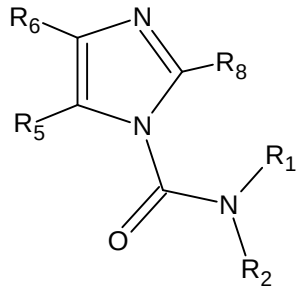
Claims

1. A compound having Formula:



wherein:

R1 is C_{1-4} alkyl;

R2 can be selected from H, C_{1-20} alkyl, C_{1-6} alkoxy, aryl, heteroaryl, partially or fully saturated heterocyclyl, C_{3-10} cycloalkyl, aryl C_{1-6} alkyl, heteroaryl C_{1-6} alkyl, heterocyclyl C_{1-6} alkyl, C_{3-10} cycloalkyl C_{1-6} alkyl, R1a, halogen, OH, OR1a, OCOR1a, SH, SR1a, SCOR1a, NH_2, NHR1a, $NHSO_2NH_2$, $NHSO_2R1a$, NR1aCOR1b, NHCOR1a, NR1aR1b, COR1a, CSR1a, CN, COOH, COOR1a, $CONH_2$, CONHOH, CONHR1a, CONHOR1a, SO_2R1a, SO_3H, SO_2NH_2, CONR1aR1b, $SO_2NR1aR1b$, wherein R1a and R1b are independently selected from C_{1-6} alkyl, substituted C_{1-6} alkyl, aryl, heteroaryl, C_{3-8} cycloalkyl and heterocyclyl, or R1a and R1b, together with the heteroatom to which they are joined, can form heterocyclyl,

wherein, when R2 is C_{1-20} alkyl, alkoxy, aryl, heteroaryl, heterocyclyl, C_{3-10} cycloalkyl, aryl C_{1-6} alkyl, heteroaryl C_{1-6} alkyl, heterocyclyl C_{1-6} alkyl, C_{3-10} cycloalkyl C_{1-6} alkyl, C_{1-6} alkyl, C_{3-8} cycloalkyl or is a group containing one or more of these moieties, each of these moieties may optionally be substituted with one or more groups selected from R1c, halogen, aryl, heteroaryl, heterocyclyl, C_{1-6} alkoxy, aryloxy, heteroaryloxy, heterocyclyloxy, aryl C_{1-6} alkyl, heteroaryl C_{1-6} alkyl, heterocyclyl C_{1-6} alkyl, aryl C_{1-6} alkoxy, heteroaryl C_{1-6} alkoxy, heterocyclyl C_{1-6} alkoxy, C_{1-6} alkylamino, C_{1-6} dialkylamino, C_{1-10} alkyl, OH, OR1c, OCOR1c, SH, SR1c, SCOR1c, NH_2, NO_2, NHR1c, $NHSO_2NH_2$, $NHSO_2R1c$, NR1cCOR1d, $NHC(NH)NH_2$, NHCOR1c, NR1cR1d, COR1c, CSR1c, CN, COOH, COOR1c, $CONH_2$, CONHOH, CONHR1c, CONHOR1c, $C(NOH)NH_2$, CONR1cR1d, SO_2R1c, SO_3H, SO_2NH_2, $SO_2NR1cR1d$, wherein R1c and R1d are independently selected from C_{1-6} alkyl, substituted C_{1-6} alkyl, aryl, heteroaryl, C_{3-8} cycloalkyl and heterocyclyl, or R1c and R1d, together with the heteroatom to which they are joined, can form heterocyclyl,

wherein, when the substituent of R2 is C_{1-10} alkyl, aryl, heteroaryl, heterocyclyl, C_{1-6} alkoxy, aryloxy, heteroaryloxy, heterocyclyloxy, aryl C_{1-6} alkyl, heteroaryl C_{1-6} alkyl, heterocyclyl C_{1-6} alkyl, aryl C_{1-6}

alkoxy, heteroaryl C_{1-6} alkoxy, heterocyclyl C_{1-6} alkoxy, C_{1-6} alkylamino, C_{1-6} dialkylamino, C_{1-6} alkyl, C_{3-8} cycloalkyl or is a group containing one or more of these moieties, each of these moieties may optionally be substituted with one or more groups selected from R1e, halogen, C_{1-10} alkyl, OH, OR1e, OCOR1e, SH, SR1e, SCOR1e, NH_2, NO_2, NHR1e, $NHSO_2NH_2$, $NHSO_2R1e$, NR1eCOR1f, $NHC(NH)NH_2$, NHCOR1e, NR1eR1f, COR1e, CSR1e, CN, COOH, COOR1e, $CONH_2$, CONHOH, CONHR1e, CONHOR1e, $C(NOH)NH_2$, CONR1eR1f, SO_2R1e, SO_3H, SO_2NH_2, $SO_2NR1eR1f$, wherein R1e and R1f are independently selected from C_{1-6} alkyl, substituted C_{1-6} alkyl, aryl, heteroaryl, C_{3-8} cycloalkyl and heterocyclyl, or R1e and R1f, together with the heteroatom to which they are joined, can form heterocyclyl,

with the exception that R1 and R2 are not both methyl,

or

R1 and R2, together with the N to which they are attached, can form a heteroaryl or heterocyclyl group, each of which may optionally be substituted with one or more oxygen atoms or one or more groups selected from aryl, heteroaryl, partially or fully saturated heterocyclyl, C_{3-8} cycloalkyl, C_{1-6} alkyl, aryl C_{1-6} alkyl, heteroaryl C_{1-6} alkyl, heterocyclyl C_{1-6} alkyl, C_{3-8} cycloalkyl C_{1-6} alkyl, C_{1-6} alkoxy, aryloxy, heteroaryloxy, heterocyclyloxy, R2a, halogen, OH, OR2a, OCOR2a, SH, SR2a, SCOR2a, NH_2, NO_2, NHR2a, $NHSO_2NH_2$, $NHSO_2R2a$, NR2aCOR2b, $NHC(NH)NH_2$, NHCOR2a, NR2aR2b, COR2a, CSR2a, CN, COOH, COOR2a, $CONH_2$, CONHOH, CONHR2a, CONHOR2a, $C(NOH)NH_2$, CONR2aR2b, SO_2R2a, SO_3H, SO_2NH_2, $SO_2NR2aR2b$, wherein R2a and R2b are independently selected from C_{1-6} alkyl, substituted C_{1-6} alkyl, aryl, heteroaryl, C_{3-8} cycloalkyl and heterocyclyl, or R2a and R2b, together with the heteroatom to which they are joined, can form heterocyclyl,

wherein, when the substituent of the heteroaryl or heterocyclyl formed by R1 and R2 together is aryl, heteroaryl, heterocyclyl, C_{3-8} cycloalkyl, C_{1-6} alkyl, aryl C_{1-6} alkyl, heteroaryl C_{1-6} alkyl, heterocyclyl C_{1-6} alkyl, C_{3-8} cycloalkyl C_{1-6} alkyl, C_{1-6} alkoxy, aryloxy, heteroaryloxy, heterocyclyloxy, or a group containing one or more of these moieties, each of these moieties may optionally be substituted with one or more groups selected from halogen, hydroxyl, C_{1-6} alkyl, aryl, heteroaryl, heterocyclyl, C_{3-8} cycloalkyl, C_{1-4} alkoxy, aryloxy, heteroaryloxy, heterocyclyloxy, C_{3-8} cycloalkyloxy, aryl C_{1-4} alkoxy, heteroaryl C_{1-6} alkoxy, heterocyclyl C_{1-4} alkoxy, C_{3-8} cycloalkyl C_{1-4} alkoxy, R2c, OR2c, OCOR2c, SH, SR2c, SCOR2c, NH_2, NO_2, NHR2c, $NHSO_2NH_2$, $NHSO_2R2c$, NR2cCOR2d, $NHC(NH)NH_2$, NHCOR2c, NR2cR2d, COR2c, CSR2c, CN, COOH, COOR2c, $CONH_2$, CONHOH, CONHR2c, CONHOR2c, $C(NOH)NH_2$, CONR2cR2d, SO_2R2c, SO_3H, SO_2NH_2, $SO_2NR2cR2d$, wherein R2c and R2d are independently selected from C_{1-6} alkyl, substituted C_{1-6} alkyl, aryl, heteroaryl, C_{3-8} cycloalkyl and heterocyclyl, or R2c and R2d, together with the heteroatom to which they are joined, can form heterocyclyl,

wherein, when the substituent of the substituent of the heteroaryl or heterocyclyl formed by R1 and R2 together is C_{1-6} alkyl, aryl, heteroaryl, heterocyclyl, C_{3-8} cycloalkyl, C_{1-6} alkoxy, aryloxy, heteroaryloxy, heterocyclyloxy, C_{3-8} cycloalkyloxy, aryl C_{1-4} alkoxy, heteroaryl C_{1-4} alkoxy, heterocyclyl C_{1-4} alkoxy, C_{3-8} cycloalkyl C_{1-4} alkoxy, or is a group containing one or more of these moieties, each of these moieties may optionally be substituted with one or more groups selected from C_{1-4} alkoxy, R2e, halogen, OH, OR2e, OCOR2e, SH, SR2e, SCOR2e, NH_2, NO_2, NHR2e, $NHSO_2NH_2$, $NHSO_2R2e$, NR2eCOR2f, $NHC(NH)NH_2$, NR2eR2f, NHCOR2e, COR2e, CSR2e, CN, COOH, COOR2e, $CONH_2$, CONHOH, CONHR2e, CONHOR2e, $C(NOH)NH_2$, CONR2eR2f, SO_2R2e, SO_3H, SO_2NH_2, $SO_2NR2eR2f$, wherein R2e and R2f are independently selected from C_{1-6} alkyl, substituted C_{1-6} alkyl, aryl, heteroaryl, C_{3-8} cycloalkyl and heterocyclyl, or R2e and R2f, together with the heteroatom to which they are joined, can form heterocyclyl;

R5 is selected from H, C_{1-2} alkyl and halogen;

R6 is selected from aryl and heteroaryl,

wherein, when R6 is heteroaryl, this moiety may optionally be substituted with one or more oxygen atoms, and when R6 is aryl or heteroaryl, each of these moieties may optionally be substituted with one or more groups selected from halogen, R6c, C_{1-6} alkyl, C_{1-6} alkynyl, aryl, heteroaryl, heterocyclyl, C_{1-6} alkoxy, aryloxy, heteroaryloxy, heterocyclyloxy, aryl C_{1-6} alkyl, heteroaryl C_{1-6} alkyl, heterocyclyl C_{1-6} alkyl, aryl C_{1-6} alkoxy, heteroaryl C_{1-6} alkoxy, heterocyclyl C_{1-6} alkoxy, OH, OR6c, OCOR6c, SH, SR6c, SCOR6c, NH_2, NO_2, NHR6c, $NHSO_2NH_2$, $NHC(NH)NH_2$, $NHSO_2R6c$, NR6cCOR6d, NHCOR6c, NR6cR6d, COR6c, CSR6c, CN, COOH, COOR6c, $CONH_2$, CONHR6c, CONHOR6c, CONHOH, $C(NOH)NH_2$, CONR6cR6d, SO_2R6c, SO_3H, SO_2NH_2, $SO_2NR6cR6d$, wherein R6c and R6d are independently selected from C_{1-6} alkyl, substituted C_{1-6} alkyl, aryl, heteroaryl, C_{3-8} cycloalkyl and heterocyclyl, or R6c and R6d, together with the heteroatom to which they are joined, can form heterocyclyl,

wherein, when the substituent of R6 is heteroaryl or heterocyclyl, each of these moieties may optionally be substituted with one or more oxygen atoms, or when the substituent of R6 is C_{1-6} alkyl, C_{1-6} alkynyl, aryl, heteroaryl, heterocyclyl, C_{1-6} alkoxy, aryloxy, heteroaryloxy, heterocyclyloxy, aryl C_{1-6} alkyl, heteroaryl C_{1-6} alkyl, heterocyclyl C_{1-6} alkyl, aryl C_{1-6} alkoxy, heteroaryl C_{1-6} alkoxy, heterocyclyl C_{1-6} alkoxy, C_{3-8} cycloalkyl, or is a group containing one or more of these moieties, each of these moieties may optionally be substituted with one or more groups selected from halogen, R6e, C_{1-6} alkyl, C_{1-4} alkoxy, OH, OR6e, OCOR6e, SH, SR6e, SCOR6e, NH_2, NO_2, NHR6e, $NHSO_2NH_2$, $NHC(NH)NH_2$, $NHSO_2R6e$, NR6eCOR6f, NHCOR6e, NR6eR6f, COR6e, CSR6e, CN, COOH, COOR6e, $CONH_2$, CONHOH, CONHR6e, CONHOR6e, $C(NOH)NH_2$, CONR6eR6f, SO_2R6e, SO_3H, SO_2NH_2, $SO_2NR6eR6f$, wherein R6e and R6f are independently selected from C_{1-6} alkyl, substituted C_{1-6} alkyl,

aryl, heteroaryl, C_{3-8} cycloalkyl and heterocyclyl, or R6e and R6f, together with the heteroatom to which they are joined, can form heterocyclyl;

R8 is H;

or a pharmaceutically acceptable salt or ester thereof;

provided that when R1 is methyl, R2 is not 4-chlorobutyl, 4-azidobutyl, or 4-isothiocyanatobutyl, and

provided that the compound is not (4-phenyl-1H-imidazol-1-yl)(4-(quinolin-2-ylmethyl)piperazin-1-yl)methanone.

2. The compound of claim 1, wherein R1 and R2, together with the N to which they are attached, form a heterocyclyl group which may optionally be substituted.

3. The compound of claim 1 or claim 2, wherein R5 is H.

4. The compound of claim 1 or claim 3, wherein R1 is methyl;

R2 is selected from monocyclic C_{5-8} cycloalkyl or monocyclic six membered saturated heterocyclyl containing a single nitrogen or oxygen heteroatom, wherein the heteroatom is at the 4-position relative to the position of attachment of the heterocyclyl group R2 to the urea nitrogen, wherein, when the heteroatom is a nitrogen atom, the nitrogen atom is optionally substituted with benzyl;

R5 is H;

R6 is selected from phenyl or pyridyl, wherein the nitrogen atom of the pyridyl group may be substituted with an oxygen atom, and wherein the phenyl may optionally be substituted with one or more groups selected from halogen, methoxy, OH, $CONH_2$, NH_2 and phenyl; and

R8 is H.

5. The compound of claim 1 or claim 3, wherein R1 is methyl;

R2 is selected from monocyclic C_{5-8} cycloalkyl, tetrahydropyranyl and piperidinyl, wherein the heteroatom in the tetrahydropyranyl and piperidinyl groups is at the 4-position relative to the position of attachment of the heterocyclyl group R2 to the urea nitrogen, and wherein the nitrogen atom of the piperidinyl group is substituted with benzyl;

R5 is H;

R6 is selected from phenyl or pyridyl, wherein the nitrogen atom of the pyridyl group is substituted with an oxygen atom, and wherein the phenyl may optionally be substituted with one or more groups selected from halogen, methoxy, CONH2, NH2 and phenyl; and

R8 is H.

6. The compound of claim 1 or claim 3, wherein R1 is methyl and R2 is a monocyclic saturated heterocyclyl containing a single nitrogen heteroatom, wherein the nitrogen heteroatom is substituted with the group CONR1cR1d.

7. The compound of claim 1 or claim 3, wherein R6 is phenyl substituted with more than one group selected from OH and C_{1-6} alkyl.

8. The compound of claim 1 or claim 3, wherein R6 is phenyl substituted with $NHSO_2NH_2$.

9. The compound of claim 1 or claim 3, wherein R1 is methyl and R2 is a monocyclic saturated heterocyclyl containing a single nitrogen heteroatom, wherein the nitrogen heteroatom is substituted with a group selected from aryl and SO_2R1c.

10. The compound of claim 1 or claim 3, wherein R6 is pyridyl substituted with a group selected from NHR6c, NR6cR6d, $NHSO_2NH_2$, NHCOR6c and $NHSO_2R6c$.

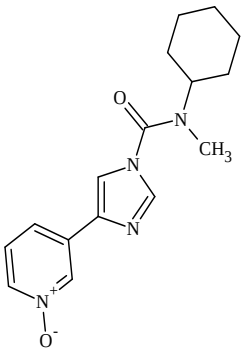
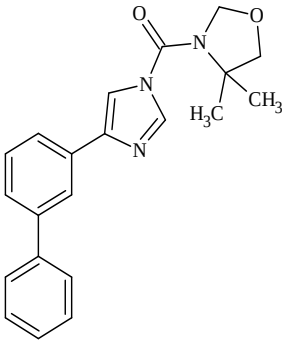
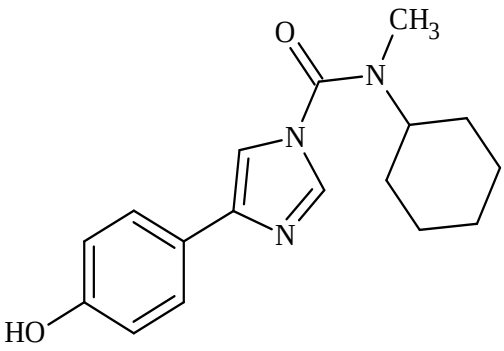
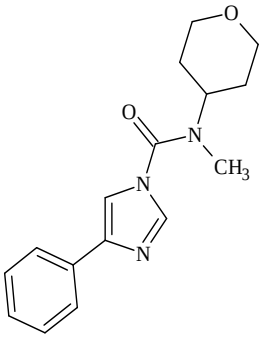
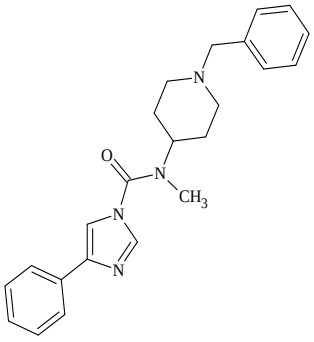
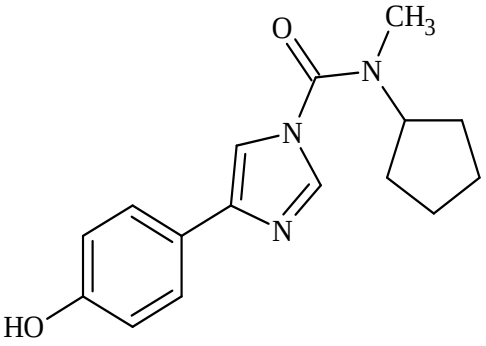
11. The compound of claim 1 or claim 3, wherein R6 is pyrazinyl or pyrimidyl.

12. The compound of any one of claims 1, 3 and 5, wherein R1c is C_{1-6} alkyl.

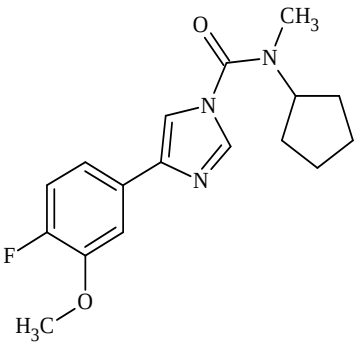
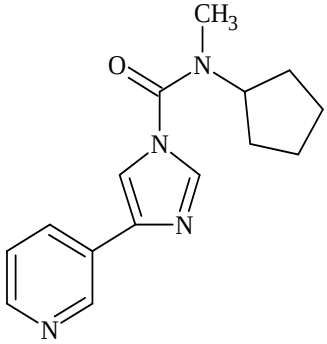
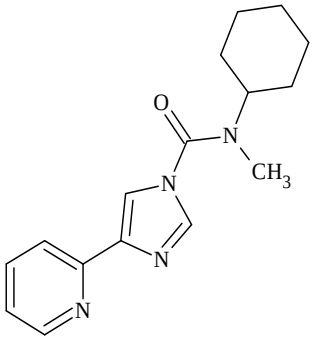
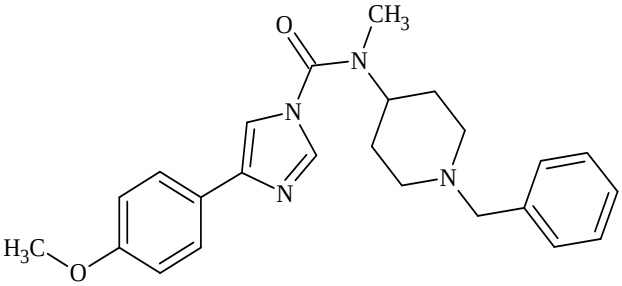
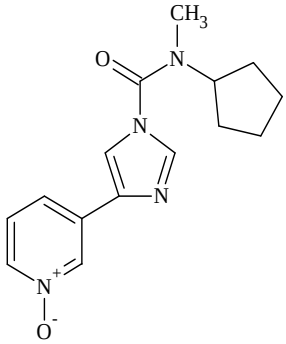
13. The compound of any one of claims 1, 3 and 5, wherein R1c is C_{3-8} cycloalkyl.

14. The compound of claim 1 or claim 3, wherein R1 is methyl and R2 is a monocyclic saturated six membered heterocyclyl containing a single nitrogen heteroatom which is substituted with aryl C_{1-4} alkyl which may be substituted or unsubstituted.

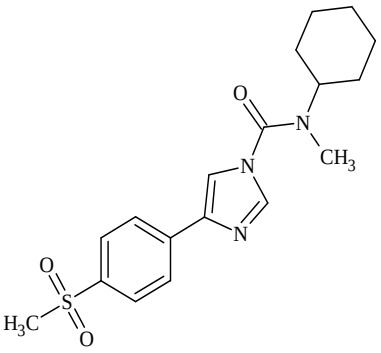
15. The compound of claim 1, selected from one of the following compounds:

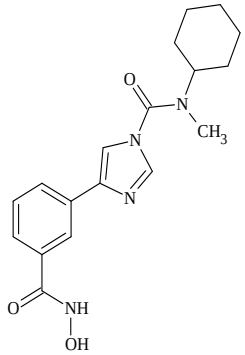







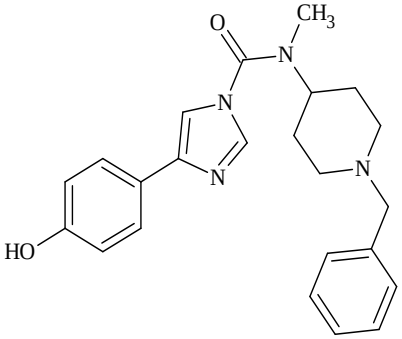
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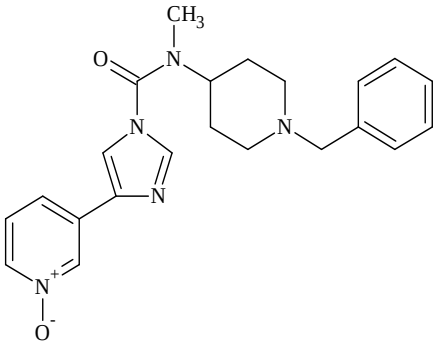






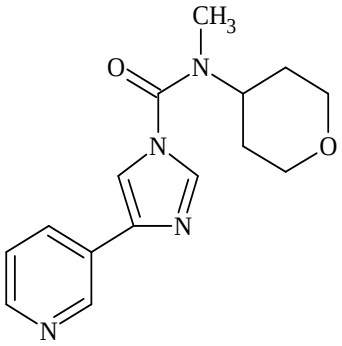
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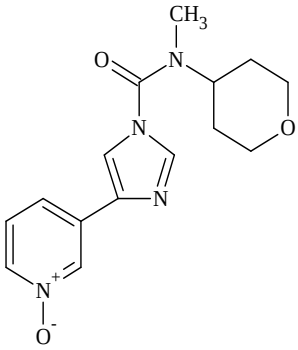


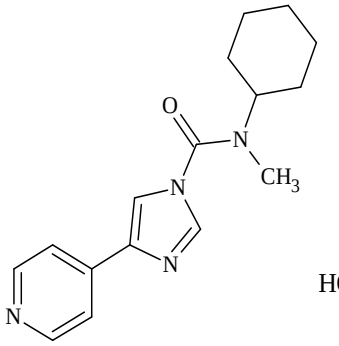


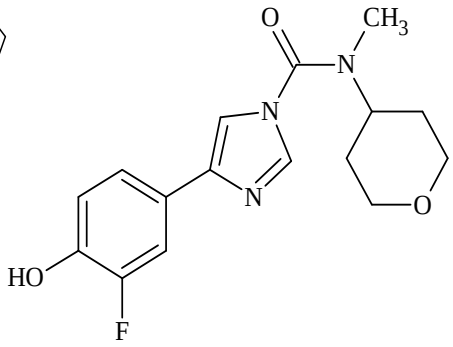


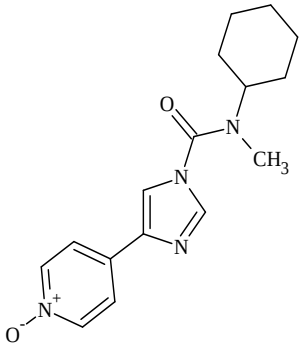












16. The compound according to claim 1, wherein R1 is selected from methyl and ethyl.

17. The compound according to claim 16, wherein R2 is selected from aryl, heteroaryl, heterocyclyl, and C_{3-10} cycloalkyl each of which may be substituted or unsubstituted.

18. A pharmaceutical composition comprising a compound according to any preceding claim, together with one or more pharmaceutically acceptable excipients.

19. The pharmaceutical composition of claim 18, further comprising one or more additional active pharmaceutical ingredients.

20. A compound according to any one of claims 1 to 17 for use in therapy.

21. Use of a compound according to any of claims 1 to 17 in the preparation of a medicament for the treatment or prevention of a condition whose development or symptoms are linked to a substrate of the FAAH enzyme, wherein the only provisos that apply are that i) when R1 is methyl, R2 is not 4-chlorobutyl, 4-azidobutyl, or 4-isothiocyanatobutyl, and ii) the compound is not (4-phenyl-1H-imidazol-1-yl)(4-(quinolin-2-ylmethyl)piperazin-1-yl)methanone.

22. Use of a compound according to claim 21, wherein the condition is a disorder associated with the endocannabinoid system.

23. Use of a compound according to claim 22, wherein the disorder is selected from appetite regulation, obesity, metabolic disorders, cachexia, anorexia, pain, inflammation, neurotoxicity, neurotrauma, stroke, multiple sclerosis, spinal cord injury, Parkinson's disease, levodopa-induced dyskinesia, Huntington's disease, Gilles de la Tourette's syndrome, tardive dyskinesia, dystonia, amyotrophic lateral sclerosis, Alzheimer's disease, epilepsy, schizophrenia, anxiety, depression, insomnia, nausea, emesis, alcohol disorders, drug addictions, hypertension, circulatory shock, myocardial reperfusion injury, atherosclerosis, asthma, glaucoma, retinopathy, cancer, inflammatory bowel disease, acute and chronic liver disease, arthritis and osteoporosis.

24. Use according to claim 23, wherein the drug addiction is opiate, nicotine, cocaine, alcohol and psychostimulant drug addiction.

25. Use according to claim 23, wherein the acute or chronic liver disease is hepatitis or liver cirrhosis.