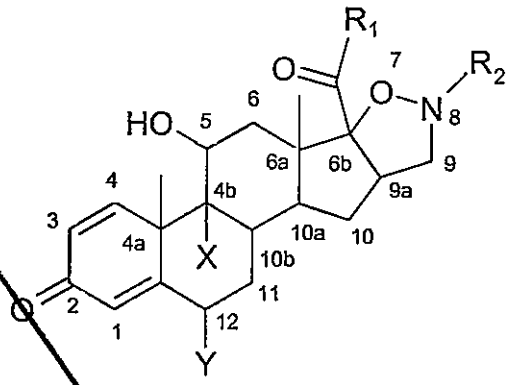
CLAIMS

1. A compound of general formula **(I)**



(I)

wherein

$\mathbf{R_1}$ is $-(CH_2)_n-Z-(CH_2)_{n'}-R_3$ wherein **n** and **n'** are each independently 0, 1 or 2;

Z is a single bond or is selected from –S-, –O- and $-OC(R_4R_5)-$;

$\mathbf{R_3}$ is selected from the group consisting of:

- H, halogen, CN, OH, $CONH_2$, (C_1-C_6)alkyl, (C_1-C_6)haloalkyl and (C_1-C_6)alkylcarbonyl;
- NR_4R_5, wherein $\mathbf{R_4}$ and $\mathbf{R_5}$ are independently selected from the group consisting of (C_1-C_6)alkyl and (C_1-C_6)alkoxy;
- (C_3-C_8)cycloalkyl which is optionally substituted by one or more halogen atoms or oxo groups or CN groups; and

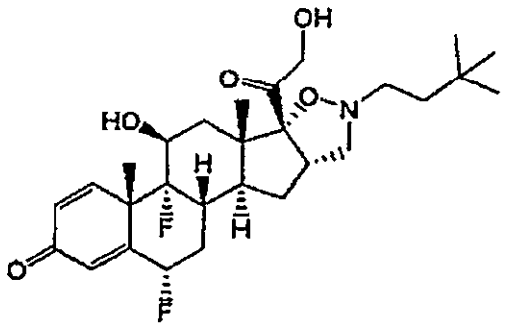
$\mathbf{R_2}$ is selected from the group consisting of:

- linear or branched (C_1-C_8)alkyl optionally substituted by one or more CN groups or halogen atoms; and

X and **Y** are a fluorine atom and

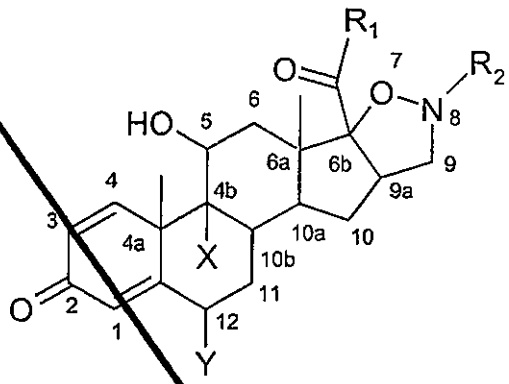
pharmaceutically acceptable salts thereof;

with the exclusion of the following compound:



;

2. A compound of general formula (I)



(I)

wherein

$\mathbf{R_1}$ is $-(CH_2)_n-Z-(CH_2)_{n'}-R_3$ wherein **n** and **n'** are each independently 0, 1 or 2;

Z is a single bond or is selected from –S-, –O- and $-OC(R_4R_5)-$;

$\mathbf{R_3}$ is selected from the group consisting of:

- H, halogen, CN, OH, $CONH_2$, (C_1-C_6)alkyl, (C_1-C_6)haloalkyl and (C_1-C_6)alkylcarbonyl;
- NR_4R_5, wherein $\mathbf{R_4}$ and $\mathbf{R_5}$ are independently selected from the group consisting of (C_1-C_6)alkyl and (C_1-C_6)alkoxy;
- (C_3-C_8)cycloalkyl which is optionally substituted by one or more halogen atoms or oxo groups or CN groups; and

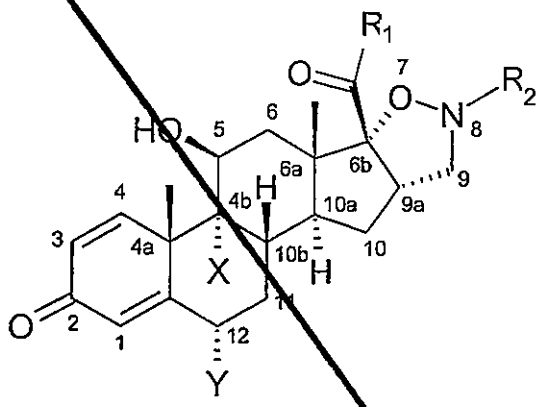
$\mathbf{R_2}$ is $-(CH_2)_mR_6$, wherein $\mathbf{R_6}$ is (C_3-C_8)cycloalkyl optionally substituted by one or more substituents selected from the group consisting of oxo, OH, halogen, CN, NH_2, $CONH_2$, NO_2, NHC(O)H, linear or branched (C_1-C_6)alkyl, linear or branched (C_1-C_6)haloalkyl, linear or branched (C_1-C_6)alkoxy, linear or

branched (C_1-C_6)haloalkoxy, (C_1-C_6)hydroxyalkoxy, (C_1-C_6)haloalkoxy, (C_1-C_6)alkoxycarbonyl, (C_1-C_6)alkylcarboxyl, (C_1-C_6)alkylsulfonyl and (C_1-C_6)alkylsulfanyl, (C_1-C_6)alkyloxysulfonyl, (C_1-C_6)haloalkylsulfonyloxy, aminosulfonyl, (C_3-C_8)cycloalkyl, (C_3-C_6)heterocycloalkyl and heteroaryl wherein **m** is an integer from 1 to 3 and

X and **Y** are a fluorine atom and

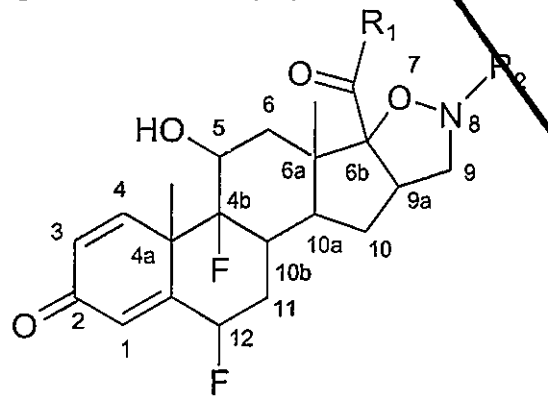
pharmaceutically acceptable salts thereof;

3. A compound according to claims 1 or 2 wherein stereogenic carbons have a stereochemistry as depicted in general formula (I')



(I')

4. A compound of general formula (**IF**)



(IF)

wherein

$\mathbf{R_1}$ is -$(CH_2)_n$-Z-$(CH_2)_{n'}$-R_3 wherein **n** is 1 and **n'** is zero;

- **Z** is a single bond;

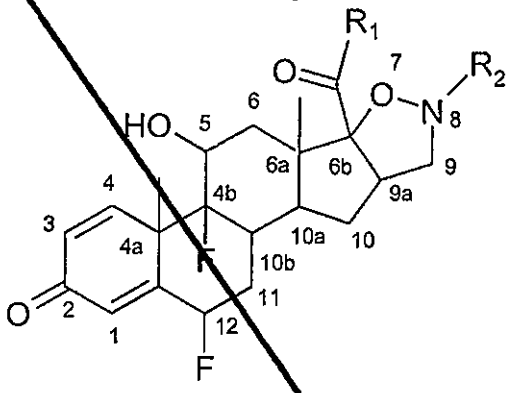
- R_3 is a fluorine atom;

R_2 is $-(CH_2)_mR_6$, wherein R_6 is aryl optionally substituted by one or more substituents selected from the group consisting of oxo, OH, halogen, CN, NH_2, NO_2, linear or branched (C_1-C_6)alkyl, (C_1-C_6)alkoxy, aryl, (C_1-C_6)hydroxyalkoxy, (C_1-C_6)haloalkoxy, straight or branched (C_1-C_6)alkoxycarbonyl, (C_1-C_6)alkylcarboxyl, arylthio, and (C_1-C_6)alkylsulfanyl, wherein **m** is an integer from 1 to 3 and

pharmaceutically acceptable salts thereof;

with the proviso that R_2 is not 4-chloro-benzyl.

5. A compound according to claim 4 of general formula (**IG**)



(IG)

wherein

R_1 is $-(CH_2)_n-Z-(CH_2)_{n'}-R_3$ wherein **n** is 1 and **n'** is zero;

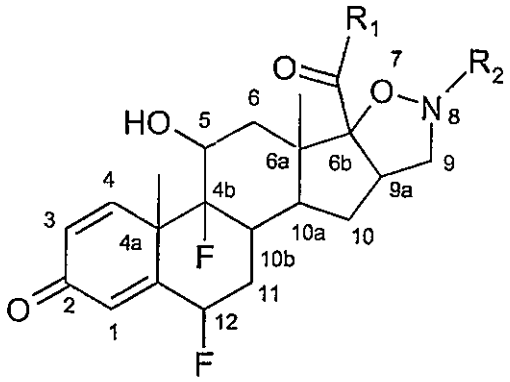
- **Z** is a single bond;
- R_3 is a fluorine atom;

R_2 is $-(CH_2)_mR_6$, wherein R_6 is aryl optionally substituted by one or more substituents selected from the group consisting of halogen, linear or branched (C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_1-C_6)alkoxycarbonyl and (C_1-C_6)alkylsulfanyl, wherein **m** is an integer from 1 to 3 and

pharmaceutically acceptable salts thereof;

with the proviso that R_2 is not 4-chloro-benzyl.

6. A compound of general formula (**IH**)



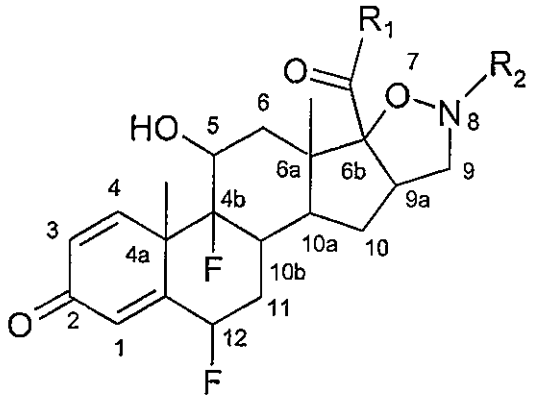
(IH)

wherein

- $\mathbf{R_1}$ is $-(CH_2)_n-Z-(CH_2)_{n'}-R_3$ wherein **n** is zero and **n'** is 1;
- **Z** is –S-;
- $\mathbf{R_3}$ is a fluorine atom;
- $\mathbf{R_2}$ is selected from the group consisting of:
- linear or branched (C_1-C_8)alkyl, (C_1-C_6)alkoxy, (C_1-C_6)haloalkyl, optionally substituted by one or more CN groups or halogen atoms;
- $-(CH_2)_mR_6$, wherein $\mathbf{R_6}$ is aryl optionally substituted by one or more substituents selected from the group consisting of oxo, OH, halogen, CN, NH_2, NO_2, linear or branched (C_1-C_6)alkyl, linear or branched (C_1-C_6)haloalkyl, linear or branched (C_1-C_6)alkoxy, aryl, (C_1-C_6)hydroxyalkoxy, (C_1-C_6)haloalkoxy, (C_1-C_6)alkoxycarbonyl, (C_1-C_6)alkylcarboxyl, arylthio, and (C_1-C_6)alkylsulfanyl, wherein **m** is an integer from 1 to 3;

with the proviso that $\mathbf{R_2}$ is neither 4-chloro-benzyl nor propyl-benzene; and pharmaceutically acceptable salts thereof.

7. A compounds according to claim 6 of general formula (**IL**)



(IL)

wherein

$\mathbf{R_1}$ is $-(CH_2)_n-Z-(CH_2)_{n'}-R_3$ wherein **n** is zero and **n'** is 1;

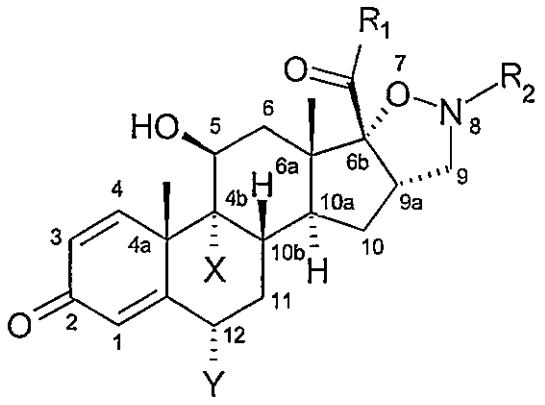
- **Z** is –S-;
- $\mathbf{R_3}$ is a fluorine atom;

$\mathbf{R_2}$ is $-(CH_2)_mR_6$, wherein $\mathbf{R_6}$ is selected from the group consisting of aryl optionally substituted by one or more substituents selected from the group consisting of halogen, linear or branched (C_1-C_6)alkyl, linear or branched (C_1-C_6)haloalkyl, linear or branched (C_1-C_6)alkoxy, (C_1-C_6)alkoxycarbonyl and (C_1-C_6)alkylsulfanyl wherein **m** is an integer from 1 to 3;

with the proviso that $\mathbf{R_2}$ is neither 4-chloro-benzyl nor propyl-benzene;

and pharmaceutically acceptable salts thereof.

8. A compound according to claims 4, 5, 6 or 7 wherein stereogenic carbons have a stereochemistry as depicted in general formula (I')



(I')

wherein X and Y are both fluorine atoms.

9. A pharmaceutical composition comprising a compound as defined in anyone of the claims 1 to 8 together with one or more pharmaceutically acceptable carriers and/or excipients.

10. A combination of a compound as defined in anyone of the claims 1 to 8 with one or more active ingredients selected from the classes of beta2-agonists, antimuscarinic agents, corticosteroids, mitogen-activated protein kinases (P38 MAP kinase) inhibitors, nuclear factor kappa-B kinase subunit beta (IKK2) inhibitors, human neutrophil elastase (HNE) inhibitors, phosphodiesterase 4 (PDE4) inhibitors, leukotriene modulators, non-steroidal anti-inflammatory agents (NSAIDs) and mucus regulators.

11. A compound as defined in anyone of claims 1 to 8, for use as a medicament.

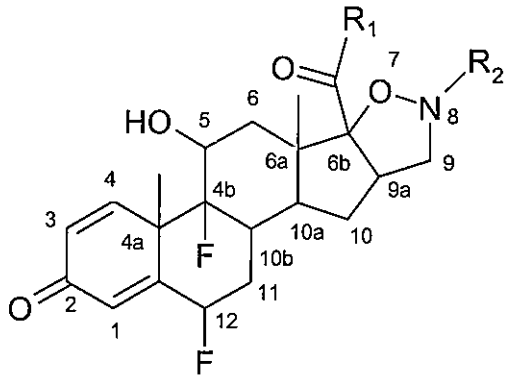
12. A compound as defined in anyone of claims 1 to 8, for use in the prevention and/or treatment of a respiratory disease.

13. A compound as defined in anyone of claims 1 to 8, for use in the prevention and/or treatment of asthma and COPD.

14. A device comprising the pharmaceutical composition according to claim 9, which may be a single- or multi-dose dry powder inhaler, a metered dose inhaler or soft mist nebulizer.

CLAIMS

1. A compound of general formula **(IN)**



(IN)

wherein

- $\mathbf{R_1}$ is $-(CH_2)_n-Z-(CH_2)_{n'}-R_3$ wherein n is zero and n' is 1;
- **Z** is a single bond;
- $\mathbf{R_3}$ is - OH;
- $\mathbf{R_2}$ is $-(CH_2)_mR_6$, wherein $\mathbf{R_6}$ is phenyl optionally substituted by one or more substituents selected from the group consisting of halogen, CN, $CONH_2$, NHC(O)H, linear or branched (C_1-C_6)alkyl, (C_1-C_6)alkylsulfonyl, linear or branched (C_1-C_6)haloalkyl, linear or branched (C_1-C_6)haloalkoxy, (C_1-C_6)alkoxycarbonyl, (C_1-C_6)alkoxysulfonyl, (C_1-C_6)haloalkylsulfonyloxy, (C_3-C_8)cycloalkyl, (C_3-C_6)heterocycloalkyl, aminosulfonyl;

m is 0;

and pharmaceutically acceptable salts thereof.

2. A compound according to claim 1, which is:

(4aS,4bR,5S,6aS,6bR,9aS,10aS,10bS,12S)-4b,12-difluoro-5-hydroxy-6b-(2-hydroxy-acetyl)-4a,6a-dimethyl-8-phenyl-4a,4b,5,6,6a,6b,8,9,9a,10,10a,10b,11,12-tetradecahydro-7-oxa-8-aza-pentaleno[2,1-a]phenanthren-2-one;

(4aS,4bR,5S,6aS,6bR,9aS,10aS,10bS,12S)-8-(4-chloro-phenyl)-4b,12-difluoro-5-hydroxy-6b-(2-hydroxy-acetyl)-4a,6a-dimethyl-4a,4b,5,6,6a,6b,8,9,9a,10,10a,10b,11,12-tetradecahydro-7-oxa-8-aza-pentaleno[2,1-a]phenanthren-2-one;

(4aS,4bR,5S,6aS,6bR,9aS,10aS,10bS,12S)-4b,12-Difluoro-5-hydroxy-6b-(2-hydroxy-acetyl)-4a,6a-dimethyl-8-p-tolyl-4a,4b,5,6,6a,6b,8,9,9a,10,10a,10b,11,12-tetradecahydro-7-oxa-8-aza-pentaleno[2,1-a]phenanthren-2-one;

(4aS,4bR,5S,6aS,6bR,9aS,10aS,10bS,12S)-4b,12-Difluoro-5-hydroxy-6b-(2-hydroxy-acetyl)-4a,6a-dimethyl-8-m-tolyl-4a,4b,5,6,6a,6b,8,9,9a,10,10a,10b,11,12-tetradecahydro-7-oxa-8-aza-pentaleno[2,1-aphenanthren-2-one;

(4aS,4bR,5S,6bR,9aS,10aS,10bS,12S)-4b,12-Difluoro-8-(4-fluoro-phenyl)-5-hydroxy-6b-((S)-2-hydroxy-acetyl)-4a,6a-dimethyl-4a,4b,5,6,6a,6b,8,9,9a,10,10a,10b,11,12-tetradecahydro-7-oxa-8-aza-pentaleno[2,1-a]phenanthren-2-one;

(4aS,4bR,5S,6aS,6bR,9aS,10aS,10bS,12S)-8-(3-Chloro-phenyl)-4b,12-difluoro-5-hydroxy-6b-(2-hydroxy-acetyl)-4a,6a-dimethyl-4a,4b,5,6,6a,6b,8,9,9a,10,10a,10b,11,12-tetradecahydro-7-oxa-8-aza-pentaleno[2,1-a]phenanthren-2-one;

(4aS,4bR,5S,6aS,6bR,9aS,10aS,10bS,12S)-4b,12-Difluoro-5-hydroxy-6b-(2-hydroxy-acetyl)-4a,6a-dimethyl-8-(4-trifluoromethyl-phenyl)-4a,4b,5,6,6a,6b,8,9,9a,10,10a,10b,11,12-tetradecahydro-7-oxa-8-aza-pentaleno[2,1-a]phenanthren-2-one;

(4aS,4bR,5S,6bR,9aS,10aS,10bS,12S)-4b,12-Difluoro-8-(3-fluoro-phenyl)-5-hydroxy-6b-((S)-2-hydroxy-acetyl)-4a,6a-dimethyl-4a,4b,5,6,6a,6b,8,9,9a,10,10a,10b,11,12-tetradecahydro-7-oxa-8-aza-pentaleno[2,1-a]phenanthren-2-one;

(4aS,4bR,5S,6aS,6bR,9aS,10aS,10bS,12S)-4b,12-Difluoro-5-hydroxy-6b-(2-

hydroxy-acetyl)-4a,6a-dimethyl-8-o-tolyl-4a,4b,5,6,6a,6b,8,9,9a,10,10a,10b,11,12-tetradecahydro-7-oxa-8-aza-pentaleno[2,1-a]phenanthren-2-one;

(4aS,4bR,5S,6bR,9aS,10aS,10bS,12S)-8-(4-Chloro-3-methyl-phenyl)-4b,12-difluoro-5-hydroxy-6b-((S)-2-hydroxy-acetyl)-4a,6a-dimethyl-4a,4b,5,6,6a,6b,8,9,9a,10,10a,10b,11,12-tetradecahydro-7-oxa-8-aza-pentaleno[2,1-a]phenanthren-2-one;

(4aS,4bR,5S,6aS,6bR,9aS,10aS,10bS,12S)-8-(4-Chloro-3-trifluoromethyl-phenyl)-4b,12-difluoro-5-hydroxy-6b-(2-hydroxy-acetyl)-4a,6a-dimethyl-4a,4b,5,6,6a,6b,8,9,9a,10,10a,10b,11,12-tetradecahydro-7-oxa-8-aza-pentaleno[2,1-a]phenanthren-2-one;

(4aS,4bR,5S,6aS,6bR,9aS,10aS,10bS,12S)-8-(3,4-Dichloro-phenyl)-4b,12-difluoro-5-hydroxy-6b-(2-hydroxy-acetyl)-4a,6a-dimethyl-4a,4b,5,6,6a,6b,8,9,9a,10,10a,10b,11,12-tetradecahydro-7-oxa-8-aza-pentaleno[2,1-a]phenanthren-2-one;

(4aS,4bR,5S,6aS,6bR,9aS,10aS,10bS,12S)-8-(4-Bromo-phenyl)-4b,12-difluoro-5-hydroxy-6b-(2-hydroxy-acetyl)-4a,6a-dimethyl-4a,4b,5,6,6a,6b,8,9,9a,10,10a,10b,11,12-tetradecahydro-7-oxa-8-aza-pentaleno[2,1-a]phenanthren-2-one;

4-[(4aS,4bR,5S,6aS,6bR,9aS,10aS,10bS,12S)-4b,12-Difluoro-5-hydroxy-6b-(2-hydroxy-acetyl)-4a,6a-dimethyl-2-oxo-2,4a,4b,5,6,6a,6b,9,9a,10,10a,10b,11,12-tetradecahydro-7-oxa-8-aza-pentaleno[2,1-a]phenanthren-8-yl]-benzamide;

(4aS,4bR,5S,6aS,6bR,9aS,10aS,10bS,12S)-4b,12-Difluoro-5-hydroxy-6b-(2-hydroxy-acetyl)-4a,6a-dimethyl-8-(4-trifluoromethoxy-phenyl)-4a,4b,5,6,6a,6b,8,9,9a,10,10a,10b,11,12-tetradecahydro-7-oxa-8-aza-pentaleno[2,1-a]phenanthren-2-one;

Methanesulfonic acid 4-[(4aS,4bR,5S,6aS,6bR,9aS,10aS,10bS,12S)-4b,12-difluoro-5-hydroxy-6b-(2-hydroxy-acetyl)-4a,6a-dimethyl-2-oxo-

2,4a,4b,5,6,6a,6b,9,9a,10,10a,10b,11,12-tetradecahydro-7-oxa-8-aza-pentaleno[2,1-a]phenanthren-8-yl]-phenyl ester;

(4aS,4bR,5S,6aS,6bR,9aS,10aS,10bS,12S)-8-(4-Cyclohexyl-phenyl)-4b,12-difluoro-5-hydroxy-6b-(2-hydroxy-acetyl)-4a,6a-dimethyl-4a,4b,5,6,6a,6b,8,9,9a,10,10a,10b,11,12-tetradecahydro-7-oxa-8-aza-pentaleno[2,1-a]phenanthren-2-one;

4-[(4aS,4bR,5S,6aS,6bR,9aS,10aS,10bS,12S)-4b,12-Difluoro-5-hydroxy-6b-(2-hydroxy-acetyl)-4a,6a-dimethyl-2-oxo-2,4a,4b,5,6,6a,6b,9,9a,10,10a,10b,11,12-tetradecahydro-7-oxa-8-aza-pentaleno[2,1-a]phenanthren-8-yl]-benzoic acid methyl ester;

(4aS,4bR,5S,6aS,6bR,9aS,10aS,10bS,12S)-4b,12-Difluoro-5-hydroxy-6b-(2-hydroxy-acetyl)-8-(4-methanesulfonyl-phenyl)-4a,6a-dimethyl-4a,4b,5,6,6a,6b,8,9,9a,10,10a,10b,11,12-tetradecahydro-7-oxa-8-aza-pentaleno[2,1-a]phenanthren-2-one;

3-[(4aS,4bR,5S,6aS,6bR,9aS,10aS,10bS,12S)-4b,12-Difluoro-5-hydroxy-6b-(2-hydroxy-acetyl)-4a,6a-dimethyl-2-oxo-2,4a,4b,5,6,6a,6b,9,9a,10,10a,10b,11,12-tetradecahydro-7-oxa-8-aza-pentaleno[2,1-a]phenanthren-8-yl]-benzonitrile;

4-[(4aS,4bR,5S,6aS,6bR,9aS,10aS,10bS,12S)-4b,12-Difluoro-5-hydroxy-6b-(2-hydroxy-acetyl)-4a,6a-dimethyl-2-oxo-2,4a,4b,5,6,6a,6b,9,9a,10,10a,10b,11,12-tetradecahydro-7-oxa-8-aza-pentaleno[2,1-a]phenanthren-8-yl]-benzene sulfonamide;

(4aS,4bR,5S,6aS,6bR,9aS,10aS,10bS,12S)-8-(4-Cyclopropyl-phenyl)-4b,12-difluoro-5-hydroxy-6b-(2-hydroxy-acetyl)-4a,6a-dimethyl-4a,4b,5,6,6a,6b,8,9,9a,10,10a,10b,11,12-tetradecahydro-7-oxa-8-aza-pentaleno[2,1-a]phenanthren-2-one;

(4aS,4bR,5S,6aS,6bR,9aS,10aS,10bS,12S)-8-(4-tert-Butyl-phenyl)-4b,12-difluoro-5-hydroxy-6b-(2-hydroxy-acetyl)-4a,6a-dimethyl-

4a,4b,5,6,6a,6b,8,9,9a,10,10a,10b,11,12-tetradecahydro-7-oxa-8-aza-pentaleno[2,1-a]phenanthren-2-one;

N-{4-[(4aS,4bR,5S,6aS,6bR,9aS,10aS,10bS,12S)-4b,12-Difluoro-5-hydroxy-6b-(2-hydroxy-acetyl)-4a,6a-dimethyl-2-oxo-2,4a,4b,5,6,6a,6b,9,9a,10,10a,10b,11,12-tetradecahydro-7-oxa-8-aza-pentaleno[2,1-a]phenanthren-8-yl]-phenyl}-formamide;

(4aS,4bR,5S,6aS,6bR,9aS,10aS,10bS,12S)-4b,12-Difluoro-5-hydroxy-6b-(2-hydroxy-acetyl)-4a,6a-dimethyl-8-(3-trifluoromethyl-phenyl)-4a,4b,5,6,6a,6b,8,9,9a,10,10a,10b,11,12-tetradecahydro-7-oxa-8-aza-pentaleno[2,1-a]phenanthren-2-one;

(4aS,4bR,5S,6aS,6bR,9aS,10aS,10bS,12S)-4b,12-Difluoro-5-hydroxy-6b-(2-hydroxy-acetyl)-4a,6a-dimethyl-8-(3-trifluoromethoxy-phenyl)-4a,4b,5,6,6a,6b,8,9,9a,10,10a,10b,11,12-tetradecahydro-7-oxa-8-aza-pentaleno[2,1-a]phenanthren-2-one;

(4aS,4bR,5S,6aS,6bR,9aS,10aS,10bS,12S)-8-(3-Bromo-phenyl)-4b,12-difluoro-5-hydroxy-6b-(2-hydroxy-acetyl)-4a,6a-dimethyl-4a,4b,5,6,6a,6b,8,9,9a,10,10a,10b,11,12-tetradecahydro-7-oxa-8-aza-pentaleno[2,1-a]phenanthren-2-one;

(4aS,4bR,5S,6aS,6bR,9aS,10aS,10bS,12S)-8-(3-Cyclopropyl-phenyl)-4b,12-difluoro-5-hydroxy-6b-(2-hydroxy-acetyl)-4a,6a-dimethyl-4a,4b,5,6,6a,6b,8,9,9a,10,10a,10b,11,12-tetradecahydro-7-oxa-8-aza-pentaleno[2,1-a]phenanthren-2-one;

or pharmaceutically acceptable salts thereof.

3. A pharmaceutical composition comprising a compound as defined in anyone of the claims 1 or 2, together with one or more pharmaceutically acceptable carriers and/or excipients.

4. A combination of a compound as defined in anyone of the claims 1 or 2 with one or more active ingredients selected from the classes of beta2-agonists,

antimuscarinic agents, corticosteroids, mitogen-activated protein kinases (P38 MAP kinase) inhibitors, nuclear factor kappa-B kinase subunit beta (IKK2) inhibitors, human neutrophil elastase (HNE) inhibitors, phosphodiesterase 4 (PDE4) inhibitors, leukotriene modulators, non-steroidal anti-inflammatory agents (NSAIDs) and mucus regulators.

5. A compound as defined in anyone of claims 1 or 2, for use as a medicament.

6. A compound as defined in anyone of claims 1 or 2, for use in the prevention and/or treatment of a disease of the respiratory tract characterized by airway obstruction.

7. A compound as defined in anyone of claims 1 or 2 for use in the prevention and treatment of a disease of the respiratory tract according to claim 6, wherein the disease is asthma or COPD.

8. A device comprising the pharmaceutical composition according to claim 3, which may be a single- or multi-dose dry powder inhaler, a metered dose inhaler or soft mist nebulizer.