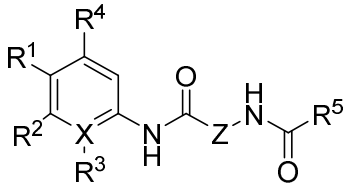
CLAIMS

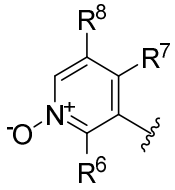
1. A compound of formula (I):



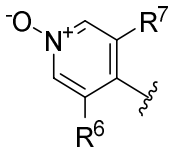
(I),

wherein,

R^1 is



or



wherein,

R^6 at each occurrence is selected from H, F, Cl, C_1-C_3alkyl and C_1-C_3fluoroalkyl;

R^7 at each occurrence is selected from H, F, Cl, C_1-C_3alkyl and C_1-C_3fluoroalkyl;

R^8 is selected from H, halo, C_1-C_3alkyl and hydroxymethyl;

X is C or N and when X is N, R^3 is absent;

R^2 is selected from H and F;

R^3 is selected from H, F and Cl;

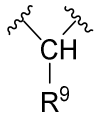
R^4 is selected from H and F;

R^5 is a 5-membered heteroaryl comprising 1 or 2 heteroatoms independently selected from N, S, and O, and wherein said heteroaryl is unsubstituted or substituted with one or two groups independently selected from C_1-C_3alkyl and C_3-C_4cycloalkyl, wherein said C_1-C_3alkyl is unsubstituted or substituted with one or more groups independently selected from F, OH, C_1-C_3alkoxy, -C(O)OH and $NR^{1b}R^{1c}$, wherein R^{1b} and R^{1c} are independently selected from H and C_1-C_3alkyl;

or

R^5 is a 5-membered heteroaryl comprising one N atom wherein said 5-membered heteroaryl is fused to a 6-membered heterocycle comprising one N atom wherein said heterocycle is unsubstituted or substituted with a group selected from C_1-C_3alkyl, C_1-C_3alkoxyC_1-C_3alkyl, -C(O)C_1-C_3alkyl, C_3-C_4cycloalkyl and oxetanyl;

Z is



, wherein R^9 is selected from

(1) monocyclic C_5-C_8cycloalkyl and C_6-bicycloalkyl,

each of which is independently unsubstituted or substituted with one or more groups independently selected at each occurrence from fluoro, C_1-C_3alkyl and C_1-C_3fluoroalkyl,

and wherein said monocyclic C_5-C_8cycloalkyl is optionally fused to phenyl; wherein said phenyl is unsubstituted or substituted with one or more groups selected from halo, C_1-C_3alkyl, C_3-C_5cycloalkyl or C_1-C_3fluoroalkyl;

(2) monocyclic C_5-C_8cycloalkenyl, which is unsubstituted or substituted with one or more fluoro;

(3) C_1-C_3alkyl, which is unsubstituted or substituted with one or two phenyl groups, wherein said phenyl at each occurrence is independently unsubstituted or substituted with one or more halo;

or a pharmaceutically acceptable salt thereof.

2. A compound of the formula (I), or a pharmaceutically acceptable salt thereof, according to claim 1, wherein R^6 at each occurrence is selected from H, F, Cl, methyl and difluoromethyl.

3. A compound of the formula (I), or a pharmaceutically acceptable salt thereof, according to claim 1 or 2, wherein R^7 at each occurrence is selected from H, F, Cl, methyl and trifluoromethyl.

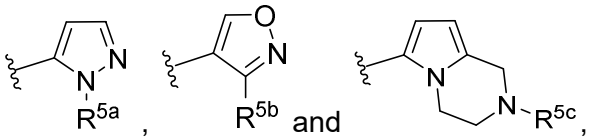
4. A compound of formula (I), or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 3, wherein R^8 is selected from H, chloro, methyl and hydroxymethyl.

5. A compound of formula (I), or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 4, wherein X is C.

6. A compound of formula (I), or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 5, wherein R^3 is H.

7. A compound of formula (I), or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 6, wherein R^4 is H.

8. A compound of formula (I), or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 7, wherein R^5 is selected from



wherein

R^{5a} is selected from methyl, ethyl, isopropyl, cyclopropyl, cyclobutyl, $-(CH_2)_2OH$, $-(CH_2)_2OCH_3$, $-CH_2C(O)OH$ and $-(CH_2)_2N(CH_3)_2$;

R^{5b} is selected from methyl, ethyl, $-CH_2OCH_3$, $-CH_2OH$, $-CH_2NH_2$ and $-CH_2N(CH_3)_2$; and

R^{5c} is selected from H, methyl, $-C(O)CH_3$, cyclopropyl, oxetanyl and $-(CH_2)_2OCH_3$.

9. A compound of formula (I), or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 8, wherein R^9 is selected from,

(1) monocyclic C_5-C_7cycloalkyl and C_6-bicycloalkyl,

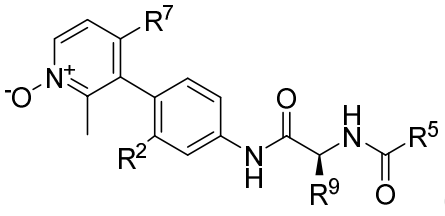
each of which is independently unsubstituted or substituted with one or two groups independently selected at each occurrence from fluoro, C_1-C_3alkyl and C_1-C_3fluoroalkyl,

and wherein said monocyclic C_5-C_7cycloalkyl is optionally fused to unsubstituted phenyl;

(2) monocyclic C_5-C_8cycloalkenyl, which is unsubstituted or substituted with one fluoro;

(3) methyl, which is unsubstituted or substituted with one or two phenyl groups, wherein said phenyl at each occurrence is independently unsubstituted or substituted with one chloro.

10. A compound, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 9, wherein the compound is of formula (IB):



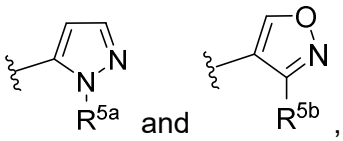
(IB),

wherein,

R^7 is selected from Cl, methyl and trifluoromethyl;

R^2 is selected from H and F;

R^5 is selected from

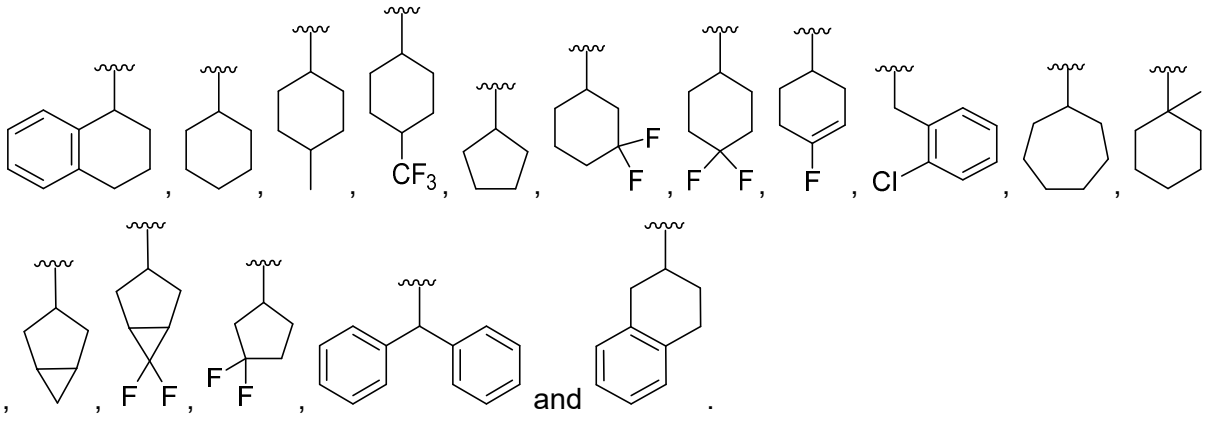


wherein,

R^{5a} is selected from methyl and ethyl; and

R^{5b} is selected from methyl and ethyl;

R^9 is selected from



and .

11. A compound, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 10, wherein the compound is selected from:

2,4-dimethyl-3-(4-((S)-2-(1-methyl-1H-pyrazole-5-carboxamido)-2-((S)-1,2,3,4-tetrahydronaphthalen-1-yl)acetamido)phenyl)pyridine 1-oxide;

4-chloro-3-(4-((S)-2-cyclohexyl-2-(1-methyl-1H-pyrazole-5-carboxamido)acetamido)-2-fluorophenyl)-2-methylpyridine 1-oxide;

2,4-dimethyl-3-(4-((S)-2-(1-methyl-1H-pyrazole-5-carboxamido)-2-((1r,4S)-4-methylcyclohexyl)acetamido)phenyl)pyridine 1-oxide;

4-chloro-3-(4-((S)-2-(3-ethylisoxazole-4-carboxamido)-2-((1r,4S)-4-(trifluoromethyl)cyclohexyl)acetamido)phenyl)-2-methylpyridine 1-oxide;

(S)-3-(4-(2-cyclopentyl-2-(3-ethylisoxazole-4-carboxamido)acetamido)phenyl)-2-methyl-4-(trifluoromethyl)pyridine 1-oxide;

4-chloro-3-(4-((S)-2-((S)-3,3-difluorocyclohexyl)-2-(3-ethylisoxazole-4-carboxamido)acetamido)phenyl)-2-methylpyridine 1-oxide;

3-(4-((S)-2-(1-ethyl-1H-pyrazole-5-carboxamido)-2-((1r,4S)-4-(trifluoromethyl)cyclohexyl)acetamido)phenyl)-2,4-dimethylpyridine 1-oxide;

3-(4-((S)-2-(3-ethylisoxazole-4-carboxamido)-2-((1r,4S)-4-(trifluoromethyl)cyclohexyl)acetamido)phenyl)-2,4-dimethylpyridine 1-oxide;

3-(4-((S)-2-((S)-3,3-difluorocyclohexyl)-2-(3-methylisoxazole-4-carboxamido)acetamido)phenyl)-2-methyl-4-(trifluoromethyl)pyridine 1-oxide;

3-(4-((S)-2-((S)-3,3-difluorocyclohexyl)-2-(1-ethyl-1H-pyrazole-5-carboxamido)acetamido)phenyl)-2-methyl-4-(trifluoromethyl)pyridine 1-oxide;

(S)-3-(4-(2-(4,4-difluorocyclohexyl)-2-(1-ethyl-1H-pyrazole-5-carboxamido)acetamido)phenyl)-2-methyl-4-(trifluoromethyl)pyridine 1-oxide;

3-(4-((2S)-2-(4-fluorocyclohex-3-en-1-yl)-2-(1-methyl-1H-pyrazole-5-carboxamido)acetamido)phenyl)-2,4-dimethylpyridine 1-oxide;
3-(4-((S)-2-((R)-4-fluorocyclohex-3-en-1-yl)-2-(1-methyl-1H-pyrazole-5-carboxamido)acetamido)phenyl)-2,4-dimethylpyridine 1-oxide; or
3-(4-((S)-2-((S)-4-fluorocyclohex-3-en-1-yl)-2-(1-methyl-1H-pyrazole-5-carboxamido)acetamido)phenyl)-2,4-dimethylpyridine 1-oxide.

12. The compound 2,4-dimethyl-3-(4-((S)-2-(1-methyl-1H-pyrazole-5-carboxamido)-2-((S)-1,2,3,4-tetrahydronaphthalen-1-yl)acetamido)phenyl)pyridine 1-oxide, or a pharmaceutically acceptable salt thereof.

13. A pharmaceutical composition comprising a compound, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 12, and a pharmaceutically acceptable carrier.

14. A combination comprising a compound, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 12, and one or more therapeutically active agents.

15. A compound, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 12, for use as a medicament.

16. Use of the~~A~~ compound, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 12, in the manufacture of a medicament for ~~use in~~ the treatment, or prevention of autoimmune disease and of inflammatory conditions, in particular inflammatory conditions with an etiology including an autoimmune component such as arthritis (for example rheumatoid arthritis, arthritis chronica progrediente and arthritis deformans) and rheumatic diseases, including inflammatory conditions and rheumatic diseases involving bone loss, inflammatory pain, spondyloarthropathies including ankylosing spondylitis and non-radiographic axial spondyloarthritis, Reiter syndrome, reactive arthritis, psoriatic arthritis, and enterophathis arthritis, osteoarthritis, tendinopathy, hypersensitivity (including both airways hypersensitivity and dermal hypersensitivity) and allergies, including eczema and dermatitis, as well as asthma; in particular autoimmune diseases such as autoimmune hematological disorders (including e.g. hemolytic anemia, aplastic anemia, pure red cell anemia and idiopathic thrombocytopenia), systemic lupus erythematosus, inflammatory muscle disorders, polychondritis, sclerodoma, Wegener granulomatosis, dermatomyositis, chronic active hepatitis, myasthenia gravis, psoriasis, Steven Johnson syndrome, idiopathic sprue, autoimmune inflammatory bowel disease (including e.g. ulcerative colitis, Crohn's disease and Irritable Bowel Syndrome), endocrine ophthalmopathy, Grave's disease, sarcoidosis,

primary biliary cirrhosis, juvenile diabetes (diabetes mellitus type I), uveitis (anterior and posterior), keratoconjunctivitis sicca and vernal keratoconjunctivitis, Behcet disease, lichen planopilaris, lichen planus, hidradenitis suppurativa, acne, recurrent aphthous stomatitis, and periodontitis, pyoderma gangraenosum, and other neutrophil dermatoses, pityriasis rubra pilaris, bullous pemphigoid and ichthyosis, endometriosis, non-alcoholic steatohepatitis, interstitial lung fibrosis, glomerulonephritis (with and without nephrotic syndrome, e.g. including idiopathic nephrotic syndrome or minimal change nephropathy), tumors, multiple sclerosis, autism, depressiona DNA, Alzheimer's disease, inflammatory disease of skin and cornea, myositis, loosening of bone implants, metabolic disorders, such as atherosclerosis, diabetes, and dislipidemia.

17. Use of the~~A~~ compound, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 12, in the manufacture of a medicament for ~~use in~~ the treatment, or prevention of psorisasis, psoriatic arthritis, ankylosing spondylitis and non-radiographic axial spondyloarthritis.