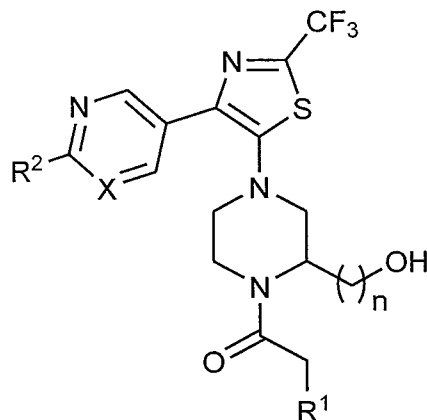


Claims

1. A compound of Formula (I)



Formula (I)

5 wherein

n represents the integer 1 or 2;

X represents N or CH;

R¹ represents heteroaryl, wherein the heteroaryl is a 5- to 10-membered monocyclic or bicyclic aromatic ring containing 1, 2 or 3 heteroatoms independently selected from oxygen, nitrogen and sulphur, and wherein the heteroaryl is independently unsubstituted or mono- or di-substituted, wherein the substituents are independently selected from the group consisting of (C₁₋₄)alkyl; (C₃₋₆)cycloalkyl; (C₁₋₄)alkoxy; (C₁₋₂)alkoxy-(C₁₋₂)alkyl; (C₁₋₂)alkyl-carbonyl; hydroxy-(C₁₋₄)alkyl; halogen; (C₁₋₂)fluoroalkyl; phenyl; and heteroaryl, wherein the heteroaryl is a 5- or 6-membered monocyclic aromatic ring containing 1, 2 or 3 heteroatoms independently selected from oxygen, nitrogen and sulphur, and wherein the heteroaryl is independently unsubstituted or mono-substituted with (C₁₋₄)alkyl; and

R² represents (C₃₋₆)cycloalkyl, (C₁₋₄)alkoxy or (C₁₋₂)fluoroalkyl; or a salt thereof.

2. A compound according to claim 1, wherein

n represents the integer 1 or 2;

X represents N;

R¹ represents a 5-membered monocyclic heteroaryl group containing 2 or 3 nitrogen atoms which is independently mono- or di-substituted, wherein the substituents are independently selected from the group consisting of (C₁₋₄)alkyl, (C₃₋₆)cycloalkyl, (C₁₋₂)alkoxy-(C₁₋₂)alkyl, hydroxy-(C₁₋₄)alkyl and (C₁₋₂)fluoroalkyl; or a 9-membered bicyclic aromatic ring containing 1, 2 or 3 nitrogen atoms which is unsubstituted or mono-substituted with (C₁₋₄)alkoxy or halogen; and

R² represents (C₃₋₆)cycloalkyl, (C₁₋₄)alkoxy or trifluoromethyl;

or a salt thereof.

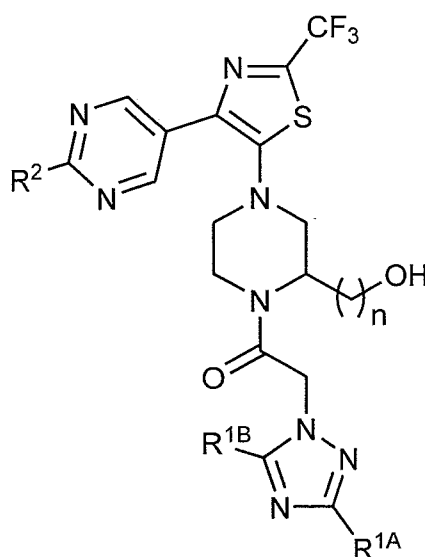
3. A compound according to any one of claims 1 or 2, wherein

R^1 represents a 5-membered monocyclic heteroaryl group containing 2 or 3 nitrogen atoms which is independently mono- or di-substituted, wherein the substituents are independently
5 selected from the group consisting of (C_{1-4}) alkyl, (C_{3-6}) cycloalkyl and (C_{1-2}) fluoroalkyl; or a salt thereof.

4. A compound according to any one of claims 1 to 3, wherein

R^2 represents trifluoromethyl;
or a salt thereof.

10 5. A compound according to claim 1, which is also a compound of Formula (I_{TA})



Formula (I_{TA})

wherein

n represents the integer 1 or 2;

15 R^{1A} represents hydrogen, (C_{1-4}) alkyl, (C_{3-6}) cycloalkyl, (C_{1-2}) alkoxy- (C_{1-2}) alkyl, (C_{1-2}) alkyl-carbonyl, hydroxy- (C_{1-4}) alkyl, (C_{1-2}) fluoroalkyl, phenyl or heteroaryl, wherein the heteroaryl is a 5- or 6-membered monocyclic aromatic ring containing 1, 2 or 3 heteroatoms independently selected from oxygen, nitrogen and sulphur, and wherein the heteroaryl is independently unsubstituted or mono-substituted with (C_{1-4}) alkyl;

20 R^{1B} represents hydrogen or (C_{1-4}) alkyl; and

R^2 represents (C_{3-6}) cycloalkyl, (C_{1-4}) alkoxy or (C_{1-2}) fluoroalkyl;
or a salt thereof.

6. A compound according to claim 5, wherein

R^{1A} represents (C_{1-4}) alkyl, (C_{3-6}) cycloalkyl, (C_{1-2}) alkoxy- (C_{1-2}) alkyl, hydroxy- (C_{1-4}) alkyl or (C_{1-2}) fluoroalkyl;

25

or a salt thereof.

7. A compound according to claim 5, wherein

R^{1A} represents (C_{1-4}) alkyl or (C_{3-6}) cycloalkyl;

or a salt thereof.

5 8. A compound according to any one of claims 5 to 7, wherein

R^{1B} represents hydrogen;

or a salt thereof.

9. A compound according to any one of claims 5 to 7, wherein

R^{1B} represents methyl;

10 or a salt thereof.

10. A compound according to any one of claims 5 to 9, wherein

R^2 represents trifluoromethyl;

or a salt thereof.

11. A compound according to claim 1 selected from the group consisting of:

- 15 2-(3-tert-Butyl-[1,2,4]triazol-1-yl)-1-{(S)-2-hydroxymethyl-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl}-ethanone;
- 2-(3,5-Dimethyl-[1,2,4]triazol-1-yl)-1-{(S)-2-hydroxymethyl-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl}-ethanone;
- 20 2-(3-Cyclopropyl-[1,2,4]triazol-1-yl)-1-{(S)-2-hydroxymethyl-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl}-ethanone;
- 1-{(S)-2-Hydroxymethyl-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl}-2-(3-isopropyl-[1,2,4]triazol-1-yl)-ethanone;
- 1-{(S)-2-Hydroxymethyl-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl}-2-(3-trifluoromethyl-[1,2,4]triazol-1-yl)-ethanone;
- 25 1-{(S)-4-[4-(2-Ethoxy-pyrimidin-5-yl)-2-trifluoromethyl-thiazol-5-yl]-2-hydroxymethyl-piperazin-1-yl}-2-(3-trifluoromethyl-[1,2,4]triazol-1-yl)-ethanone;
- 2-(3,5-Dimethyl-[1,2,4]triazol-1-yl)-1-{(S)-4-[4-(2-ethoxy-pyrimidin-5-yl)-2-trifluoromethyl-thiazol-5-yl]-2-hydroxymethyl-piperazin-1-yl}-ethanone;
- 1-{(S)-4-[4-(2-Cyclopropyl-pyrimidin-5-yl)-2-trifluoromethyl-thiazol-5-yl]-2-hydroxymethyl-piperazin-1-yl}-2-(3,5-dimethyl-[1,2,4]triazol-1-yl)-ethanone;
- 30 1-{(S)-4-[4-(2-Cyclopropyl-pyrimidin-5-yl)-2-trifluoromethyl-thiazol-5-yl]-2-hydroxymethyl-piperazin-1-yl}-2-(3-trifluoromethyl-[1,2,4]triazol-1-yl)-ethanone;
- 1-{(R)-2-Hydroxymethyl-4-[2-trifluoromethyl-4-(6-trifluoromethyl-pyridin-3-yl)-thiazol-5-yl]-piperazin-1-yl}-2-(3-isopropyl-[1,2,4]triazol-1-yl)-ethanone;

- 1-((R)-2-Hydroxymethyl-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl)-2-(3-isopropyl-[1,2,4]triazol-1-yl)-ethanone;
- 2-(3,5-Dimethyl-[1,2,4]triazol-1-yl)-1-((R)-2-hydroxymethyl-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl)-ethanone;
- 5 2-Benzoimidazol-1-yl-1-((R)-2-hydroxymethyl-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl)-ethanone;
- 2-(5-Fluoro-indol-1-yl)-1-((R)-2-hydroxymethyl-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl)-ethanone;
- 1-((R)-2-Hydroxymethyl-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl)-2-(5-methoxy-indol-1-yl)-ethanone;
- 10 1-((R)-2-Hydroxymethyl-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl)-2-(3-methyl-[1,2,4]triazol-1-yl)-ethanone;
- 1-((R)-2-Hydroxymethyl-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl)-2-(3-methoxymethyl-[1,2,4]triazol-1-yl)-ethanone;
- 15 1-((R)-2-Hydroxymethyl-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl)-2-[3-(5-methyl-[1,2,4]oxadiazol-3-yl)-[1,2,4]triazol-1-yl]-ethanone;
- 1-((R)-2-Hydroxymethyl-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl)-2-(3-phenyl-[1,2,4]triazol-1-yl)-ethanone;
- 2-(3-Acetyl-[1,2,4]triazol-1-yl)-1-((R)-2-hydroxymethyl-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl)-ethanone;
- 20 2-[3-(1-Hydroxy-ethyl)-[1,2,4]triazol-1-yl]-1-((R)-2-hydroxymethyl-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl)-ethanone;
- 1-((R)-2-Hydroxymethyl-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl)-2-(3-methyl-pyrazol-1-yl)-ethanone;
- 25 1-((R)-2-Hydroxymethyl-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl)-2-(3-pyridin-2-yl-[1,2,4]triazol-1-yl)-ethanone;
- 2-(3-Ethyl-5-methyl-[1,2,4]triazol-1-yl)-1-((R)-2-hydroxymethyl-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl)-ethanone;
- 2-(5-Ethyl-3-methyl-[1,2,4]triazol-1-yl)-1-((R)-2-hydroxymethyl-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl)-ethanone;
- 30 1-((R)-2-Hydroxymethyl-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl)-2-imidazo[4,5-b]pyridin-3-yl)-ethanone;
- 2-(3,5-Dimethyl-[1,2,4]triazol-1-yl)-1-((R)-2-(2-hydroxy-ethyl)-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl)-ethanone;
- 35 1-((R)-2-(2-Hydroxy-ethyl)-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl)-2-(3-trifluoromethyl-[1,2,4]triazol-1-yl)-ethanone;

2-(3-Cyclobutyl-[1,2,4]triazol-1-yl)-1-{(R)-2-(2-hydroxy-ethyl)-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl}-ethanone;

2-(3-tert-Butyl-[1,2,4]triazol-1-yl)-1-{(R)-2-(2-hydroxy-ethyl)-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl}-ethanone;

5 2-(3-Cyclopropyl-[1,2,4]triazol-1-yl)-1-{(R)-2-(2-hydroxy-ethyl)-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl}-ethanone;

2-(3-Ethyl-[1,2,4]triazol-1-yl)-1-{(R)-2-(2-hydroxy-ethyl)-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl}-ethanone;

10 2-(5-Ethyl-[1,2,4]triazol-1-yl)-1-{(R)-2-(2-hydroxy-ethyl)-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl}-ethanone;

1-{(R)-2-(2-Hydroxy-ethyl)-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl}-2-(3-isopropyl-[1,2,4]triazol-1-yl)-ethanone;

1-{(R)-2-(2-Hydroxy-ethyl)-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl}-2-(3-methyl-[1,2,4]triazol-1-yl)-ethanone;

15 1-{(R)-2-(2-Hydroxy-ethyl)-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl}-2-(5-methyl-[1,2,4]triazol-1-yl)-ethanone;

1-{(R)-2-(2-Hydroxy-ethyl)-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl}-2-(3-methoxymethyl-[1,2,4]triazol-1-yl)-ethanone; and

20 2-(3-Difluoromethyl-[1,2,4]triazol-1-yl)-1-{(R)-2-hydroxymethyl-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl}-ethanone;

or a salt thereof.

12. A compound according to claim 1 selected from the group consisting of:

1-{(R)-2-(2-Hydroxy-ethyl)-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl}-2-(3-methyl-pyrazol-1-yl)-ethanone;

25 2-(3-Ethyl-pyrazol-1-yl)-1-{(R)-2-(2-hydroxy-ethyl)-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl}-ethanone;

2-(3-Cyclopropyl-pyrazol-1-yl)-1-{(R)-2-(2-hydroxy-ethyl)-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl}-ethanone;

30 1-{(S)-2-Hydroxymethyl-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl}-2-(3-methyl-pyrazol-1-yl)-ethanone;

2-(3-Ethyl-pyrazol-1-yl)-1-{(S)-2-hydroxymethyl-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl}-ethanone; and

2-(3-Cyclopropyl-pyrazol-1-yl)-1-{(S)-2-hydroxymethyl-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl}-ethanone;

35 or a salt thereof.

13. A compound according to claim 1, wherein the compound is

1-{(R)-2-Hydroxymethyl-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl}-2-(3-methyl-pyrazol-1-yl)-ethanone;

or a pharmaceutically acceptable salt thereof.

14. A compound according to claim 1, wherein the compound is

5 2-(3-Ethyl-[1,2,4]triazol-1-yl)-1-{(R)-2-(2-hydroxy-ethyl)-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl}-ethanone;

or a pharmaceutically acceptable salt thereof.

15. A compound according to claim 1, wherein the compound is

10 1-{(R)-2-(2-Hydroxy-ethyl)-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl}-2-(3-methyl-[1,2,4]triazol-1-yl)-ethanone;

or a pharmaceutically acceptable salt thereof.

16. A pharmaceutical composition comprising, as active principle, a compound according to any one of claims 1 to 15, or a pharmaceutically acceptable salt thereof, and at least one therapeutically inert excipient.

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

18. A compound according to any one of claims 1 to 15, or a pharmaceutically acceptable salt thereof, for use in the prevention or treatment of a disease selected from the group consisting of autoimmune disorders, inflammatory diseases, infectious diseases, transplant rejection, fibrosis, neurodegenerative disorders and cancer.

20 19. Use of a compound according to any one of claims 1 to 15, or a pharmaceutically acceptable salt thereof, for the preparation of a medicament for the prevention or treatment of a disease selected from the group consisting of autoimmune disorders, inflammatory diseases, infectious diseases, transplant rejection, fibrosis, neurodegenerative disorders and cancer.

25 20. Use of a compound according to any one of claims 1 to 15, or a pharmaceutically acceptable salt thereof, for the preparation of a medicament for the prevention or treatment of a disease selected from the group consisting of rheumatoid arthritis, multiple sclerosis, neuromyelitis optica, inflammatory bowel disease, Crohn's disease, ulcerative colitis, systemic lupus erythematosus, psoriasis, psoriatic arthritis, lupus nephritis, interstitial cystitis, celiac disease, myasthenia gravis, type I diabetes, uveitis, asthma, chronic obstructive pulmonary disorder, atherosclerosis, myocarditis, inflammatory myopathies, dry eye disease, sarcoidosis, influenza, cerebral malaria, transplant rejection, liver cirrhosis, systemic sclerosis, pulmonary arterial hypertension, neurodegeneration, Alzheimer's disease, HIV associated dementia, Huntington's chorea, Guillain-Barré syndrome, chronic

inflammatory demyelinating polyneuropathy, brain tumor, colon cancer, breast cancer, and metastatic spread of cancer.