{R(2)} \) and \( \text{R(3)} \)

is \( \text{R(6)}-\text{A-B-D} \);

\( \text{R(6)} \) is a basic protonatable radical, i.e. an amino group

\(-\text{NR(7)}\text{R(8)}\), an amidino group \( \text{R(7)}\text{R(8)}\text{N-}\text{C[\text{N-R(9)}]} \) - or a

guanidino group

\[
\begin{align*}
\text{R(7)} & \quad \text{R(10)} \\
\text{R(8)} & \quad \text{N} \\
\text{R(9)} & \quad \text{N}
\end{align*}
\]

\( \text{R(7)}, \text{R(8)}, \text{R(9)} \) and \( \text{R(10)} \)

independently of one another are hydrogen or alkyl

having 1, 2, 3 or 4 carbon atoms;

or

\( \text{R(7)} \) and \( \text{R(8)} \)

together are \( \text{C}_a\text{H}_{2a} \);

\( a \) is 4, 5, 6 or 7;

where if \( a = 5, 6 \) or 7 a methylene group of the group

\( \text{C}_a\text{H}_{2a} \) can be replaced by a heteroatom group \( \text{O, SO}_m \)

or \( \text{NR(11)} \),

or

\( \text{R(8)} \) and \( \text{R(9)} \) or \( \text{R(9)} \) and \( \text{R(10)} \) or \( \text{R(7)} \) and \( \text{R(10)} \)

are a group \( \text{C}_a\text{H}_{2a} \);

\( a \) is 2, 3, 4 or 5;
where if \( a = 3, 4 \) or \( 5 \) a methylene group of the 
group \( C_{a}H_{2a} \) can be replaced by a heteroatom 
group O, \( SO_{m} \) or \( NR(11) \); 
\[ m \text{ is zero, 1 or 2;} \]

\[ R(11) \text{ is hydrogen or methyl;} \]
or

\[ R(6) \text{ is a basic heteroaromatic ring system having 1 - 9 carbon atoms;} \]
\[ A \text{ is } C_{b}H_{2b}; \]
\[ b \text{ is } 1, 2, 3, 4, 5, 6, 7, 8, 9 \text{ or } 10; \]

where in the group \( C_{b}H_{2b} \) one or two methylene groups 
can be replaced by one of the groupings selected from 
the group consisting of \(-O-, -CO-, -CH[OR(20)]-, \]
\(-SO_{m}-, -NR(20)-, -NR(20)-CO-, -NR(20)-CO-NH-, \]
\[ -NR(20)-CO-NH-SO_{2}- \]
\[ \begin{array}{c}
(0)_{aa} \\
\| \\
- R(20) N - S - \\
\| \\
\text{INR}(19)_{bb} 
\end{array} \]

\[ \text{and } -SO_{aa}[NR(19)]_{bb}^{-}; \]

and where in the group \( C_{b}H_{2b} \) a methylene group can 
be replaced by \(-CH-R(99)\), where \( R(99) \) together with 
\( R(7) \) forms a pyrrolidine or piperidine ring;
\[ aa \text{ is 1 or 2;} \]
\[ bb \text{ is 0 or 1;} \]
\[ aa + bb = 2; \]

\[ R(19) \text{ is hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;} \]
\[ R(20) \text{ is hydrogen or methyl;} \]
B is a phenylene or naphthylene radical

\[
\begin{array}{c}
\text{R(12)} \\
\text{R(13)}
\end{array}
\]

\[
\begin{array}{c}
\text{R(12)} \\
\text{R(13)}
\end{array}
\]

R(12) and R(13) independently of one another are hydrogen, methyl, F, Cl, Br, I, CF₃ or -SOₓ-R(14);
R(14) is methyl or NR(15)R(16);
R(15) and R(16) independently of one another are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;
w is zero, 1 or 2;
D is \(-\text{C}_d\text{H}_{2d}\text{-X}_f\);
d is zero, 1, 2, 3 or 4;
X is \(-\text{O}_x\), \(-\text{CO}_x\), \(-\text{CH[OR(21)]}_x\), \(-\text{SO}_m\text{-}x\) or \(-\text{NR(21)}_x\);
f is zero or 1;
R(21) is hydrogen or methyl;
m is zero, 1 or 2;
and the other substituents R(1) and R(2) and R(3) in each case independently of one another are hydrogen, F, Cl, Br, I, -CN, -(C₁-C₄)-alkyl, -(C₂-C₃)-alkenyl, -NR(35)R(36) or R(17)-C₇H₁₇-Zₙ-;
g is zero, 1, 2, 3 or 4;
h is zero or 1;
R(35) and R(36) independently of one another are hydrogen or alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms;
or
R(35) and R(36) together are 4 - 7 methylene groups, of which one CH₂ group.
can be replaced by oxygen, -S-, -NH-, -NCH₃ or -N-benzyl;

Z is -O-, -CO-, -SO₂-, -NR(18)-, -NR(18)-CO-, -NR(18)-CO-NH-
or -NR(18)-SO₂-;
R(18) is hydrogen or methyl;

v is zero, 1 or 2;
R(17) is hydrogen, cycloalkyl having 3, 5 or 6 carbon atoms or
C₃F₇₂k₊₁;
k is 1, 2 or 3,
or
R(17) is pyrrol-1-yl, pyrrol-2-yl or pyrrol-3-yl,
which is not substituted or is substituted by 1 - 4
substituents selected from the group consisting of F,
Cl, Br, I, -CN, (C₂₋C₈)-alkanoyl, (C₂₋C₈)-alkoxycarbonyl,
formyl, carboxyl, -CF₃, methyl and methoxy;

or
R(17) is (C₃₋C₈)-cycloalkyl or phenyl,
which is not substituted or is substituted by 1 - 3
substituents selected from the group consisting of F
and Cl, -CF₃, methyl, hydroxyl, methoxy,
-NR(37)R(38), CH₃SO₂- and H₂NO₂S-;
R(37) and R(38)
are hydrogen or -CH₃;

R(4) and R(5)
independently of one another are hydrogen, alkyl having 1, 2, 3 or 4
carbon atoms, F, Cl, -OR(32), -NR(33)R(34) or -C₁F₂k₊₁;
R(32), R(33) and R(34)
independently of one another are hydrogen or alkyl having 1,
2 or 3 carbon atoms;
r is 1, 2, 3 or 4;

and their pharmacologically tolerable salts;

ah) indenoylguanidines of the formula I
in which:

R(1) and R(2) independently of one another are hydrogen, alkyl having 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 carbon atoms, cycloalkyl having 3, 4, 5 or 6 carbon atoms, O-alkyl having 1, 2, 3 or 4 carbon atoms, O-C(=O)-alkyl having 1, 2, 3 or 4 carbon atoms or C_{m}H_{2m}-NR(12)R(13);

R(12) and R(13) independently of one another are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

m is zero, 1, 2, 3 or 4;

NH-C(=O)-NH_{2}, C(=O)-O-alkyl having 1, 2, 3 or 4 carbon atoms, C(=O)-NH_{2}, C(=O)-NH-alkyl having 1, 2, 3 or 4 carbon atoms, C(=O)-N(alkyl)_{2} having 1, 2, 3 or 4 carbon atoms in each alkyl group, alkenyl having 2, 3, 4, 5, 6, 7, 8, 9 or 10 carbon atoms, alkynyl having 2, 3, 4, 5, 6, 7, 8, 9 or 10 carbon atoms, alkylaryl having 1, 2, 3 or 4 carbon atoms in the alkyl group, alkenylaryl having 2, 3, 4, 5, 6, 7, 8, 9 or 10 carbon atoms in the alkenyl group, alkynylaryl having 2, 3, 4, 5, 6, 7, 8, 9 or 10 carbon atoms in the alkynyl group, C_{1}-C_{4} alkyl-substituted aryl, C_{1}-C_{4} alkylheteroaryl, C_{1}-C_{4} alkenylheteroaryl, aminoalkylaryl having 1, 2, 3 or 4 carbon atoms in the alkyl group, substituted aryl, heteroaryl and substituted heteroaryl;

R(3), R(4), R(5) and R(6) independently of one another are hydrogen, alkyl having 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 carbon atoms, O-alkyl having 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 carbon atoms, halogen, (such as F, Cl, Br, I), OH, aryl,
substituted aryl, heteroaryl, substituted heteroaryl, O-lower alkyl, O-aryl, O-lower alkylaryl, O-substituted aryl, O-lower alkyl-substituted aryl, O-C(=O)-C\textsubscript{1}-C\textsubscript{4}-alkylaryl, O-C(=O)-NH-C\textsubscript{1}-C\textsubscript{4}-alkyl, O-C(=O)-N(C\textsubscript{1}-C\textsubscript{4}-alkyl)\textsubscript{2}, NO\textsubscript{2}, CN, CF\textsubscript{3}, NH\textsubscript{2}, NH-C(=O)-C\textsubscript{1}-C\textsubscript{4}-alkyl, NH-C(=O)-NH\textsubscript{2}, COOH, C(=O)-O-C\textsubscript{1}-C\textsubscript{4}-alkyl, C(=O)-NH\textsubscript{2}, C(=O)-NH-C\textsubscript{1}-C\textsubscript{4}-alkyl, C(=O)-N(C\textsubscript{1}-C\textsubscript{4}-alkyl)\textsubscript{2}, C\textsubscript{1}-C\textsubscript{4}-COOH, C\textsubscript{1}-C\textsubscript{4}-alkyl-C(=O)-C\textsubscript{4}-alkyl, SO\textsubscript{3}H, SO\textsubscript{2}-alkyl, SO\textsubscript{2}-alkylaryl, SO\textsubscript{2}-N-(alkyl)\textsubscript{2}, SO\textsubscript{2}-N(alkyl)(alkylaryl), C(=O)-R(11), C\textsubscript{1}-C\textsubscript{10}-alkyl-C(=O)-R(11), C\textsubscript{2}-C\textsubscript{10}-alkenyl-C(=O)-R(11), C\textsubscript{2}-C\textsubscript{10}-alkynyl-C(=O)-R(11), NH-C(=O)-C\textsubscript{1}-C\textsubscript{10}-alkyl-C(=O)-R(11), O-C\textsubscript{1}-C\textsubscript{11}-alkyl-C(=O)-R(11); R(11) is C\textsubscript{1}-C\textsubscript{4}-alkyl, C\textsubscript{1}-C\textsubscript{4}-alkynyl, aryl, substituted aryl, NH\textsubscript{2}, NH-C\textsubscript{1}-C\textsubscript{4}-alkyl, N-(C\textsubscript{1}-C\textsubscript{4}-alkyl)\textsubscript{2}, SO\textsubscript{3}H, SO\textsubscript{2}-alkyl, SO\textsubscript{2}-alkylaryl, SO\textsubscript{2}-N-(alkyl)\textsubscript{2}, SO\textsubscript{2}-N(alkyl)(alkylaryl);

X is O, S or NH;

15 R(7), R(8), R(9) and R(10) independently of one another are hydrogen, alkyl, cycloalkyl, aryl, alkylaryl;

or R(8) and R(9) together are part of a 5, 6 or 7-membered heterocyclic ring;

A is absent or is a nontoxic organic or inorganic acid.

ai) benzyloxycarbonylguanidines of the formula I

\[
\begin{array}{c}
\text{R(2)} \quad \text{R(1)} \\
\text{R(3)} \quad \text{X} \quad \text{N} \quad \text{NH}_2 \\
\text{R(4)} \quad \text{R(5)} \quad \text{R(6)} \quad \text{R(7)} \\
\end{array}
\]

30 in which:

R(1), R(2) and R(3) independently of one another are -Y-[4-R(8)-phenyl], -Y-[3-R(8)-}
phenyl] or -Y-[2-R(8)-phenyl],

where the phenyl is in each case unsubstituted or substituted by 1 - 2 substituents from the group consisting of F, Cl, -CF₃, methyl, hydroxyl, methoxy and -NR(96)R(97);

R(96) and R(97)

independently of one another are hydrogen or -CH₃;

Y is a bond, CH₂, oxygen, -S- or -NR(9);

R(9) is hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

R(8) is SOₐ[NR(98)]ₐNR(99)R(10);

a is 1 or 2;

b is 0 or 1;

a + b = 2;

R(98), R(99) and R(10)

independently of one another are hydrogen, -(C₁-Cₙ)-alkyl, benzyl, -(C₂-Cₙ)-alkylene-NR(11)R(12), (C₂-Cₙ)-alkylene-NR(13)-(C₂-Cₙ)-alkylene-NR(37)R(38) or (C₀-Cₙ)-alkylene-CR(39)R(40)CR(41)R(42)(C₀-Cₙ)-alkylene-NR(43)R(44);

R(11), R(12), R(13), R(37), R(38), R(43) and R(44)

independently of one another are hydrogen, -(C₁-Cₙ)-alkyl or benzyl;

R(39), R(40), R(41) and R(42)

independently of one another are hydrogen, -(C₁-Cₙ)-alkyl or -(C₂-Cₙ)-alkylenephosphoryl, where the phenyl is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F, Cl, -CF₃, methyl and methoxy;

or

R(99) and R(10)

together are 4 - 6 methylene groups, of which one CH₂ group can be replaced by oxygen, -S-, -NH-, -N-CH₃ or
-N-benzyl;

or

R(8) is SO₂[NR(95)]₆NR(95)-C[=N-R(94)]-NR(93)R(92);
R(92), R(93), R(94) and R(95) independently of one another are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

or

R(1), R(2) and R(3) independently of one another are pyrrol-1-yl, pyrrol-2-yl or pyrrol-3-yl, which is not substituted or is substituted by 1 - 4 substituents selected from the group consisting of F, Cl, Br, I, -CN, (C₂-C₆)-alkanoyl, (C₂-C₆)-alkoxycarbonyl, formyl, carboxyl, -CF₃, methyl, methoxy;

or

R(1), R(2) and R(3) independently of one another are hydrogen, -(C₁-C₅)-alkyl, -(C₂-C₆)-alkenyl or -(CH₂)ₘR(14);

m is zero, 1 or 2;

R(14) is -(C₃-C₇)-cycloalkyl or phenyl, which is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F and -Cl, -CF₃, methyl, methoxy and -NR(15)R(16);

R(15) and R(16) are hydrogen or -CH₃;

or

R(1), R(2) and R(3) independently of one another are -Q-₄-[(CH₂)ₜ-CHR(17)-(C=O)R(20)]-phenyl, -Q-₃-(CH₂)ₜ-CHR(17)-(C=O)R(20)]-phenyl or

-Q-₂-[(CH₂)ₜ-CHR(17)-(C=O)R(20)]-phenyl, where the phenyl in each case is unsubstituted or substituted by 1 - 2 substituents from the group F, Cl, -CF₃, methyl,
hydroxyl, methoxy and -NR(35)R(36);
R(35) and R(36)
  independently of one another are hydrogen or -CH₃;
Q is a bond, oxygen, -S- or -NR(18);
5 R(18) is hydrogen or -(C₁-C₄)-alkyl;
R(17) is -OR(21) or -NR(21)R(22);
R(21) and R(22)
  independently of one another are hydrogen, -(C₁-C₈)-
  alkyl, -(C₁-C₉)-alkanoyl, -(C₁-C₈)-alkoxycarbonyl,
10  benzyl, benzyloxy carbonyl;
or
R(21) is trityl;
R(20) is -OR(23) or -NR(23)R(24);
R(23), R(24) independently of one another are
15  hydrogen, -(C₁-C₈)-alkyl or benzyl;
k is zero, 1, 2, 3 or 4;
or
R(1), R(2) and R(3)
  independently of one another are (C₁-C₉)-heteroaryl,
20  which is linked via C or N and which is unsubstituted or
  substituted by 1 - 3 substituents from the group F, Cl, CF₃,
  CH₃, methoxy, hydroxyl, amino, methylamino and
  dimethylamino;
or
25 R(1), R(2) and R(3)
  are -SR(25), -OR(25), -NR(25)R(26), -CR(25)R(26)R(27);
R(25) is -C₂H₂r-(C₁-C₉)-heteroaryl,
  which is unsubstituted or substituted by 1 - 3
  substituents from the group F, Cl, CF₃, CH₃, methoxy,
30  hydroxyl, amino, methylamino and dimethylamino;
f is zero, 1 or 2;
R(26) and R(27)
independently of one another are defined as \( R(25) \) or

or

\( R(1), R(2) \) and \( R(3) \)

individually of one another are \( \text{(C}_1\text{-C}_4\text{-alkyl)} \),

or

\( R(1), R(2) \) and \( R(3) \)

individually of one another are \( \text{(C}_1\text{-C}_9\text{-heteroaryl-N-oxide)} \),

which is linked via \( C \) or \( N \) and which is unsubstituted or

substituted by 1 - 3 substituents selected from the group

consisting of \( F, \text{Cl, CF}_3, \text{CH}_3, \text{methoxy, hydroxyl, amino, methylamino and dimethylamino} \);

or

\( R(1), R(2) \) and \( R(3) \)

individually of one another are \(-\text{SR}(28), -\text{OR}(28), -\text{NR}(28)\text{R}(29)\)

or \(-\text{CR}(28)\text{R}(29)\text{R}(30)\);

\( R(28) \) is \(-\text{C}_g\text{H}_{2g}\text{-(C}_1\text{-C}_9\text{-heteroaryl-N-oxide)}\),

which is unsubstituted or substituted by 1 - 3

substituents selected from the group consisting of \( F, \text{Cl, CF}_3, \text{CH}_3, \text{methoxy, hydroxyl, amino, methylamino and dimethylamino} \);

\( g \)

is zero, 1 or 2;

\( R(29), R(30) \)

individually of one another are defined as \( R(28) \),

hydrogen or \( \text{(C}_1\text{-C}_4\text{-alkyl)} \);

or

\( R(1), R(2) \) and \( R(3) \)

individually of one another are hydrogen, \( F, \text{Cl, Br, I, -C=N} \),

\( \text{T-(CH}_2\text{)}^\text{h-}(\text{CF}_2\text{)}^{\text{2h+1-}}, \text{R(31)SO}^-\text{, R(32)R(33)N-CO-}, \text{R(34)-CO- or} \)

\( \text{R(45)R(46)N-SO}_2 \) where the perfluoroalkyl group is straight-chain or

branched;

\( \text{T} \)

is a bond, oxygen, \(-\text{S- or -NR}(47)\);

\( i \)

is zero, 1 or 2;

\( h \)

is zero, 1 or 2;

\( i \)

is 1, 2, 3, 4, 5 or 6;
R(31), R(32), R(34) and R(45) independently of one another are -(C_1-C_8)-alkyl, -(C_3-C_6)-alkenyl, (CH_2)_nR(48) or -CF_3; 

n is zero, 1, 2, 3 or 4;

R(47) is hydrogen or alkyl with 1, 2 or 3 carbon atoms; R(48) is -(C_3-C_7)-cycloalkyl or phenyl, which is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F, Cl, -CF_3, methyl, methoxy and -NR(49)R(50); 

R(49) and R(50) are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms; 

or 

R(32), R(34) and R(45) are hydrogen; 

R(33) and R(46) independently of one another are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms; 

or 

R(32) and R(33), and R(45) and R(46) together are 5 or 6 methylene groups, of which one CH_2 group can be replaced by oxygen, -S-, -NH-, -NCH_3 or -N-benzyl; 

or 

R(1), R(2) and R(3) independently of one another are R(51)-A-G-D--; R(51) is a basic protonatable radical, i.e. an amino group -NR(52)R(53), an amidino group R(52)R(53)N-C[=N-R(54)]- or a guanidino group R(52)R(53)N-C[=N-R(54)]-NR(55)--; 

R(52), R(53), R(54) and R(55) independently of one another are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;
or
R(52) and R(53) are
a group $C_\alpha H_{2\alpha}$;
$\alpha$ is 4, 5, 6 or 7;

where if $\alpha = 5, 6 \text{ or } 7$ a carbon atom of the group
$C_\alpha H_{2\alpha}$ can be replaced by a heteroatom group O, SO$_d$
or NR(56),
or
R(53) and R(54) or R(54) and R(55) or R(52) and R(55) are
a group $C_\gamma H_{2\gamma}$;
$\gamma$ is 2, 3, 4 or 5;
where if $\gamma = 3, 4 \text{ or } 5$ a carbon atom of the group $C_\gamma H_{2\gamma}$
can be replaced by a heteroatom group O, SO$_d$ or
NR(56);

$R(56)$ is zero, 1 or 2;

$R(56)$ is hydrogen or methyl;
or
R(51) is a basic heteroaromatic ring system having 1 - 9 carbon
atoms;

$A$ is a group $C_e H_{2e}$;
e is zero, 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10;
where in the group $C_e H_{2e}$ a carbon atom can be replaced by
one of the groupings -O-, -CO-, -CH[OR(57)]-, -SO$_r$-, -
NR(57)-, -NR(57)-CO-, -NR(57)-CO-NH-, -NR(57)-CO-NH-
SO$_2$- or -NR(57)-SO$_2$-;

$r$ is zero, 1 or 2;

$G$ is a phenylene radical
R(58) and R(59) independently of one another are hydrogen, methyl, methoxy, F, Cl, Br, I, CF₃ or -SO₂-R(60);
R(60) is methyl or NR(61)R(62);
R(61) and R(62) independently of one another are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

D is \(-CₙH_{2v}\)-;
v is zero, 1, 2, 3 or 4;

E is -O-, -CO-, -CH[OR(63)]-, -SO₃- or -NR(63)-;
w is zero or 1;

aa is zero, 1 or 2
R(63) is hydrogen or methyl,

or

R(1), R(2) and R(3) independently of one another are -CF₂R(64), -CF[R(65)][R(66)], -CF[CF₂]ₚ-CF₃[R(65)], -C[(CF₂)ₚ-CF₃]=CR(65)R(66);
R(64) is alkyl having 1, 2, 3 or 4 carbon atoms or cycloalkyl having 3, 4, 5, 6 or 7 carbon atoms;
R(65) and R(66) independently of one another are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;
q is zero, 1 or 2;
p is zero, 1 or 2;

or

R(1), R(2) and R(3) independently of one another are -OR(67) or -NR(67)R(68);
R(67) and R(68)
independently of one another are hydrogen or alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms;

or

R(67) and R(68)

together are 4, 5, 6 or 7 methylene groups, of which one CH₂ group can be replaced by oxygen, -S-, SO₂, -NH-, -NCH₃ or -N-benzyl;

R(4) and R(5)
independently of one another are hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms, F, Cl, -OR(69), -NR(70)R(71) or -C₂F₃; R(69), R(70) and R(71)
independently of one another are hydrogen or alkyl having 1, 2 or 3 carbon atoms;

z is 1, 2, 3 or 4;

R(6) and R(7)
independently of one another are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

X is oxygen or NR(72);

R(72) is hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

and their pharmaceutically tolerable salts;

ak) alkenylcarboxylic acid guanidides, carrying fluorophenyl groups, of the formula I

in which:

R(6) is hydrogen, (C₁-C₆)-alkyl, (C₂-C₆)-cycloalkyl or phenyl,

where the phenyl group is not substituted or is substituted by
1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(9)R(10);

R(9) and R(10) are hydrogen, (C₁-C₄)-alkyl or (C₁-C₄)-perfluoroalkyl;

R(7) independently is defined as R(6);

R(1), R(2), R(3), R(4) and R(5)

independently of one another are hydrogen or F;

where, however, at least one of the radicals R(4), R(2), R(3), R(4)

and R(5) must be fluorine;

and their pharmaceutically tolerable salts;

al) benzoylguanidines of the formula I

in which:

R(1) is R(4)-SO₃⁻ or R(5)R(6)N-SO₂⁻;

m is 1 or 2;

R(4) and R(5) independently of one another are alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, alkenyl having 3, 4, 5 or 6 carbon atoms, CF₃ or -CₙH₂ₙ₋₁-R(7);

n is zero, 1, 2, 3 or 4;

R(3) is H or alkyl having 1, 2, 3 or 4 carbon atoms;

R(7) is cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms or phenyl,

which is not substituted or is substituted by 1 - 3 substituents selected from the group consisting
of F, Cl, CF₃, methyl, methoxy and NR(8)R(9); R(8) and R(9) are H or alkyl having 1, 2, 3 or 4 carbon atoms;

or

R(5) is also hydrogen;

or

R(5) and R(6) together are 4 or 5 methylene groups, of which a CH₂ group can be replaced by oxygen, S, NH, N-CH₃ or N-benzyl;

or

R(1) is -O_p-(CH₂)_q-(CF₂)_r-CF₃;
p is zero or 1;
q is zero, 1 or 2;
r is zero, 1, 2 or 3;

or

R(1) is -SR(10), -OR(10) or -CR(10)R(11)R(12);

R(10), R(11) and R(12) independently of one another are hydrogen, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, -C₆H₄-(C₃- C₈)-cycloalkyl or an aromatic system selected from the group consisting of pyridyl, pyrrolyl, quinolyl, isoquinolyl, imidazolyl or phenyl;
s is zero, 1 or 2;

where the aromatic systems pyridyl, pyrrolyl, quinolyl, isoquinolyl, imidazolyl and phenyl are unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino and dimethylamino;

R(2) is -(CH₂)_t-(CF₂)_u-CF₃;
t is zero, 1, 2 or 3;
u is zero or 1;
R(3) is hydrogen or independently is defined as R(1); and their pharmaceutically tolerable salts;

am) substituted cinnamic acid guanidides of the formula I

\[
\begin{align*}
R(1) & \quad R(2) \\
R(3) & \quad R(4) \\
R(5) & \quad R(6) \\
R(7) & \quad \text{NH}_2 \\
\end{align*}
\]

in which:

at least one of the substituents R(1), R(2), R(3), R(4) and R(5) is

\[-X_a-\text{Y}_{b-L_n-U};\]

\[X \quad \text{is CR(16)R(17), O, S or NR(18);}\]

\[R(16), R(17) \text{ and } R(18) \quad \text{independently of one another are } H, \text{ alkyl having 1, 2, 3 or 4 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;}\]

\[a \quad \text{is zero or 1;}\]

\[Y \quad \text{is alkylene having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, alkylene-T having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms in the alkylene group, T, T-alkylene having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms in the alkylene group;}\]

\[T \quad \text{is NR(20), O, S or phenylene,}\]

\[\text{where the phenylene is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF}_3, \text{ methyl, methoxy and NR(21)R(22);}\]

\[R(20), R(21) \text{ and } R(22) \quad \text{independently of one another are } H, \text{ alkyl having 1, 2, 3 or 4 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon}\]
 atoms;

\[ b \] is zero or 1;
\[ L \] is O, S, NR(23) or \( \mathrm{C}_x\mathrm{H}_{2x} \);
\[ k \] is 1, 2, 3, 4, 5, 6, 7, 8;
\[ n \] is zero or 1;
\[ \text{U} \] is NR(24)R(25) or an N-containing heterocycle having 1, 2, 3, 4, 5, 6, 7, 8 or 9 carbon atoms;
\[ \text{R}(24) \text{ and } \text{R}(25) \] independently of one another are hydrogen, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms or perfluoroalkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms;
\[ \text{or} \]
\[ \text{R}(24) \text{ and } \text{R}(25) \] together are 4 or 5 methylene groups, of which one \( \text{CH}_2 \) group can be replaced by oxygen, S, NH, N-CH\(_3\) or N-benzyl; where the N-containing heterocycles are N- or C-bridged and are not substituted or are substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF\(_3\), methyl, methoxy and \( \text{NR}(27)\text{R}(28) \);
\[ \text{R}(23), \text{R}(27) \text{ and } \text{R}(28) \] independently of one another are H, alkyl having 1, 2, 3 or 4 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;
\[ \text{and the other substituents } \text{R}(1), \text{R}(2), \text{R}(3), \text{R}(4) \text{ and } \text{R}(5) \text{ in each case independently of one another are } \text{H, F, Cl, Br, I, CN, -O}_n\text{-C}_m\text{H}_{2m+1}, \]
\[ \text{-O}_p\text{-}(\text{CH}_2)_q\text{-C}_r\text{F}_{2q+1} \text{ or } \text{-C}_t\text{H}_{2t} \text{R}(10); \]
\[ n \] is zero or 1;
\[ m \] is zero 1, 2, 3, 4, 5, 6, 7 or 8;
\[ p \] is zero or 1;
\[ q \] is 1, 2, 3, 4, 5, 6, 7 or 8;
s is zero, 1, 2, 3 or 4;

r is zero, 1, 2, 3 or 4;

R(10) is cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, or phenyl,

where the phenyl is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(11)R(12);

R(11) and R(12) independently of one another are H, alkyl having 1, 2, 3 or 4 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;

R(6) and R(7) independently of one another are hydrogen, F, Cl, Br, I, CN, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, perfluoroalkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, or phenyl, which is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(14)R(15);

R(14) and R(15) independently of one another are H, alkyl having 1, 2, 3 or 4 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;

and their pharmaceutically tolerable salts;
an) benzoylguanidines of the formula I

\[
\begin{align*}
\text{R(1)} & \quad \text{R(2)} \\
\text{R(3)} & \quad \text{R(4)} \quad \text{R(5)} \\
\text{R(6)} & \quad \text{R(7)} \quad \text{R(8)} \\
\text{N} & \quad \text{N} \quad \text{NH}_2 \\
\end{align*}
\]

in which:

10 at least one of the substituents \(R_1\), \(R_2\) and \(R_3\)

\[
\text{R(6)} \quad \text{is perfluoroalkyl having 1, 2 or 3 carbon atoms, which is}
\]

straight-chain or branched;

and the other substituents \(R(1), R(2)\) and \(R(3)\)

15 independently of one another are hydrogen, OH, F, Cl, Br, I, alkyl

having 1, 2, 3, 4, 5 or 6 carbon atoms, cycloalkyl with 3, 4, 5 or 6

carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms or phenoxy,

which is unsubstituted or is substituted by 1 - 3 substituents

selected from the group consisting of F, Cl, methyl and

methoxy;

or

the other substituents \(R(1), R(2)\) and \(R(3)\)

25 independently of one another are alkyl\(-\text{SO}_x\), \(-\text{CR(7)}=\text{CR(8)}\text{R(9)}\) or

\(-\text{C}=\text{CR(9)}\);

\(x\) is zero, 1 or 2;

\(\text{R(7)}\) is hydrogen or methyl;

\(\text{R(8)}\) and \(\text{R(9)}\)

independently of one another are hydrogen, alkyl having 1, 2,

3 or 4 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7 or 8

carbon atoms or phenyl,

which is unsubstituted or is substituted by 1 - 3

substituents selected from the group consisting of F,
CI, CF₃, methyl and methoxy;

or

the other substituents R(1), R(2) and R(3)

independently of one another are phenyl, C₆H₅-(C₁-C₄)-alkyl,

naphthyl, biphenyl, quinolinyl, isoquinolinyl or imidazolyl,

where quinolinyl, isoquinolinyl or imidazolyl are bonded via C

or N and where phenyl, C₆H₅-(C₁-C₄)-alkyl, naphthyl,

biphenyl, quinolinyl, isoquinolinyl and imidazolyl are

unsubstituted or are substituted by 1 - 3 substituents selected

from the group consisting of F, CI, CF₃, CH₃, methoxy,

hydroxyl, amino, methylamino and dimethylamino;

or

the other substituents R(1), R(2) and R(3)

independently of one another are SR(10), -OR(10),

-CR(10)R(11)R(12);

R(10)

is -C₆H₅-C₆H₅-(C₃-C₅)-cycloalkyl, quinolinyl, isoquinolinyl, pyridinyl,

imidazolyl or phenyl,

where the aromatic systems quinolinyl, isoquinolinyl,

pyridinyl, imidazolyl and phenyl are unsubstituted or

are substituted by 1 - 3 substituents selected from the

group consisting of F, CI, CF₃, CH₃, methoxy, hydroxyl,

amino, methylamino and dimethylamino;

f is zero, 1 or 2;

R(11) and R(12)

independently of one another are defined as R(10), hydrogen

or alkyl having 1, 2, 3 or 4 carbon atoms;

R(4) and R(5)

independently of one another are hydrogen, alkyl having 1, 2 or 3

carbon atoms, F, CI, Br, I, CN, OR(13), NR(14)R(15), -(CH₂)n-(CF₂)ₙ-

CF₃;

R(13), R(14) and R(15)
independently of one another are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

\[ n \text{ is zero or } 1; \]
\[ o \text{ is zero, } 1 \text{ or } 2; \]

and their pharmacologically acceptable salts;

ao) sulfonimidamides of the formula I

\[
\begin{aligned}
N & \quad R_1 \\
O=S & \quad R_2 \\
R_4 & \quad N \\
R_3 & \quad N
\end{aligned}
\]

in which:

at least one of the three substituents \( R(2) \) and \( R(3) \)

is a benzyolguanidine,

which is unsubstituted or substituted in the phenyl moiety by 1 - 4 radicals selected from the group consisting of alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, alkenyl having 2, 3, 4, 5, 6, 7 or 8 carbon atoms, -(CH\(_2\))\(^m\)-R(14), F, Cl, Br, I, -C=N, CF\(_3\), R(22)SO\(_2\), R(23)R(24)N-CO-, R(25)-CO-, R(26)R(27)N=SO\(_2\), -OR(35), -SR(35) or -NR(35)R(36);

\[ m \text{ is zero, } 1 \text{ or } 2; \]

\[ R(14) \]

is -(C\(_3\)-C\(_8\))-cycloalkyl or phenyl,

which is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F and Cl, -CF\(_3\), methyl, methoxy and -NR(15)R(16);
R(15) and R(16) independently of one another are hydrogen or \(-\text{CH}_3\);

R(22), R(23), R(25) and R(26) independently of one another are alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, alkenyl having 2, 3, 4, 5, 6, 7 or 8 carbon atoms, \((\text{CH}_2)_n\)R(29) or -\(\text{CF}_3\);

\(n\) is zero, 1, 2, 3 or 4;

R(29) is \(-(\text{C}_3-\text{C}_7)\)-cycloalkyl or phenyl,

which is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F, Cl, -\(\text{CF}_3\), methyl, methoxy and -\(\text{NR}(30)\)R(31);

R(30) and R(31) are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

or

R(23), R(25) and R(26) are hydrogen;

R(24) and R(27) independently of one another are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

or

R(23) and R(24), and also R(26) and R(27) together are 5 or 6 methylene groups, of which one \(\text{CH}_2\) group can be replaced by oxygen, -S-, -\(\text{NH}_2\), -N\(\text{CH}_3\) or -N-benzyl;

R(35) and R(36) independently of one another are hydrogen or alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms;

or
R(35) and R(36) together are 4 - 7 methylene groups, of which one \( \text{CH}_2 \) group can be replaced by oxygen, -S-, -NH-, -NCH\(_3\) or -N-benzyl;

or

R(35) is phenyl,

which is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F, Cl, -CF\(_3\), methyl, methoxy, SO\(_2\)R(5), SO\(_2\)NR(6)R(7) and -NR(32)R(33);

R(5) is alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms

R(6) and R(7) independently of one another are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

R(32) and R(33) independently of one another are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

or

R(35) is \( \text{C}_1-\text{C}_9 \)-heteroaryl,

which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF\(_3\), CH\(_3\), methoxy, hydroxyl, amino, methylamino and dimethylamino;

and the other substituents R(1), R(2) and R(3) in each case independently of one another are alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, \((\text{CH}_2)_p\)R(10)

\( p \) is zero, 1, 2, 3 or 4;
is phenyl, which is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F, Cl, -CF₃, methyl, methoxy, -SO₂NR(17)R(8) and -SO₂R(9); R(17) and R(8) independently of one another are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms; R(9) is alkyl having 1, 2, 3 or 4 carbon atoms; or the other radicals R(1) and R(3) in each case are hydrogen, R(4) is hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms; and their pharmaceutically tolerable salts; ap) benzoylguanidines of the formula I

\[
\begin{align*}
\text{O} & \\
\text{O=S-R1} & \\
\text{R2-N} & \\
\text{R3} & \\
\text{R4} & \\
\text{R5} & \\
\text{I} & \\
\text{R6} & \\
\text{N} & \\
\text{NH₂} & \\
\text{NH₂} & \\
\end{align*}
\]

in which:
R(1) is alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms or NR(7)R(8);
R(7) and R(8) independently of one another are hydrogen or alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms;
R(2) is hydrogen, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms or -SO₂R(9);
R(9) independently is defined as R(1);
R(3) is hydrogen, -SR(25), -OR(25), -NR(25)R(26) or -CR(25)R(26)R(27);
R(25) is hydrogen, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms,
or phenyl,

which is unsubstituted or substituted by 1 - 3
substituents selected from the group consisting of F,
Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino

and dimethylamino;

or

R(25)

is -(C₁₋₃)-heteroaryl,

which is unsubstituted or substituted by 1 - 3
substituents selected from the group consisting of F,
Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino
and dimethylamino;

R(26) and R(27)

independently of one another are defined as R(25) or

are hydrogen or alkyl having 1, 2, 3, 4, 5, 6, 7 or 8
carbon atoms;

R(4) is hydrogen, F, Cl, Br, I, OH, -C≡N, CF₃, alkyl having 1, 2, 3, 4, 5, 6,
7 or 8 carbon atoms, alkenyl having 2, 3, 4, 5, 6, 7 or 8 carbon
atoms or -(CH₂)ₘR(14);

m is zero, 1 or 2;

R(14) is -(C₃₋₈)-cycloalkyl or phenyl,

which is not substituted or is substituted by 1 - 3
substituents selected from the group consisting of F
and Cl, -CF₃, methyl, methoxy and -NR(15)R(16);

R(15) and R(16)

independently of one another are hydrogen or
-CH₃;

R(5) and R(6)

independently of one another are hydrogen, alkyl having 1, 2, 3 or 4
carbon atoms, F, Cl, -OR(32), -NR(33)R(34) or CF₃;

R(32), R(33) and R(34)

independently of one another are hydrogen or alkyl having 1,
2, 3 or 4 carbon atoms;
and their pharmaceutically tolerable salts;
aq) benzenedicarboxylic acid diguanidides of the formula I

in which:
one of the radicals R(1), R(2), R(3) and R(4)
is -CO-N=C(NH₂)₂;
and the other radicals R(1), R(2), R(3) and R(4) in each case are:
R(1) is hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms, F, Cl, Br, I,
-OR(32), -NR(33)R(34) or CF₃;
R(32), R(33) and R(34)
independently of one another are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;
R(2) and R(4)
independently of one another are hydrogen, F, Cl, Br, I, OH, -CN, CF₃, -CO-N=C(NH₂)₂, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, alkenyl having 2, 3, 4, 5, 6, 7 or 8 carbon atoms or -(CH₂)ₘR(14);
m is zero, 1 or 2;
R(14) is -(C₃-C₄)-cycloalkyl or phenyl,
which is not substituted or is substituted by 1 - 3
substituents selected from the group consisting of F
and Cl, -CF₃, methyl, methoxy and -NR(15)R(16);
R(15) and R(16)
are hydrogen or -CH₃;
or
R(2) and R(4)
independently of one another are pyrrol-1-yl, pyrrol-2-yl or pyrrol-3-yl,
each of which is not substituted or is substituted by 1-4 substituents selected from the group consisting of F, Cl, Br, I,
-CN, (C₂₋₆)-alkanoyl, (C₂₋₆)-alkoxycarbonyl, formyl, carboxyl, -CF₃, methyl, methoxy;
or
R(2) and R(4)
independently of one another are R(22)-SO₂-, R(23)R(24)N-CO-,
R(28)-CO- or R(29)R(30)N-SO₂;
R(22) and R(28)
independently of one another are methyl or -CF₃;
R(23), R(24), R(29) and R(30)
independently of one another are hydrogen or methyl;
or
R(2) and R(4)
independently of one another are -OR(35) or -NR(35)R(36);
R(35) and R(36)
independently of one another are hydrogen or alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms;
or
R(35) and R(36)
together are 4-7 methylene groups, of which one CH₂ group can be replaced by oxygen, -S-, -NH-, -NCH₃ or -N-benzyl;
R(3) is hydrogen, -SR(25), -OR(25), -NR(25)R(26), -CR(25)R(26)R(27);
R(25) is hydrogen, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms or phenyl,
which is unsubstituted or substituted by 1-3 substituents selected from the group consisting of F,
Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino and dimethylamino;
R(25) is $\text{-C}_1\text{-C}_9\text{-heteroaryl}$, which is unsubstituted or substituted by 1-3 substituents selected from the group consisting of F, Cl, CF$_3$, CH$_3$, methoxy, hydroxyl, amino, methylamino and dimethylamino;

R(26) and R(27) independently of one another are defined as R(25) or are hydrogen or alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms;

R(5) is alkyl having 1, 2, 3 or 4 carbon atoms, F, Cl, Br, I, X-(CH$_2$)$_y$-CF$_3$ or phenyl, which is not substituted or is substituted by 1-3 substituents selected from the group consisting of F and Cl, -CF$_3$, methyl, methoxy and -NR(6)R(7);

R(6) and R(7) independently of one another are hydrogen or -CH$_3$;

X is a bond or oxygen;

y is zero, 1 or 2;

and their pharmaceutically tolerable salts;

ar) benzenedicarboxylic acid diguanidides of the formula I

\[
\text{R(1)}\text{-N} = \text{C(NH}_2\text{)}_2
\]

in which:

one of the radicals R(1), R(2), R(3) and R(5) is -CO-N=C(NH$_2$)$_2$;

and the other radicals R(1), R(2), R(3) and R(5) in each case are:

R(1) and R(5) independently of one another are hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms, F, Cl, -OR(32), -NR(33)R(34) or CF$_3$.\]
R(32), R(33) and R(34) independently of one another are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

R(2) is hydrogen, F, Cl, Br, I, OH, -CN, CF₃, -CO-N(C(NH₂)₂, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, alkenyl having 2, 3, 4, 5, 6, 7 or 8 carbon atoms or -(CH₂)ₘR(14);

m is zero, 1 or 2;

R(14) is -(C₃-C₈)-cycloalkyl or phenyl, which is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F and Cl, -CF₃, methyl, methoxy and -NR(15)R(16);

R(15) and R(16) independently of one another are hydrogen or -CH₃;

or

R(2) is R(22)-SO₂-, R(23)R(24)N-CO-, R(28)-CO- or R(29)R(30)N-SO₂;

R(22) and R(28) independently of one another are methyl or -CF₃;

R(23), R(24), R(29) and R(30) independently of one another are hydrogen or methyl;

or

R(2) is -OR(35) or -NR(35)R(36);

R(35) and R(36) independently of one another are hydrogen or alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms;

or

R(35) and R(36) together are 4 - 7 methylene groups, of which one CH₂ group can be replaced by oxygen, -S-, -NH-, -NCH₃ or -N-benzyl;

R(3) is hydrogen, -SR(25), -OR(25), -NR(25)R(26), -CR(25)R(26)R(27);

R(25) is hydrogen, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms or phenyl,
which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino and dimethylamino;

or

R(25) is -(C₁-C₆)-heteroaryl,

which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino and dimethylamino;

R(26) and R(27) independently of one another are defined as R(25) or are hydrogen or alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms;

R(4) is CF₃, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, alkenyl having 2, 3, 4, 5, 6, 7 or 8 carbon atoms, -(C₃-C₆)-cycloalkyl or -(CH₉)ₘR(14);

m is 1 or 2;

R(14) is -(C₃-C₆)-cycloalkyl or phenyl,

which is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F and Cl, -CF₃, methyl, methoxy and -NR(15)R(16);

R(15) and R(16) independently of one another are hydrogen or -CH₃;

or

R(4) is phenyl,

which is substituted by 2, 3, 4 or five substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and -NR(15)R(16);

R(15) and R(16) independently of one another are hydrogen or CH₃;
and their pharmaceutically tolerable salts;

as) diaryldicarboxylic acid diguanidides of the formula (I)

\[
\begin{array}{c}
R_1 \quad R_2 \\
R_3 \quad R_4 \\
R_5 \quad R_6 \\
R_7 \quad R_8 \\
R_9 \\
A
\end{array}
\]

in which:

one of the radicals R(1), R(2), R(3), R(4) and R(5) is \(-\text{CO-N}=\text{C(NH}_2\text{)}_2\);

the other radicals R(1) and R(5) in each case independently of one another are hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms, F, Cl, \(-\text{OR}(32)\), \(-\text{NR}(33)\text{R}(34)\) or \(\text{CF}_3\);

R(32), R(33) and R(34) independently of one another are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

the other radicals R(2) and R(4) in each case independently of one another are hydrogen, F, Cl, Br, I, OH, \(-\text{CN}\), \(\text{CF}_3\), \(-\text{CO-N}=\text{C(NH}_2\text{)}_2\), alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, alkenyl having 2, 3, 4, 5, 6, 7 or 8 carbon atoms or \(-\langle\text{CH}_2\rangle_m\text{R}(14)\);

\(m\) is zero, 1 or 2;

R(14) is \(-(\text{C}_3-\text{C}_8)\)-cycloalkyl or phenyl, which is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F and Cl, \(-\text{CF}_3\), methyl, methoxy and \(-\text{NR}(15)\text{R}(16)\);

R(15) and R(16) are hydrogen or \(-\text{CH}_3\);

or

the other radicals R(2) and R(4) in each case independently of one another are pyrrol-1-yl, pyrrol-2-yl or pyrrol-3-yl,
which is not substituted or is substituted by 1-4 substituents selected from the group consisting of F, Cl, Br, I, -CN, (C<sub>2</sub>-C<sub>6</sub>)-alkanoyl, (C<sub>2</sub>-C<sub>6</sub>)-alkoxycarbonyl, formyl, carboxyl, -CF<sub>3</sub>, methyl, methoxy;

or

the other radicals R(2) and R(4) in each case are R(22)-SO<sub>2</sub>-, R(23)R(24)N-CO-, R(28)-CO- or R(29)R(30)N-SO<sub>2</sub>;

R(22) and R(28)

independently of one another are methyl or -CF<sub>3</sub>;

R(23), R(24), R(29) and R(30)

independently of one another are hydrogen or methyl;

or

the other radicals R(2) and R(4) in each case independently of one another are -OR(35) or -NR(35)R(36);

R(35) and R(36)

independently of one another are hydrogen or alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms;

or

R(35) and R(36)

together are 4-7 methylene groups, of which one CH<sub>2</sub> group can be replaced by oxygen, -S-, -NH-, -NCH<sub>3</sub> or -N-benzyl;

the other radical R(3) in each case is hydrogen, -SR(25), -OR(25), -NR(25)R(26), -CR(25)R(26)R(27);

R(25) is hydrogen, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms or phenyl,

which is unsubstituted or substituted by 1-3 substituents selected from the group consisting of F, Cl, CF<sub>3</sub>, CH<sub>3</sub>, methoxy, hydroxyl, amino, methylamino and dimethylamino;

or

R(25) is -(C<sub>1</sub>-C<sub>9</sub>)-heteroaryl,

which is unsubstituted or substituted by 1-3
substituents selected from the group consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino and dimethylamino;

R(26) and R(27)

independently of one another are defined as R(25) or are hydrogen or alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms;

one of the radicals R(6), R(7), R(8), R(9) and R(10)

is -CO-N=C(NH₂)₂;

the other radicals R(6) and R(10) in each case

independently of one another are hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms, F, Cl, -OR(132), -NR(133)R(134) or CF₃;

R(132), R(133) and R(134)

independently of one another are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

the other radicals R(7) and R(9) in each case

independently of one another are hydrogen, F, Cl, Br, I, OH, -CN, CF₃, -CO-N=C(NH₂)₂, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, alkenyl having 2, 3, 4, 5, 6, 7 or 8 carbon atoms or -(CH₂)ₘₙR(114);

mm is zero, 1 or 2;

R(114)

is -(C₃-C₈)-cycloalkyl or phenyl,

which is not substituted or is substituted by 1 - 3 substituents selected from the group consisting of F and Cl, -CF₃, methyl, methoxy and -NR(115)R(116);

R(115) and R(116)

are hydrogen or -CH₃;

or

the other radicals R(7) and R(9) in each case

independently of one another are pyrrol-1-yl, pyrrol-2-yl or pyrrol-3-yl,

which is not substituted or is substituted by 1 - 4 substituents
selected from the group consisting of F, Cl, Br, I, -CN, (C₂-C₈)-alkanoyl, (C₂-C₈)-alkoxycarbonyl, formyl, carboxyl, -CF₃, methyl and methoxy;

or

the other radicals R(7) and R(9) in each case

are R(122)-SO₂-, R(123)R(124)N-CO-, R(128)-CO- or R(129)R(130)N-SO₂;

R(122) and R(128)

independently of one another are methyl or -CF₃;

R(123), R(124), R(129) and R(130)

independently of one another are hydrogen or methyl;

or

the other radicals R(7) and R(9) in each case

independently of one another are -OR(135) or -NR(135)R(136);

R(135) and R(136)

independently of one another are hydrogen or alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms;

or

R(135) and R(136)

together are 4 - 7 methylene groups, of which one CH₂ group can be replaced by oxygen, -S-, -NH-, -NCH₃ or -N-benzyl;

the other radical R(8) in each case

is hydrogen, -SR(125), -OR(125), -NR(125)R(126) or -CR(125)R(126)R(127);

R(125)

is hydrogen, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms or phenyl,

which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino and dimethylamino;

or
R(125) is -(C$_1$-C$_9$)-heteroaryl,
which is unsubstituted or substituted by 1 - 3
substituents selected from the group consisting of F, Cl, CF$_3$, CH$_3$, methoxy, hydroxyl, amino, methylamino
and dimethylamino;
R(126) and R(127) independently of one another are defined as R(125) or are
hydrogen or alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms;

A is absent or is -NR(11)-CO-, -NR(12)-CO-NR(13)-,
-NR(17)-CO-NR(18)-SO$_2$-, -NR(19)-SO$_2$-, -SO$_2$-NR(19)-SO$_2$-, -SO$_2$-NR(19)-CO-, -O-CO-NR(19)-SO$_2$- or -CR(20)=CR(21)-;
R(11), R(12), R(13), R(17), R(18), R(19), R(20) and R(21)
independently of one another are hydrogen or alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms
and their pharmaceutically tolerable salts;
at) substituted thiophenylalkenylcarboxylic acid guanidides of the formula I

in which:

at least one of the substituents R(1), R(2) and R(3)
is -O$_p$-(CH$_2$)$_s$-C$_q$F$_{2q+1}$, R(40)CO- or R(31)SO$_k$-;
p is zero or 1;
s is zero, 1, 2, 3 or 4;
q is 1, 2, 3, 4, 5, 6, 7 or 8;
k is zero, 1 or 2;
R(40) is alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms,
298

perfluoroalkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms,
cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, or phenyl,
    which is not substituted or is substituted by 1 - 3
substituents selected from the group consisting of F,
5
    Cl, CF₃, methyl and methoxy;

R(31) is alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms,
    perfluoroalkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms,
cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, or phenyl,
    which is not substituted or is substituted by 1 - 3
10
substituents selected from the group consisting of F,
    Cl, CF₃, methyl or methoxy;

or
R(31) is NR(41)R(42);
    R(41) and R(42)
15
    independently of one another are hydrogen, alkyl
having 1, 2, 3 or 4 carbon atoms, perfluoroalkyl having
    1, 2, 3 or 4 carbon atoms,
or
R(41) and R(42)
20
together are 4 or 5 methylene groups, of which one
    CH₂ group can be replaced by oxygen, S, NH, N-CH₃
    or N-benzyl;

and the other substituents R(1), R(2) and R(3) in each case
    independently of one another are H, F, Cl, Br, I, CN, -O⁻Na-C⁺M₄H₂Na+1
    or -O⁻Ga-C⁺RaH₂RaR(10);
    na is zero or 1;
    ma is zero, 1, 2, 3, 4, 5, 6, 7 or 8;
    ga is zero or 1;
    ra is zero, 1, 2, 3 or 4;
30
R(10) is cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms or phenyl,
    where the phenyl is not substituted or is substituted by
    1 - 3 substituents selected from the group consisting of
F, Cl, CF₃, methyl and methoxy;

R(4) and R(5)

independently of one another are hydrogen, F, Cl, Br, I, CN, alkyl
having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, perfluoroalkyl having 1,
2, 3, 4, 5, 6, 7 or 8 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7 or 8
carbon atoms or phenyl,

which is not substituted or is substituted by 1 - 3 substituents
selected from the group consisting of F, Cl, CF₃, methyl,
methoxy and NR(14)R(15);

R(14) and R(15)

independently of one another are H, alkyl having 1, 2,
3 or 4 carbon atoms or perfluoroalkyl having 1, 2, 3 or
4 carbon atoms;

and their pharmaceutically tolerable salts;

au) ortho-substituted benzoylguanidines of the formula I

\[
\begin{array}{c}
\text{F} \\
\text{R(2)} \\
\text{R(3)} \\
\text{Cl} \\
\text{O} \\
\text{NH}_2 \\
\text{NH}_2
\end{array}
\]

in which:

R(2) and R(3)

independently of one another are hydrogen, Cl, Br, I, (C₁-C₈)-alkyl,
(C₃-C₈)-cycloalkyl or -OR(5);

R(5) is (C₁-C₈)-alkyl or \(-C_dH_{2d}(C₃-C₈)\)-cycloalkyl;

\(d\) is zero, 1 or 2;

where one of the two substituents R(2) and R(3) is always hydrogen but
both substituents R(2) and R(3) are not simultaneously hydrogen,

and their pharmaceutically tolerable salts;
av) benzoylguanidines of the formula I

\[
\begin{align*}
& \text{R(1) is H, F, Cl, Br, I, CN, NO}_2, \text{alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, alkoxy having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, cycloalkoxy having 3, 4, 5, 6, 7 or 8 carbon atoms or X}_{a(\text{CH}_2)b}\text{-CF}_2\text{-CF}_3;}
\end{align*}
\]

\[
\begin{align*}
& \text{X is oxygen, S, NR(5),}
\end{align*}
\]

\[
\begin{align*}
& \text{a is zero or 1;}
\end{align*}
\]

\[
\begin{align*}
& \text{b is zero, 1 or 2;}
\end{align*}
\]

\[
\begin{align*}
& \text{c is zero, 1, 2 or 3;}
\end{align*}
\]

\[
\begin{align*}
& \text{R(5) is H, alkyl having 1, 2, 3 or 4 carbon atoms or -C}_9\text{H}_{20}\text{R(6);}
\end{align*}
\]

\[
\begin{align*}
& \text{d is zero, 1, 2, 3 or 4;}
\end{align*}
\]

\[
\begin{align*}
& \text{R(6) is cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, phenyl, biphenyl or naphthyl,}
\end{align*}
\]

\[
\begin{align*}
& \text{where the aromatics phenyl, biphenyl or naphthyl are not substituted or are substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF}_3, \text{methyl, methoxy and NR(7)R(8);}
\end{align*}
\]

\[
\begin{align*}
& \text{R(7) and R(8) independently are H or alkyl having 1, 2, 3 or 4 carbon atoms;}
\end{align*}
\]

\[
\begin{align*}
& \text{or}
\end{align*}
\]

\[
\begin{align*}
& \text{R(1) is -SR(10), -OR(10) or -CR(10)R(11)R(12);}
\end{align*}
\]

\[
\begin{align*}
& \text{R(10) is -C}_8\text{H}_{2r}\text{-cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms in the cycloalkyl ring, or phenyl,}
\end{align*}
\]
where phenyl is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino and dimethylamino;

5 \( f \) is zero, 1 or 2;

\[ \text{R}(11) \text{ and } \text{R}(12) \]

independently of one another are defined as \( \text{R}(10) \) or are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

or

10 \( \text{R}(1) \) is phenyl, naphthyl, biphenyl or heteroaryl having 1, 2, 3, 4, 5, 6, 7, 8 or 9 carbon atoms, with the latter being linked via a carbon atom or a nitrogen atom of the ring,

which are in each case unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino and dimethylamino,

or

\[ \text{R}(1) \] is -SR(13), -OR(13), -NHR(13), -NR(13)R(14), -CHR(13)R(15), -C[R(15)R(16)OH], -C=CR(18), -C[R(19)]=CHR(18),

20 -C[R(20)R(21)]ₖ-(CO)-[CR(22)R(23)]ₗ-R(24),

\( k \) is zero, 1, 2, 3 or 4;

\( l \) is zero, 1, 2, 3 or 4;

\[ \text{R}(13) \text{ and } \text{R}(14) \]

identically or differently are -(CH₂)ₜ-(CHOH)ₜ-(CH₂)ₜ-(CHOH)ₜ-(CH₂)ₜ-(CHOH)ₜ-(CH₂)ₜ-(CHOH)ₜ-(CH₂)ₜ-

25 \( \text{R}(17) \) or -(CH₂)ₜ-O-(CH₂-CH₂O)ₜ-R(24);

\( \text{R}(17) \) is hydrogen or methyl,

\( g, h \) and \( i \)

identically or differently are zero, 1, 2, 3 or 4;

\( j \) is 1, 2, 3 or 4;
R(15) and R(16)
identically or differently are hydrogen, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms or, together with the carbon atom
carrying them, are cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon
5 atoms;

R(18)
is phenyl,
which is unsubstituted or substituted by 1 - 3
substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(25)R(26);
R(25) and R(26)
are H or alkyl having 1, 2, 3 or 4 carbon atoms;
or
R(18) is heteroaryl having 1, 2, 3, 4, 5, 6, 7, 8 or 9 carbon atoms,
which is unsubstituted or substituted as phenyl;
or
R(18) is alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms,
which is unsubstituted or substituted by 1 - 3 OH;
or
20 R(18)
is cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms;
R(19), R(20), R(21), R(22) and R(23)
identically or differently are hydrogen or methyl;
R(24) is H, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, cycloalkyl
having 3, 4, 5, 6, 7 or 8 carbon atoms or -CₘH₂ₘ-R(18);
m is 1, 2, 3 or 4;
R(2) and R(3)
are defined as R(1);
R(4) is alkyl having 1, 2, 3 or 4 carbon atoms;
30 and their pharmaceutically tolerable salts;
aw) ortho-substituted benzoylguanidines of the formula I

![Chemical Structure](image)

in which:

- **R(1)** is H, F, Cl, Br, I, CN, NO₂, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, alkoxy having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, or Xₐ-(CH₂)ₐ-(CF₂)ₐ-CF₃;
- **X** is oxygen, S, NR(5);
- **a** is zero or 1;
- **b** is zero, 1 or 2;
- **c** is zero, 1, 2 or 3;
- **R(5)** is H, alkyl having 1, 2, 3 or 4 carbon atoms or -C₄H₂dR(6);
- **d** is zero, 1, 2, 3 or 4;
- **R(6)** is cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, phenyl, biphenylyl or naphthyl, where the aromatics phenyl, biphenylyl or naphthyl are unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(7)R(8);
- **R(7)** and **R(8)** independently are H or alkyl having 1, 2, 3 or 4 carbon atoms;
- or

- **R(1)** is -SR(10), -OR(10) or -CR(10)R(11)R(12);
- **R(10)** is -C₇H₆-cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms in the cycloalkyl ring, or phenyl,
where phenyl is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino and dimethylamino;

\[ f \]  is zero, 1 or 2;

\[ R(11) \text{ and } R(12) \]

independently of one another are defined as \( R(10) \), or are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

\[ R(1) \]
is phenyl, naphthyl, biphenyl or heteroaryl having 1, 2, 3, 4, 5, 6, 7, 8 or 9 carbon atoms, with the latter being linked via a carbon atom or a nitrogen atom of the ring, which are in each case unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF₃, CH₃, methoxy, hydroxyl, amino, methylamino and dimethylamino,

\[ R(1) \text{ is } -SR(13), -OR(13), -NHR(13), -NR(13)R(14), -CHR(13)R(15), -C[R(15)R(16)OH], -C=CR(18), -C[R(19)]=CHR(18), -C[R(20)R(21)]_k-(CO)-[CR(22)R(23)]_l-R(24), \]
\[ k \]
is zero, 1, 2, 3 or 4;

\[ I \]
is zero, 1, 2, 3 or 4;

\[ R(13) \text{ and } R(14) \]
identically or differently are -(CH₂)ₙ-(CHOH)ₘ-(CH₂)ᵢ-(CHOH)ⱼ-R(17) or -(CH₂)ₙ-O-(CH₂-CH₂O)ₘ-R(24);

\[ R(17) \]
is hydrogen or methyl, g, h and i identically or differently are zero, 1, 2, 3 or 4;

\[ j \]
is 1, 2, 3 or 4;

\[ R(15) \text{ and } R(16) \]
identically or differently are hydrogen, alkyl having 1, 2, 3, 4,
5 or 6 carbon atoms or, together with the carbon atom carrying them, are cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms;

\( R(18) \) is phenyl,
which is unsubstituted or substituted by 1 - 3 substituents selected from the group consisting of F, Cl, CF\(_3\), methyl, methoxy and NR(25)R(26);

\( R(25) \) and \( R(26) \)

\( 10 \) are \( H \) or alkyl having 1, 2, 3 or 4 carbon atoms;
or

\( R(18) \) is heteroaryl having 1, 2, 3, 4, 5, 6, 7, 8 or 9 carbon atoms,
which is unsubstituted or substituted as phenyl;
or

\( R(18) \) is alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms,
which is unsubstituted or substituted by 1 - 3 OH;
or

\( R(18) \) is cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms;

\( R(19), R(20), R(21), R(22) \) and \( R(23) \)
identically or differently are hydrogen or methyl;

\( R(24) \) is \( H \), alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms or \(-C_mH_{2m}^{-}\)R(18);

\( m \) is 1, 2, 3 or 4;

\( 25 \) one of the two substituents \( R(2) \) and \( R(3) \)
is hydroxyl;

and

the other of the substituents \( R(2) \) and \( R(3) \) in each case
is defined as \( R(1) \);

\( R(4) \) is alkyl having 1, 2, 3 or 4 carbon atoms; alkoxy having 1, 2, 3 or 4 carbon atoms, F, Cl, Br, I or \(-(CH_2)_n-(CF_2)_o-CF_3\);

\( n \) is zero or 1;
o is zero or 1;
and their pharmaceutically tolerable salts;
ay) bisortho-substituted benzoylguanidines of the formula
\[
\begin{align*}
R(1) \\
R(2) & \\
R(3) & \\
R(4) & \\
\end{align*}
\]
in which:
\[
\begin{align*}
R(1), R(2) \text{ and } R(3) & \text{ independently of one another are } R(10)-SO_2- \text{ or } R(14)R(15)N-SO_2^-; \\
a & \text{ is zero, 1 or 2,} \\
R(10), R(14) \text{ and } R(15) & \text{ independently of one another are alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, perfluoroalkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, alkenyl having 3, 4, 5 or 6 carbon atoms or } -C_{ab}H_{2ab}-R(16); \\
ab & \text{ is zero, 1, 2, 3 or 4;} \\
R(16) & \text{ is cycloalkyl having 3, 4, 5, 6 or 7 carbon atoms or phenyl, which is unsubstituted or substituted by 1-3 substituents selected from the group consisting of } F, Cl, CF_3, \text{ methyl, methoxy and } NR(17)R(18); \\
R(17) \text{ and } R(18) & \text{ independently of each other are hydrogen, } CF_3 \text{ or alkyl having 1, 2, 3 or 4 carbon atoms;} \\
or \[
\begin{align*}
R(14) & \text{ and } R(15) \\
\text{ together are 4 or 5 methylene groups, of which one } CH_2 \text{ group can be replaced by oxygen, sulfur, NH, N-CH}_3 \text{ or N-benzyl;} \\
or \\text{ } R(14) \text{ and } R(15) & \text{ are hydrogen;} \\
or \\text{ } R(1), R(2) \text{ and } R(3) & \end{align*}
\]
independently of each other are SR(21), -OR(22), -NR(23)R(24) or -CR(25)R(26)R(27);

R(21), R(22), R(23) and R(25)

independently of one another are -CgH2g-(C1-Cg)-heteroaryl,

which is unsubstituted or substituted by 1-3
substituents selected from the group consisting of F, Cl, CF3, CH3, methoxy, hydroxyl, amino, methylamino
and dimethylamino;

b is zero, 1 or 2;

R(24), R(26) and R(27)

independently of each other are hydrogen, alkyl having 1, 2,
3 or 4 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4
carbon atoms;

or

R(1), R(2) and R(3)

independently of one another are hydrogen, F, Cl, Br, I, CN,

-(Xa)dg-CdgH2dg+1, -(Xb)dh-(CH2)db-CdbF2db+1, alkenyl having 3, 4, 5, 6, 7
or 8 carbon atoms or -CdfH2dfR(30);

(Xa) is oxygen, sulfur or NR(33);

R(33) is hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or
perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;

dg is zero or 1;

(Xb) is oxygen, sulfur or NR(34);

R(34) is hydrogen, alkyl having 1, 2, 3, or 4 carbon atoms or
perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;

dh is zero or 1;

da is zero, 1, 2, 3, 4, 5, 6, 7 or 8;

db is zero, 1, 2, 3 or 4;

de is zero, 1, 2, 3, 4, 5, 6 or 7;

df is zero, 1, 2, 3 or 4;

R(30) is cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, phenyl,
biphenylyl or naphthyl,
where the aromatics phenyl, biphenyl or naphthyl are not substituted or substituted by 1-3 substituents selected from the group consisting of F, Cl, CF$_3$, methyl, methoxy and NR(31)R(32);

R(31) and R(32) are hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;

or

R(1), R(2) and R(3) independently of one another are NR(40)R(41) or -\(\text{Xe}\)-(CH$_2$)$_{ab}$R(45);

R(40) and R(41) independently of one another are hydrogen, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, perfluoroalkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms or (CH$_2$)$_e$-R(42);

e is zero, 1, 2, 3 or 4;

R(42) is cycloalkyl having 3, 4, 5, 6 or 7 carbon atoms or phenyl, which is not substituted or substituted by 1-3 substituents selected from the group consisting of F, Cl, CF$_3$, methyl, methoxy and NR(43)R(44);

R(43) and R(44) independently of one another are hydrogen, CF$_3$ or alkyl having 1, 2, 3 or 4 carbon atoms;

or

R(40) and R(41) together are 4 or 5 methylene groups, of which one CH$_2$ group can be replaced by oxygen, sulfur, NH, N-CH$_3$ or N-benzyl;

\(\text{Xe}\) is oxygen, sulfur or NR(47);
\( R(47) \) is hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;

\( eb \) is zero, 1, 2, 3 or 4;

\( R(45) \) is cycloalkyl having 3, 4, 5, 6 or 7 carbon atoms or phenyl, which is not substituted or substituted by 1-3 substituents selected from the group consisting of F, Cl, CF\(_3\), methyl, methoxy, NR(50)R(51) and \(-(Xfa)-(CH\(_2\))\(_{ed}\)-(Xfb)R(46)\);

\( Xfa \) is CH\(_2\), oxygen, sulfur or NR(48);

\( Xfb \) is oxygen, sulfur or NR(49);

\( R(48), R(49), R(50) \) and \( R(51) \) independently of one another are hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;

\( ed \) is 1, 2, 3 or 4;

\( R(46) \) is hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;

or

\( R(1), R(2) \) and \( R(3) \) independently of one another are \(-\text{CHR}(52)\text{R}(53)\);

\( R(52) \) is \(-(\text{CH}\(_2\))\(_{g}\)-(\text{CHOH})\(_h\)-(\text{CH})\(_i\)-(\text{CHOH})\(_k\)-\text{R}(54)\) or \(-(\text{CH}\(_2\))\(_g\)-O-(\text{CH}_2-\text{CH}_2\text{O})\(_h\)\text{R}(54)\);

\( R(54) \) is hydrogen or methyl;

\( g, h, i \) are identical or different and are zero, 1, 2, 3 or 4;

\( k \) is 1, 2, 3 or 4;

\( R(53) \) is hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

or

\( R(1), R(2) \) and \( R(3) \) independently of one another are \(-\text{C(OH)}\text{R}(55)\text{R}(56)\);

\( R(55) \) and \( R(56) \) are identical or different and are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;
or
R(55) and R(56)

together are cycloalkyl having 3, 4, 5 or 6 carbon atoms;
or

R(55) is \(-\text{CH}_2\text{OH}\);

and

R(4) and R(5)

independently of one another are alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, OH, F, Cl, Br, I, CN,

\(-\text{O}_n(\text{CH}_2)_o(\text{CF}_2)_p\text{-CF}_3;\)

\(n\) is zero or 1;

\(o\) is zero, 1 or 2;

\(p\) is zero, 1 or 2;

and their pharmaceutically tolerable salts;

az) substituted 1-naphthoylguanidines of the formula I

\[
\begin{align*}
\text{I} & \\
\text{R}_2, \text{R}_3, \text{R}_4, \text{R}_5, \text{R}_6, \text{R}_7 & \text{R}_8 \\
\text{N} & \text{O} \\
\text{H}_2\text{N} & \text{NH}_2
\end{align*}
\]

in which:
R2, R3, R4, R5, R6, R7 and R8

independently of one another are H, F, Cl, Br, I, CN, NO\(_2\), CF\(_3\), C\(_2\)F\(_5\)

or \(X_aY_bZ;\)

\(X\) is O, S, NR(10), CR(11)R(12), C=O, C(=O)NR(10), C(=O)O, SO, SO\(_2\), SO\(_2\)NR(10), OC=O, NR(10)C=O or NR(10)SO\(_2\),

where the linkage with the naphthalene ring is in each case effected through the atom on the left;

R(10), R(11) and R(12)

independently of one another are H, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, perfluoroalkyl having 1, 2, 3
or 4 carbon atoms or cycloalkyl having 3, 4, 5, 6 or 7 carbon atoms;

a is zero or 1;

Y is alkylene having 1, 2, 3, 4, 5, 6, 7 or 8 CH₂ groups;

it being possible for one of these CH₂ groups to be replaced by O, S, NR(13) or o-, p- or m-phenylene;

R(13) is H, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, perfluoroalkyl having 1, 2, 3 or 4 carbon atoms or cycloalkyl having 3, 4, 5 or 6 carbon atoms;

b is zero or 1;

Z is H, alkyl having 1, 2, 3, 4, 5, 6 or 7 carbon atoms, cycloalkyl having 3, 4, 5, 6 or 7 carbon atoms, C(=O)R(15), SO₂R(15), NR(16)R(17) or phenyl, which is not substituted or substituted by 1-3 substituents selected from the group consisting of F, Cl, Br, CF₃, methyl, methoxy, NR(21)R(22);

R(21) and R(22) independently of one another are H or alkyl having 1, 2, 3 or 4 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;

R(15) is N=C(NH₂)₂, NR(18)R(19), N(CH₂)₄NR(18)R(19) or OR(20);

c is 2 or 3;

R(18) and R(19) independently of one another are H, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;

or

R(18) and R(19) together are 4 or 5 methylene groups,

of which one CH₂ group can be replaced by oxygen, S, NH, N-CH₃, N-benzyl or
N-(p-chlorophenyl);
R(20) is H, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms,
perfluoroalkyl having 1, 2, 3 or 4 carbon atoms or
cycloalkyl having 3, 4, 5, 6 or 7 carbon atoms;

R(16) and R(17) independently of one another are H, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;
or
R(16) and R(17) together are 4 or 5 methylene groups, of which one CH₂ group can be replaced by oxygen, S, NH, N-CH₃, N-benzyl or N-(p-chlorophenyl);
or
Z is a N-containing heterocycle having 1, 2, 3, 4, 5, 6, 7, 8 or 9 carbon atoms,
where the N-containing heterocycle is linked via N or C and is not substituted or substituted by 1-3 substituents selected from the group consisting of F, Cl, Br, CF₃ methyl, methoxy and NR(21)R(22);
but where in the case that R(4) is an alkoxy radical, at least one of the substituents R(2), R(3), R(5), R(6), R(7) and R(8) is not hydrogen;
and their pharmaceutically tolerable salts;

ba) substituted 2-naphthoylguanidines of the formula I

in which:
at least one of the substituents R1, R3, R4, R5, R6, R7 and R8
is \( XY_a W Z \) or \( X'Y_a W Z' \);

\[ X \] is O, S, NR(10) or CR(11)R(12);

R(10), R(11) and R(12) independently of one another are H, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, perfluoroalkyl having 1, 2, 3 or 4 carbon atoms or cycloalkyl having 3, 4, 5, 6 or 7 carbon atoms;

\[ Y \] is alkylene having 1, 2, 3, 4, 5, 6, 7 or 8 CH\(_2\) groups, where one of these CH\(_2\) groups can be replaced by O, S, NR(13) or o-, p- or m-phenylene;

R(13) is H, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, perfluoroalkyl having 1, 2, 3 or 4 carbon atoms or cycloalkyl having 3, 4, 5 or 6 carbon atoms;

\[ a \] is zero or 1;

\[ W \] is CH\(_2\), SO\(_2\), S(=O)(=NH) or - if W does not immediately follow a hetero atom of the group \( XY_a \) - also O or NR(14);

R(14) is H, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, perfluoroalkyl having 1, 2, 3 or 4 carbon atoms or cycloalkyl having 3, 4, 5 or 6 carbon atoms;

\[ Z \] is \( C(=O)R(15) \), SO\(_2\)R(15) or - if W is not O or NR(14) - also NR(16)R(17);

R(15) is \( N=C(NH_2)_2 \), NR(18)R(19), N(CH\(_2\))\(_b\)NR(18)R(19) or OR(20);

\[ b \] is 2 or 3;

R(18) and R(19) independently of one another are H, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;
R(18) and R(19) together are 4 or 5 methylene groups, of which one CH$_2$ group can be replaced by oxygen, S, NH, N-CH$_3$, N-benzyl or N-(p-chlorophenyl);

R(20) is H, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, perfluoroalkyl having 1, 2, 3 or 4 carbon atoms or cycloalkyl having 3, 4, 5, 6 or 7 carbon atoms;

R(16) and R(17) independently of one another are H, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;

or

R(16) and R(17) together are 4 or 5 methylene groups, of which one CH$_2$ group can be replaced by oxygen, S, NH, N-CH$_3$, N-benzyl or N-(p-chlorophenyl);

X' is C=O, C(=O)NR(30), C(=O)O, SO, SO$_2$, SO$_2$NR(30), OC=O, NR(30) C=O or NR(30)SO$_2$,

where the linkage with the naphthalene ring is in each case effected through the atom on the left;

R(30) is H, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, perfluoroalkyl having 1, 2, 3 or 4 carbon atoms or cycloalkyl having 3, 4, 5, 6 or 7 carbon atoms;

Z' is C(=O)R(15), SO$_2$R(15), an N-containing heterocycle having 1, 2, 3, 4, 5, 6, 7, 8 or 9 carbon atoms,

where the N-containing heterocycle is linked via N or C and is not substituted or substituted by 1-3 substituents selected from the group consisting of F, Cl, Br, C$^{+}$, methyl, methoxy and NR(21)R(22);
R(21) and R(22)
individually of one another are H, alkyl having 1, 2, 3 or 4 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;

R(15)
is N=C(NH$_2$)$_2$, NR(18)R(19), N(CH$_2$)$_n$NR(18)R(19) or OR(20);
R(18) and R(19)
individually of one another are H, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;
or
R(18) and R(19)
together are 4 or 5 methylene groups,
of which one CH$_2$ group can be replaced by

R(20) is H, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, perfluoroalkyl having 1, 2, 3 or 4 carbon atoms or
cycloalkyl having 3, 4, 5, 6 or 7 carbon atoms;
or
- if W is not O or NR(14) - is NR(16)R(17);
R(16) and R(17)
individually of one another are H, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;
or
R(16) and R(17)
together are 4 or 5 methylene groups,
of which one CH$_2$ group can be replaced by oxygen S, NH, N-CH$_3$, N-benzyl or N-(p-chlorophenyl);

and in each case the remaining substituents R1, R3, R4, R5, R6, R7 and
R8, to which none of the abovementioned definitions has been assigned,  
individually of one another are H, I, Cl, Br, I, CN, NO₂, Cl, C₂F₆,  
or V₃Q₂U;

V is O, S, SO₂, NR(00), CO₂O, C=O, C(=O)NR(00),  
R(00), R(00) and R(07),

independently of one another are H, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, perfluoroalkyl having 1, 2, 3 or 4 carbon atoms or cycloalkyl having 3, 4, 5, 6 or 7 carbon atoms;

p is zero or 1;

Q is alkylone having 1, 2, 3, 4, 5, 6, 7 or 8 CH₂ groups,
where one of these CH₂ groups can be replaced by O,
S, NR(68) or a-, p- or m-phenylene;

R(68)

is H, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, perfluoroalkyl having 1, 2, 3 or 4 carbon atoms or cycloalkyl having 3, 4, 5 or 6 carbon atoms;

q is zero or 1;

U is H, alkyl having 1, 2, 3, 4, 5, 6 or 7 carbon atoms, cycloalkyl having 3, 4, 5, 6 or 7 carbon atoms, C(=O)R(65), SO₂R(65), NR(61)R(62) or phenyl,

which is not substituted or substituted by 1-3 substituents

selected from the group consisting of F, Cl, Br, CF₃, methyl, methoxy and NR(63)R(64);

R(63) and R(64)

independently of one another are H, alkyl having 1, 2, 3 or 4 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;

R(65) is N=C(NH₂)₂, NR(61)R(62) or OR(60);

R(61) and R(62)
independently of one another are H, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;

or

R(61) and R(62)
together are 4 or 5 methylene groups,
of which one CH₂ group can be replaced by oxygen, S, NH, N-CH₃, N-benzyl or N-(p-chlorophenyl);

or

U is an N-containing heterocycle having 1, 2, 3, 4, 5, 6, 7, 8 or 9 carbon atoms,
where the N-containing heterocycle is linked via N or C and is not substituted or substituted by 1-3 substituents selected from the group consisting of F, Cl, Br, CF₃, methyl, methoxy

and NR(63)R(64);
where, however, at least one of the substituents R5,R6, R7 and R8 is not hydrogen;
and their pharmaceutically tolerable salts;
bb) ortho-substituted benzoylguanidines of the formula I

in which:

R(1) is H, F, Cl, Br, I, CN, NO₂, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, alkoxy having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, cycloalkoxy having 3, 4, 5, 6, 7 or 8 carbon atoms or Xa-(CH₂)ₐ-(CF₂)ₐ-CF₃;

X is oxygen, sulfur or NR(9),
a is zero or 1;
b is zero, 1 or 2;
c is zero, 1, 2 or 3;

R(9) is H, alkyl having 1, 2, 3 or 4 carbon atoms or
\(-\text{C}_n\text{H}_{2n}\)R(6);

d is zero, 1, 2, 3 or 4;

R(6) is cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, phenyl, biphenyl or naphthyl,

where the aromatics phenyl, biphenyl or naphthyl are not substituted or
substituted by 1-3 substituents selected from the group consisting of F, Cl, CF₃,
methyl, methoxy and NR(7)R(8);

R(7) and R(8) independently of one another are
H or alkyl having 1, 2, 3 or 4 carbon atoms;

or

R(1) is -SR(10), -OR(10) or -CR(10)R(11)R(12);

R(10) is \(-\text{C}_n\text{H}_{2n}\)cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms in

the cycloalkyl ring,

heteroaryl having 1, 2, 3, 4, 5, 6, 7, 8 or 9 carbon atoms or

phenyl,

where heteroaryl and phenyl are unsubstituted or
substituted by 1-3 substituents selected from the group
consisting of F, Cl, CF₃, CH₃ methoxy, hydroxyl,

amino, methylamino and dimethylamino;

f is zero, 1 or 2;

R(11) and R(12) independently of one another are as defined for R(10) or are
hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

or

R(1) is phenyl, naphthyl, biphenyl or heteroaryl having 1, 2, 3, 4, 5, 6, 7, 8 or 9 carbon atoms, the latter being linked via a carbon or a
nitrogen ring atom,
each of the radicals being unsubstituted or substituted by 1-3 substituents selected from the group consisting of F, Cl, CF₃, CH₃ methoxy, hydroxyl, amino, methylamino and dimethylamino,
or
R(1) is -SR(13), -OR(13), -NHR(13), -NR(13)R(14), -CHR(13)R(15),
-C[R(15)R(16)]OH, -C≡CR(18), -C[R(19)]=CHR(18),
-C[R(20)R(21)]_l-(CO)-[CR(22)R(23)]_m-R(24),
k is zero, 1, 2, 3 or 4;
l is zero, 1, 2, 3 or 4;
R(13) and R(14) are identical or different and are
-(CH₂)ᵣ-(CHOH)ₗ-(CH₂)ᵫ-(CHOH)ₖ-R(17) or
-(CH₂)ᵣ-O-(CH₂-CH₂O)ₗ-R(24);
R(17) is hydrogen or methyl,
g, h and i are identical or different and are zero, 1, 2, 3 or 4;
kk is 1, 2, 3 or 4;
R(15) and R(16) are identical or different and are hydrogen, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, or together with the carbon atom carrying them are cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms;
R(18) is phenyl,
which is unsubstituted or substituted by 1-3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(25)R(26);
R(25) and R(26) are H or alkyl having 1, 2, 3 or 4 carbon atoms;
R(18) is heteroaryl having 1, 2, 3, 4, 5, 6, 7, 8 or 9 carbon atoms
  which is unsubstituted or substituted as for phenyl;

or

R(18) is alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms,
  which is unsubstituted or substituted by 1-3 OH;

or

R(18)
  is cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms;

R(19), R(20), R(21), R(22) and R(23)
  are identical or different and are hydrogen or methyl;

R(24) is H, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, cycloalkyl
  having 3, 4, 5, 6, 7 or 8 carbon atoms or -C\textsubscript{m}H\textsubscript{2m}-R(18);
  \(m\) is 1, 2, 3 or 4;

one of the two substituents R(2) and R(3)
  is -O-CO-R(27);

R(27) is alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, cycloalkyl
  having 3, 4, 5, 6, 7 or 8 carbon atoms, phenyl, biphenylyl,
  naphthyl, pyridyl or quinolyl,

  where phenyl, biphenylyl, naphthyl, pyridyl or quinolyl
  are unsubstituted by 1-3 substituents selected from the
  group consisting of F, Cl, CF\textsubscript{3}, methyl, methoxy and
  NR(7)R(8);

R(7) and R(8)

  independently of one another are hydrogen or
  alkyl having 1, 2, 3 or 4 carbon atoms;

one of the substituents R(2) and R(3)
  always being defined as R(1);

R(4) and R(5)

  independently of one another are hydrogen, alkyl having 1, 2, 3 or 4
  carbon atoms;
  \(\cdot\)koxoxy having 1, 2, 3 or 4 carbon atoms, F, Cl, Br, I, CN or
-(CH₂)ₙ-(CF₂)o-CF₃;

n is zero or 1;
o is zero or 1;

and their pharmaceutically tolerable salts;

bc) benzoylguanidines of the formula I

\[
\begin{align*}
&\text{R(1)} \quad \text{R(2)} \\
&\text{R(3)} \quad \text{N} \quad \text{NH}_2 \text{R(4)}
\end{align*}
\]

which:

R(1) is R(13)-SOₘ or R(14)R(15)N-SO₂⁻;

m is 1 or 2;

R(13) is alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms,
perfluoroalkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms,
alkenyl having 3, 4, 5, 6, 7 or 8 carbon atoms or -CₙH₂ₙ-R(16),
n is zero, 1, 2, 3 or 4;

R(16) is cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms,
phenyl, biphenyl or naphthyl,
where phenyl, biphenyl and naphthyl are not substituted or substituted by 1-3 substituents
selected from the group consisting of F, Cl, CF₃,
methyl, methoxy and NR(25)R(26);

R(25) and R(26)

independently of one another are hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or perfluoroalkyl having 1,
2, 3 or 4 carbon atoms;

R(14) is hydrogen, alkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms,
perfluoroalkyl having 1, 2, 3, 4, 5, 6, 7 or 8 carbon atoms, alkenyl
having 3, 4, 5, 6, 7 or 8 carbon atoms or \(-\text{C}_n\text{H}_{2n}\)-R(27),

\(n\) is zero, 1, 2, 3 or 4;

R(27) is cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, phenyl, biphenyl or naphthyl,

where phenyl, biphenyl and naphthyl are not substituted or substituted by 1-3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy and NR(28)R(29);

R(28) and R(29) independently of one another are hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;

R(15) is hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or perfluoroalkyl having 1, 2, 3 or 4 carbon atoms;

or

R(14) and R(15) together are 4 or 5 methylene groups, of which one CH₂ group can be replaced by oxygen, S, NH, N-CH₃ or N-benzyl;

one of the substituents R(2) and R(3) is hydrogen;

and the other substituent R(2) and R(3) in each case is \(-\text{CHR}(30)\text{R}(31)\);

R(30)

\[\text{is } -(\text{CH}_2)_g-(\text{CHOH})_h-(\text{CH}_2)_i-(\text{CHOH})_k-R(32) \text{ or } -(\text{CH}_2)_g-\text{O-}(\text{CH}_2-\text{CH}_2\text{O})_h-R(24);\]

R(24) and R(32) independently of one another are hydrogen or methyl;

\(g, h, i\)

are identical or different and are zero, 1, 2, 3 or 4;

\(k\) is 1, 2, 3 or 4;

or the other substituent R(2) and R(3) in each case
is-C(OH)R(33)R(34);
R(31), R(33) and R(34)
are identical or different and are hydrogen or alkyl having 1,
2, 3 or 4 carbon atoms

or
R(33) and R(34)
together are cycloalkyl having 3, 4, 5 or 6 carbon
atoms;
or
R(33) is -CH₂OH;
R(4) is alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4
carbon atoms, F, Cl, Br, I, CN, -(CH₂)n-(CF₂)ₙ-CF₃;
n is zero or 1;
o is zero, 1 or 2;
and their pharmaceutically tolerable salts;

bd) indanylidineacetylguanidines of formula I

in which
R1, R2, R3, R4, R5 and R6
independently of one another are H, C₁₋C₁₀-alkyl; haloalkyl having
1-6 carbon atoms, O-C₁₋C₁₀-alkyl, haloalkoxy having 1-6 carbon
atoms, F, Cl, Br, I, aryl, substituted aryl, heteroaryl, substituted
heteroaryl, OH, O-lower alkyl, O-aryl, O-lower alkylaryl, O-
substituted aryl, O-lower alkyl-substituted aryl, O-C(=O)-C₁₋C₄-
alkylaryl, O-C(=O)-NH-C₁₋C₄-alkyl, O-C(=O)-N(C₁₋C₄-alkyl)₂, NO₂,
CN, CF₃, NH₂, NH-C(=O)-C₁₋C₄-alkyl, NH-C(=O)-NH₂, COOH,
C(=O)-O-C₁₋C₄-alkyl, C(=O)-NH₂, C(=O)-NH-C₁₋C₄-alkyl,
C(=O)-N(C₁₋C₄-alkyl)₂, C₁₋C₄-COOH,
C₁₋C₄-alkyl-C(=O)-O-C₁₋C₄-alkyl, SO₃H, SO₂-alkyl, SO₂-alkylaryl,
SO₂-N-(alkyl)₂, SO₂-N(alkyl)(alkylaryl), C(=O)-R₁₁,
C₁₋C₁₀-alkyl-C(=O)-R₁₁, C₂₋C₁₀-alkenyl-C(=O)-R₁₁,
C₂₋C₁₀-alkynyl-C(=O)-R₁₁, NH-C(=O)-C₁₋C₁₀-alkyl-C(=O)-R₁₁ or
O-C₁₋C₁₁-alkyl-C(=O)-R₁₁;

R₁₁ is C₁₋C₄-alkyl, C₁₋C₄-alkynyl, aryl, substituted aryl, NH₂,
NH-C₁₋C₄-alkyl, N-(C₁₋C₄-alkyl)₂, SO₃H, SO₂-alkyl,
SO₂-alkylaryl, SO₂-N-(alkyl)₂ or SO₂-N(alkyl)(alkylaryl);  

X is O, S or NH;

R₇, R₈, R₉ and R₁₀ independently of one another are H, alkyl, cycloalkyl, aryl,
alkylaryl,  

or

R₈ and R₉ together are part of a 5-, 6- or 7-membered heterocyclic ring;

or their pharmaceutically tolerable salts;  

be) phenyl-substituted alkenylcarboxylic acid guanidines of the formula I

in which:

T is

R(A) is hydrogen, F, Cl, Br, I, CN, OH, OR(6), (C₁₋C₄)-alkyl,
O_{r}(CH_{2})_{a}C_{b}\text{F}_{2b+1}, (C_{3}-C_{9})\text{-cycloalkyl or NR(7)R(8)

r is zero or 1;
a is zero, 1, 2, 3 or 4;
b is 1, 2, 3 or 4;

R(6) is (C_{1}-C_{4})\text{-alkyl, (C}_{1}-C_{4})\text{-perfluoroalkyl, (C}_{3}-C_{9})\text{-alkenyl,
(C}_{3}-C_{9})\text{-cycloalkyl, phenyl or benzyl,

where the phenyl ring is not substituted or substituted
by 1-3 substituents selected from the group consisting
of F, Cl, CF_{3}, methyl, methoxy and NR(9)R(10);

R(9) and R(10)
are H, (C_{1}-C_{4})\text{-alkyl or (C}_{1}-C_{4})\text{-perfluoroalkyl;

R(7) and R(8)
independently of one another are defined as R(6);
or

R(7) and R(8)
together are 4, or 5, methylene groups, of which one
CH_{2} group can be replaced by oxygen, sulfur, NH,
N-CH_{3} or N-benzyl;

R(B), R(C) and R(D)
independently are as defined for R(A);

x is zero, 1 or 2;
y is zero, 1 or 2;

R(F) is hydrogen, F, Cl, Br, I, CN, OR(12), (C_{1}-C_{8})\text{-alkyl, O}_{p}(CH_{2})_{q}C_{g}\text{F}_{2g+1},
(C_{3}-C_{9})\text{-cycloalkyl or (C}_{1}-C_{9})\text{-heteroaryl;

p is zero or 1;
f is zero, 1, 2, 3 or 4;
g is 1, 2, 3, 4, 5, 6, 7 or 8;

R(12) is (C_{1}-C_{8})\text{-alkyl, (C}_{1}-C_{4})\text{-perfluoroalkyl, (C}_{3}-C_{9})\text{-alkenyl,
(C}_{3}-C_{9})\text{-cycloalkyl, phenyl or benzyl,

where the phenyl ring is not substituted or substituted
by 1-3 substituents selected from the group consisting
of F, Cl, CF_{3}, methyl, methoxy and NR(13)R(14);
R(13) and R(14) are H, (C₁-C₄)-alkyl or (C₁-C₄)-perfluoroalkyl;
R(E) independently is as defined for R(F);
R(1) independently is as defined for T;
or
R(1) is hydrogen, \(-O_kC_mH_{2m+1}\), \(-O_n(CH_2)_pC_qF_{2q+1}\), F, Cl, Br, I, CN,
-(C=O)-N=C(NH₂)₂, -SO₁R(17), -SO₂NR(31)R(32), -O₁(CH₂)aC₈H₅,
-O₂-(C₉-C₉)-heteroaryl or -S₂-(C₉-C₉)-heteroaryl;
k is zero or 1;
m is zero, 1, 2, 3, 4, 5, 6, 7 or 8;
n is zero or 1;
p is zero, 1, 2, 3 or 4;
q is 1, 2, 3, 4, 5, 6, 7 or 8;
r is zero, 1, 2;
r₂ is zero, 1, 2;
R(31) and R(32) independently of one another are hydrogen, (C₁-C₈)-alkyl or (C₁-C₈)-perfluoroalkyl;
or
R(31) and R(32) together are 4 or 5 methylene groups, of which one CH₂ group can be replaced by oxygen, S, NH, N-CH₃ or N-benzyl;
R(17) is (C₁-C₈)-alkyl;
u is zero or 1;
u₂ is zero or 1;
v is zero, 1, 2, 3 or 4;
where the phenyl ring is not substituted or substituted by 1-3 substituents selected from the group consisting of F, Cl, CF₃, methyl, methoxy, \(-(CH₂)wNR(21)R(22)\), NR(18)R(19) and (C₁-C₈)-heteroaryl;
R(18), R(19), R(21) and R(22) independently of one another are (C₁-C₄)-alkyl or
(C₁-C₄)-perfluoroalkyl;

w is 1, 2, 3 or 4;

where the heterocycle of the (C₁-C₆)-heteroaryl is
unsubstituted or substituted by 1-3 substituents

selected from the group consisting of F, Cl, CF₃,
methyl or methoxy;

R(2), R(3), R(4) and R(5)

independently of one another are as defined for R(1),

or

R(1) and R(2) or R(2) and R(3)

in each case together are -CH-CH=CH-CH-,

which is unsubstituted or substituted by 1-3 substituents

selected from the group consisting of F, Cl, CF₃, methyl,

methoxy, -(CH₂)₂NR(24)R(25) and NR(26)R(27);

R(24), R(25), R(26) and R(27)

are H, (C₁-C₄)-alkyl or (C₁-C₄)-perfluoroalkyl;

w₂ is 1, 2, 3 or 4;

the radical T being present in the molecule at least twice, but at most three
times;

and their pharmaceutically tolerable salts;

bf) benzoylguanidines of the formula I

in which:

R(1) is CF₃;

one of the substituents R(2) and R(3)

is hydrogen;
and the other substituent R(2) and R(3) in each case
is -C(OH)(CH₃)-CH₂OH, -CH(CH₃)-CH₂OH or -C(OH)(CH₃)_2;
R(4) is methyl, methoxy, Cl or CF₃;
and their pharmaceutically tolerable salts;

(DE 195 02 895, DE 44 30 212, EP 667 341, DE 44 04 183, EP 708 088,
EP 726 254, US 4 251 545, DE 35 02 629, WO 84/00875, Kumamoto et

II. or compounds of the formula

in which:

W, Y and Z
are a nitrogen atom or a carbon atom substituted by R(2) or R(3) or
R(4);
R(1) is hydrogen, A, Hal, -CF₃, -CH₂F, -CHF₂, -CH₂CF₃, -C₂F₅, -CN,
-NO₂, -ethynyl, or an X-R';
A is alkyl having 1 to 6 carbon atoms;
Hal is F, Cl, Br or I;
X is oxygen, S or NR";
R" is hydrogen, A or a cyclic methylene chain having 3 to
7 carbon atoms;
R' is H, A, HO-A-, HOOC-A-, (C₃-C₇)-cycloalkyl, (C₆-C₈)-
cycloalkylalkyl, CF₃, CH₂F, CHF₂, CH₂-CF₃, Ph, -CH₂-Ph or
Het;
Ph is phenyl, naphthyl or biphenyl, which is unsubstituted or mono-, di- or trisubstituted by A, OA, NR'R'', Hal, CF$_3$;

Het is a mono- or binuclear saturated, unsaturated or aromatic heterocycle having 1 to 4 nitrogen, oxygen and/or sulfur atoms, which is unsubstituted or mono-, di- or trisubstituted by Hal, CF$_3$, A, OH, OA, -X-R', -CN, -NO$_2$, and/or carbonyl oxygen, where Het is bonded via N or an alkylene chain C$_m$H$_{2m}$ where m = zero to 6;

or

R' and R''
together are alkylene having 4 - 5 carbon atoms, in which one CH$_2$ group can also be replaced by oxygen, S, NH, N-A, N-Ph and N-CH$_2$-Ph;

R(2) and R(3)

independently of one another are hydrogen, Hal, A, HO-A, -X-R', -C(=N-OH)-A, A-O-CO-(C$_1$-C$_4$)-alkyl-, CN, NO$_2$, COOH, halogen-substituted A, in particular CF$_3$, CH$_2$F, CHF$_2$, C$_2$F$_5$, CH$_2$CF$_3$, or S(O)$_n$R''';

R''' is A, Ph or -Het;

n is zero, 1 or 2;

or

R(2) and R(3)

independently of one another are SO$_2$NR'R'', Ph or -O-Ph, -O-CH$_2$-Ph, -CO-A, -CHO, -COOA, -CSNR'R'', CONR'R'', -CH=CH-COOH, -CH=CH-COOA, indenyl, indanyl, decahydronaphthyl, cyclopentenyl, dihydrothien, I, dihydrofuryl, heterobicyclyl, alkylthienyl, halothienyl, haloalkyl: ienyl, acylthienyl, halofuryl, haloalkylfuryl or pyrrolyl;

or
R(2) and R(3) independently of one another are R(5)-O-;
R(5) is hydrogen, A, (C₁-C₆)-alkenyl or (C₃-C₇)-cycloalkyl;
R(4) is Ph, Het, -O-Het; CF₃, S(O)ₙR‴, -SO₂NR'R″, alk;

or
two of the substituents R(1) to R(4) together are a group
-O-CR(6)R(7)-CO-NR(8)-,
or R₆ or N[R(2)]O₀ to₄ R₇)

where R(2) has the meaning indicated;

R(6), R(7), R(8) and R(9) independently of one another are H or A;
or
R(8) is (C₅-C₇)-cycloalkyl;
or
R(9) is cyano;

alk is straight-chain or branched (C₁-C₈)-alkyl or (C₃-C₈)-cycloalkyl,

which is unsubstituted or mono-, di- or trisubstituted by A;
or
alk is an ethenyl or ethynyl radical which is substituted by H, A, Ph or
Het;
or

III. compounds of the formula

in which:
X is H, Hal, (Hal)3C-, (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl, substituted phenyl, (C₁-C₆)-alkyl-S- or (C₁-C₆)-alkyl-SO₂-;

Y is NH₂ or substituted amino;

or

5 X and Z
together are a -(CH₂)₄- or a 1,3-butadienylene chain;

or

Z is H, Hal, OH, HS, (C₁-C₆)-alkyl, (C₃-C₆)-cycloalkyl, substituted phenyl;

or

10 is an amino group -NR(1)R(2);

R(1) is H, straight- or branched-chain, optionally substituted (C₁-C₆)-alkyl,

which can be interrupted by oxygen;

or

15 R(1) is (C₃-C₆)-alkenyl, (C₃-C₆)-alkynyl, (C₃-C₇)-cycloalkyl or OH-substituted phenyl or OH-substituted phenyl-(C₁-C₄)-alkyl or OH-substituted (C₃-C₇)-cycloalkyl;

R(2) is 1-morpholino, hydrogen or a straight or branched (C₁-C₆)-alkyl chain,

which can be interrupted by oxygen or an amino group,

which straight or branched (C₁-C₆)-alkyl chain is unsubstituted or substituted by

20 a substituted or unsubstituted mono- or polynuclear heterocycle which contains nitrogen, oxygen or sulfur atoms;

or

which alkyl chain is substituted by phenyl,

25 unsubstituted or mono- or polysubstituted by (C₁-C₄)-alkoxy, optionally substituted by OH, alkylamino, alkyl or phenyl;
by an aminocarbonyl group
or
by hydroxyl or (C₁-C₄)-alkoxy groups,

5

or

R(2) is phenyl,

unsubstituted or substituted by alkyl, alkoxy, an amino group, which as substituents carries:

- H, a mono- or polynuclear heterocycle which contains nitrogen, oxygen or sulfur atoms,

10

- which is unsubstituted or substituted by H, Hal or (C₁-C₄)-alkyl;

- a phenyl radical,

15

- unsubstituted or substituted by a substituent selected from the group consisting of (C₁-C₄)-alkyl, (C₁-C₄)-alkoxy, Hal and OH;

or

R(2) is 1-piperidino,

unsubstituted or substituted in the 4-position by an acyl radical of an aliphatic, alicyclic, aromatic or heteroaromatic carboxylic acid, (C₁-C₄)-alkyl, which for its part can be substituted by OH or (C₁-C₄)-alkoxy or a (C₁-C₄)-alkoxy-substituted phenyl radical;

20

or

R(2) is amidino,

which is unsubstituted or substituted by phenyl,

which is unsubstituted or substituted by Hal or alkyl;

30

or

R(2) is an acyl radical of an aliphatic, alicyclic, aromatic or heteroaromatic carboxylic acid,
or

R(2) is a (C₁-C₈)-alkyl chain, which can be substituted by a phenyl radical carrying OH, alkoxy or alkyl radicals,
or

5  
R(1) and R(2)

together with the nitrogen atom to which they are bonded, are

a piperazine ring,

which is unsubstituted or via a (C₁-C₆)-methylene chain carries a mono- or polynuclear heterocycle,

10  
Hal is F, Cl, Br or I;

or

IV. indoloylguanidine derivatives of the formula

in which

R(2) is hydrogen, unsubstituted or substituted (C₁-C₈)-alkyl, (C₃-C₇)-cycloalkyl, OH, (C₁-C₆)-alkyl-O-, an aromatic radical or a group -CH₂-R(20);

R(20) is (C₂-C₆)-alkenyl or (C₂-C₆)-alkynyl;

R(1) is 1 to 5 identical or different substituents, which are:

hydrogen, unsubstituted or substituted (C₁-C₈)-alkyl, (C₂-C₆)-alkenyl, (C₂-C₆)-alkynyl, (C₃-C₇)-cycloalkyl, halogen, -NO₂, (C₂-C₆)-alkanoyl, arylalkanoyl having up to 10 carbon atoms, aroyl having up to 11 carbon atoms, -COOH, (C₂-C₆)-alkoxycarbonyl, an aromatic group or one of the following mentioned groups: -OR(3), -NR(6)R(7) or -S(O)₂R(40);

R(3) is hydrogen, (C₂-C₆)-alkyl, substituted (C₁-C₆)-alkyl, (C₃-C₇)-cycloalkyl, an aromatic radical or a group -CH₂-R(30)

R(30) is alkenyl or alkynyl;
R(6) and R(7) independently of one another are hydrogen, unsubstituted or substituted (C₁-C₆)-alkyl, (C₃-C₇)-cycloalkyl, (C₂-C₆)-alkanoyl, an arylalkanoyl group having up to 10 carbon atoms, an aroyl group having up to 11 carbon atoms, an aromatic group or -CH₂-R(60);

R(60) is (C₂-C₆)-alkenyl or (C₂-C₆)-alkynyl;

or

R(6) and R(7) together with the nitrogen atom are a 5-7-membered cyclic amine, which can additionally contain further heteroatoms in the ring;

n is zero, 1 or 2;

R(40) is unsubstituted or substituted (C₁-C₆)-alkyl, or an aromatic group, or a group -A-CH₂-H-R'

A is oxygen, -S(O)ₙ⁻ or -N(R₅₀)-;

R(5₀) is hydrogen or (C₁-C₆)-alkyl;

R' is hydrogen, unsubstituted or substituted (C₁-C₆)-alkyl, in which the ring represents a saturated 3-8-membered heterocycle having a nitrogen atom,

said substituted alkyl carries one or more groups selected from the group consisting of halogen, -OH, (C₁-C₆)-alkoxy, -CN, -COOH, (C₂-C₆)-alkoxycarbonyl, (C₂-C₆)-alkanoyl, arylalkanoyl having up to 10 carbon atoms, aroyl having up to 11 carbon atoms, an aromatic group, -CONR(4)R(5),

R(4) and R(5) identically or differently are hydrogen or (C₁-C₆)-alkyl;

or

R(4) and R(5) are connected to one another and together form a 5-7-membered cyclic amine which can additionally contain
further heteroatoms in the ring,
or said substituted alkyl carries a group

\[ \text{A} - \text{CH} \text{E} - \text{R}'' \]

in which:

- \( E \) is a nitrogen atom or a CH group;
- \( R'' \) is hydrogen, \((C_1-C_6)\)-alkyl which is unsubstituted or
  substituted by OH, \((C_1-C_6)\)-alkoxy, -CN, -COOH, \((C_2-C_6)\)-alkoxycarbonyl, \((C_2-C_8)\)-alkanoyl, aralkanoyl having up to
  10 carbon atoms, aroyl having up to 11 carbon atoms, an
  aromatic group, \(-\text{NR}(6)\text{R}(7)\), \(-\text{CONR}(4)\text{R}(5)\);

\( R(4) \) and \( R(5) \) independently of one another are hydrogen or \((C_1-C_6)\)-alkyl;

where the cyclic system of the formula

\[ \text{A} - \text{CH} \text{E} - \]

is a 3-8-membered saturated aliphatic or heterocyclic ring system having a nitrogen atom,

and where the aromatic groups mentioned are an aryl radical having up to

- 10 carbon atoms, a 5- or 6-membered heteroaryl radical having
  1 - 4 nitrogen atoms, a 5- or 6-membered heteroaryl group containing 1 or
  2 nitrogen atoms and a heteroatom which is oxygen or sulfur, or furyl,

and where the aryl radicals mentioned can be unsubstituted or substituted
by unsubstituted \((C_1-C_6)\)-alkyl or substituted \((C_1-C_6)\)-alkyl, halogen, -NO\(_2\),

\((C_2-C_6)\)-alkoxycarbonyl, COOH, -OR(3), NR(6)R(7), -CONR(4)R(5),
-SO\(_2\)NR(6)R(7) or S(O)\(_n\)R(40),

where \( R(1) \) and the guanidinocarbonyl radical can be in any desired
position of the 5- or 6-membered ring of the indole system,

and the appropriate pharmaceutically tolerable salts;

or
V. heterocyclic guanidine derivatives of the formula

![Chemical Structure]

in which:

- $X$ is $\text{O}^-, \text{S}^-, \text{NH}^-, \text{N}\left[(\text{C}_1-\text{C}_4)-\text{alkyl}\right]^-, \text{or} \text{-N(phenyl)}^-;

- $R(1)$, $R(2)$ and $R(3)$ are hydrogen, halogen, $(\text{C}_1-\text{C}_4)$-alkyl, $(\text{C}_1-\text{C}_4)$-alkyl-O-, phenyl, benzyl;

or

- two of the substituents $R(1)$, $R(2)$ and $R(3)$ together with one side of the benzo system are a 4-6-membered carbocyclic ring;

- $R(4)$ and $R(5)$ independently of one another are hydrogen, $(\text{C}_1-\text{C}_{12})$-alkyl, benzhydryl, aralkyl,

  which is unsubstituted or substituted by one or more substituents from the groups halogen, $(\text{C}_1-\text{C}_4)$-alkyl, $(\text{C}_1-\text{C}_4)$-alkyl-O- or $\text{-CF}_3$, $\text{-CH}_2\text{-CF}_3$, $\text{-CH}_2\text{-CH}_2\text{-T}$,

  - $m$ is zero to 3;
  - $T$ is $\text{-CO-O}\text{-T}(1)$;
  - $T(1)$ is hydrogen or $(\text{C}_1-\text{C}_4)$-alkyl;

- $\text{Cy}$ is a benzo fused unsaturated or dihydro-5-membered ring heterocycle

![Chemical Structure]

a pyrazole or imidazole ring of the formula

![Chemical Structure]
a naphthyl radical or a dihydro- or tetrahydronaphthyl radical

\[
\begin{array}{c}
\text{R(6)} \\
\end{array}
\]

5 a 2-, 3- or 4-pyridyl radical

\[
\begin{array}{c}
\text{R(6)} \\
\text{Z} \\
\text{R(7)}
\end{array}
\]

\[Z \text{ is } N- \text{ or } CH;\]

a thienyl radical

\[
\begin{array}{c}
\text{S} \\
\text{R(6)} \\
\text{R(7)}
\end{array}
\]

10 \(R(6)\) is hydrogen, halogen, hydroxyl, \((C_1-C_{10})\)-alkyl, \((C_1-C_{10})\)-alkyl-O-, phenoxy, \((C_1-C_{10})\)-alkyloxymethyloxy- or \(-(O)_nS\)-R(9);

\[R(9) \text{ is } (C_1-C_{10})\)-alkyl, thienyl, pyridyl, thiazolyl, thiadiazolyl, imidazolyl, pyrazolyl or phenyl,

each of which is unsubstituted or mono- or disubstituted by halogen, \((C_1-C_4)\)-alkyl or \((C_1-C_4)\)-alkyl-O-;

\[R(7) \text{ and } R(8)\]

is hydrogen, halogen, hydroxyl, \((C_1-C_{10})\)-alkyl, \((C_1-C_{10})\)-alkyl-O-, phenyl, phenoxy or \((C_1-C_{10})\)-alkyloxymethyloxy;

or

Cy is phenyl,

which is unsubstituted or mono- or disubstituted by halogen,

\[R(3)\]

\[Cy \text{ is } -Gr-Am;\]

Gr is \(-R(13)-R(12)-(CH_2)_q-C[W][W(1)]-(CH_2)_p-; R(13)R(14)- \text{ or } -R(15)-;\]

30 \[R(12) \text{ is a single bond, } -O-, -(O)_nS-, -CO- \text{ or } -CONH-;\]

\[R(13) \text{ is a single bond, phenyl, thienyl, pyridyl, thiazolyl, thiadiazolyl, imidazolyl or pyrazolyl;}\]
R(14) is a single bond or SO$_2$-;
R(15) is (C$_2$-C$_{10}$)-alkenyl- or (C$_2$-C$_{10}$)-alkynyl;
W and W(1)

independently of one another are hydrogen, (C$_1$-C$_4$)-alkyl;

or

W and W(1)
cyclically connected to one another are a (C$_3$-C$_6$)-hydrocarbon ring;

q and q'

are zero to 9;

Am is -NR(10)R(11);
R(10) is hydrogen, (C$_1$-C$_4$)-alkyl or benzyl,
R(11) is (C$_1$-C$_4$)-alkyl, phenyl or benzyl;

or

R(10) and R(11)
together are a (C$_3$-C$_{10}$)-alkylene group,

which is unsubstituted or substituted by -COOH,
(C$_1$-C$_3$)-alkoxycarbonyl, (C$_2$-C$_4$)-hydroxyl-
alkylene or benzyl;

or

Am is pyrrolyl, pyridyl, pyrazolyl, morpholinyl, dihydropyridyl,
tetrahydropyridyl, quinuclidinyl, imidazolyl,
3-azabicyclo[3.2.1]octyl,

which is unsubstituted or substituted by (C$_1$-C$_4$)-alkyl,

or

Am is azabicyclo[3.2.2]nonyl;

or

Am is a piperazine group of the formula

\[ \text{R(16) is hydrogen, (C}_1\text{-C}_4\text{-alkyl, (C}_3\text{-C}_6\text{-cycloalkyl, phenyl,}
\text{ tolyl, methoxyphenyl, halophenyl, diphenylmethylene,} \]
benzyl or pyridyl;

or

Am is an azido group \(-(O)t-(CH_2)q-C[W][W(1)]-(CH_2)q'-.N_3;\)

t is zero or 1;

where \(W\) and \(W(1)\) have the previously indicated meaning;

and the optical enantiomers and the pharmacologically tolerable salts;

or

VI. Guanidine compounds as described in


where \(R_1 = R_2\) is H, halo, alkyl, CN, NO_2, perfluoroalkyl, SO_3CF_3;

\(R_3\) = CH=CH_2, CH_2=CH=CH_2, CH_2=CH_2=CH=CH_2, cycloalkenyl,

cycloalkenylalkyl; \(R_4\) = alkyl, (substituted) phenyl,

or as described in DE 195 48 708, WO 97 25 310, WO 97 27 183,


3. The pharmaceutical combination preparation as claimed in claim 2,

comprising an NHE inhibitor and a medicament for lowering the blood

pressure for the treatment of hypertension under cardioprotective

conditions.

4. The pharmaceutical combination preparation as claimed in claim 2,

comprising an NHE inhibitor and a beta-receptor blocker for the treatment

of hypertension and the treatment of arrhythmia under cardioprotective

conditions.
5. The pharmaceutical combination preparation as claimed in claim 2, comprising an NHE inhibitor and a calcium antagonist for the treatment of hypertension under cardioprotective conditions.

6. The pharmaceutical combination preparation as claimed in claim 2, comprising an NHE inhibitor and an angiotensin conversion enzyme inhibitor for the treatment of hypertension under cardioprotective conditions.

7. The pharmaceutical combination preparation as claimed in claim 2, comprising an NHE inhibitor and a diuretic or an aldosterone antagonist for the treatment of hypertension and cardiac insufficiency under cardioprotective conditions.

8. The pharmaceutical combination preparation as claimed in claim 2, comprising an NHE inhibitor and a medicament which strengthens the contractile force of the heart, for the treatment of cardiac insufficiency and congestive heart failure under cardioprotective conditions.

9. The pharmaceutical combination preparation as claimed in claim 2, comprising an NHE inhibitor and a cardiac glycoside for the treatment of cardiac insufficiency and congestive heart failure under cardioprotective conditions.

10. The pharmaceutical combination preparation as claimed in claim 2, comprising an NHE inhibitor and an antiarrhythmic for the treatment of cardiac arrhythmias of various genesis under cardioprotective conditions.

11. The pharmaceutical combination preparation as claimed in claim 2, comprising an NHE inhibitor and an antiarrhythmic of the classes I, II, III or IV for the treatment of cardiac arrhythmias of various genesis under cardioprotective conditions.
12. The pharmaceutical combination preparation as claimed in claim 2, comprising an NHE inhibitor and a nitrate having cardiovascular activity.

13. The pharmaceutical combination preparation as claimed in claim 2, comprising an NHE inhibitor and an opener of the K(ATP) channel.

14. The pharmaceutical combination preparation as claimed in claim 2, comprising an NHE inhibitor and a K(ATP) blocker.

15. The pharmaceutical combination preparation as claimed in claim 2, comprising the NHE inhibitor cariporide (Hoe 642) in combination with an inhibitor of the non-inactivating sodium channel.

16. A commercial pack, comprising as pharmaceutically active compound an inhibitor of the Na⁺/H⁺ exchanger and another substance having cardiovascular activity, together with instructions for the combined use of these active compounds for simultaneous or separate use or use at graded time intervals in the treatment or prophylaxis of cardiovascular diseases.

DATED this 26th day of August 1998.

HOECHST MARION ROUSSEL DEUTSCHLAND GMBH
Abstract

Pharmaceutical combination preparation of an inhibitor of the sodium/hydrogen exchanger and a medicament for the treatment of cardiovascular diseases

These combinations of an NHE inhibitor can comprise one or more therapeutically active compounds having cardiovascular activity. The combination of the cardioprotective properties with known therapies of cardiovascular diseases leads on the one hand to an improvement of the quality of the treatment and on the other hand in a large number of combinations to an additive or potentiated increase of the cardiovascular effects of the individual active compounds alone.