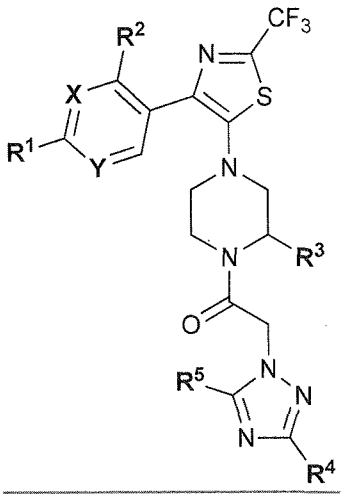
R^6 represents hydrogen, (C_{1-4})alkyl or fluoro; or **R**^{1} and **R**^{6} form, together with the carbon atoms to which they are attached, a 5- or 6-membered heterocyclic ring, wherein the moiety needed to complete said heterocyclic ring is selected from -OCH_2CH_2-*, -OCH_2O-*, -$OCH_2CH_2CH_2$-* and -OCH_2CH_2O-*, wherein the asterisks indicate the bond which is linked to the **R**^{6} bearing carbon atom;

R^7 represents (C_{1-2})alkyl; and

R^8 represents (C_{1-2})alkyl;

and to the salts (in particular pharmaceutically acceptable salts) of such compounds.

In an aspect, the invention relates to a compound of Formula (I_P)



Formula (I_P)

wherein

X represents N or CH;

Y represents N or CR^6;

R^1 represents (C_{1-4})alkyl; (C_{3-6})cycloalkyl; (C_{1-4})alkoxy; (C_{3-6})cycloalkoxy; (C_{1-3})fluoroalkyl; (C_{1-3})fluoroalkoxy; halogen; cyano; (C_{1-2})alkoxy-(C_{2-3})alkoxy; (C_{1-3})alkyl which is mono-substituted with -NR^{7}R^8; (C_{2-3})alkoxy which is mono-substituted with -NR^{7}R^8; heterocyclyl, wherein the heterocyclyl is a 4- to 6-membered mono-cyclic saturated ring containing one or two heteroatoms independently selected from nitrogen and oxygen and wherein said heterocyclyl is unsubstituted or mono-substituted with (C_{1-2})alkyl; or heterocyclyloxy, wherein the heterocyclyl is a 4- to 6-membered mono-cyclic saturated ring containing one oxygen atom;

R^2 represents hydrogen, (C_{1-4})alkoxy or fluoro;

R^3 represents hydrogen or methyl;

R^4 represents (C_{1-4})alkyl, or (C_{1-2})alkyl which is mono-substituted with -NR^{7}R^8;

R^5 represents (C_{1-4})alkyl;

R^6 represents hydrogen, (C_{1-4})alkyl or fluoro; or R^1 and R^6 form, together with the carbon atoms to which they are attached, a 5- or 6-membered heterocyclic ring, wherein the moiety needed to complete said heterocyclic ring is selected from $-OCH_2CH_2-*$, $-OCH_2O-*$, $-OCH_2CH_2CH_2-*$ and $-OCH_2CH_2O-*$, wherein the asterisks indicate the bond which is linked to the R^6 bearing carbon atom;
R^7 represents (C_{1-2})alkyl; and
R^8 represents (C_{1-2})alkyl;
or a pharmaceutically acceptable salt thereof.

Another aspect of the invention relates to a pharmaceutical composition comprising, as active principle, a compound as disclosed herein, or a pharmaceutically acceptable salt thereof, and at least one therapeutically inert excipient.

Another aspect relates to a compound as defined herein, or a pharmaceutically acceptable salt thereof, for use as a medicament.

Another aspect relates to the use of a compound as defined herein, 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 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, or metastatic spread of those cancers~~autoimmune disorders, inflammatory diseases, infectious diseases, transplant rejection, fibrosis, neurodegenerative disorders and cancer~~.

Definitions provided herein are intended to apply uniformly to the compounds of Formulae (I), (I_P), (II), (III), (IV) and (V) as defined in any one of embodiments 1) to 45), and, *mutatis mutandis*, throughout the description and the claims unless an otherwise expressly set out definition provides a broader or narrower definition. It is well understood that a definition or preferred definition of a term defines and may replace the respective term independently of (and in combination with) any definition or preferred definition of any or all other terms as defined herein.

The compounds of Formula (I) as defined in any one of embodiments 1) to 45), may contain one or more stereogenic or asymmetric centers, such as one or more asymmetric carbon

atoms. The compounds of Formula (I) may thus be present as mixtures of stereoisomers or in stereoisomerically enriched form, preferably as pure stereoisomers. Mixtures of stereoisomers may be separated in a manner known to a person skilled in the art.

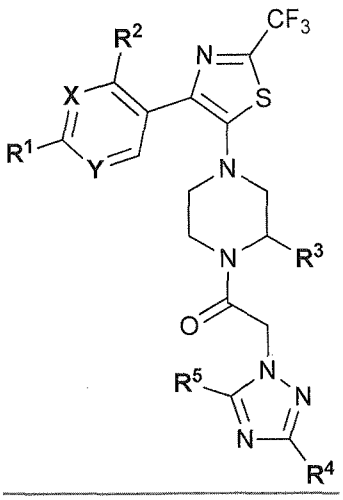
The term "enriched", for example when used in the context of enantiomers, is understood in the context of the present invention to mean especially that the respective enantiomer is present in a ratio (mutatis mutandis: purity) of at least 70:30, and notably of at least 90:10 (mutatis mutandis: purity of 70% / 90%) with respect to the respective other enantiomer. Preferably the term refers to the respective essentially pure enantiomer. The term “essentially”, for example when used in a term such as "essentially pure" is understood in the context of the present invention to mean especially that the respective stereoisomer / composition / compound etc. consists in an amount of at least 90, especially of at least 95, and notably of at least 99 per cent by weight of the respective pure stereoisomer / composition / compound etc..

The term "halogen" means fluorine, chlorine, or bromine, preferably fluorine or chlorine.

The term "alkyl", used alone or in combination, refers to a straight or branched saturated hydrocarbon chain containing one to four carbon atoms. The term "(C_{x-y})alkyl" (x and y each being an integer), refers to an alkyl group as defined before containing x to y carbon atoms. For example a (C_{1-4})alkyl group contains from one to four carbon atoms. Examples of (C_{1-4})alkyl groups are methyl, ethyl, *n*-propyl, *iso*-propyl, *n*-butyl, *iso*-butyl, *sec.*-butyl and *tert.*-

Claims

1. A compound of Formula (I_P)



Formula (I_P)

wherein

X represents N or CH;

Y represents N or CR^6;

R^1 represents (C_{1-4})alkyl; (C_{3-6})cycloalkyl; (C_{1-4})alkoxy; (C_{3-6})cycloalkoxy; (C_{1-3})fluoroalkyl; (C_{1-3})fluoroalkoxy; halogen; cyano; (C_{1-2})alkoxy-(C_{2-3})alkoxy; (C_{1-3})alkyl which is mono-substituted with $-NR^7R^8$; (C_{2-3})alkoxy which is mono-substituted with $-NR^7R^8$; heterocyclyl, wherein the heterocyclyl is a 4- to 6-membered mono-cyclic saturated ring containing one or two heteroatoms independently selected from nitrogen and oxygen and wherein said heterocyclyl is unsubstituted or mono-substituted with (C_{1-2})alkyl; or heterocyclyloxy, wherein the heterocyclyl is a 4- to 6-membered mono-cyclic saturated ring containing one oxygen atom;

R^2 represents hydrogen, (C_{1-4})alkoxy or fluoro;

R^3 represents hydrogen or methyl;

R^4 represents (C_{1-4})alkyl, or (C_{1-2})alkyl which is mono-substituted with $-NR^7R^8$;

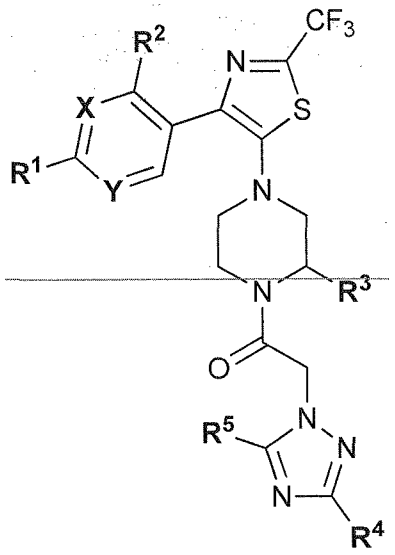
R^5 represents (C_{1-4})alkyl;

R^6 represents hydrogen, (C_{1-4})alkyl or fluoro; or R^1 and R^6 form, together with the carbon atoms to which they are attached, a 5- or 6-membered heterocyclic ring, wherein the moiety needed to complete said heterocyclic ring is selected from $-OCH_2CH_2-*$, $-OCH_2O-*$, $-OCH_2CH_2CH_2-*$ and $-OCH_2CH_2O-*$, wherein the asterisks indicate the bond which is linked to the R^6 bearing carbon atom;

R^7 represents (C_{1-2})alkyl; and

R^8 represents (C_{1-2})alkyl;

or a pharmaceutically acceptable salt thereof.



Formula (I)

wherein

X represents N or CH;

Y represents N or CR^6;

R^1 represents (C_{1-4})alkyl; (C_{3-6})cycloalkyl; (C_{1-4})alkoxy; (C_{3-6})cycloalkoxy; (C_{1-3})fluoroalkyl; (C_{1-3})fluoroalkoxy; halogen; cyano; (C_{1-2})alkoxy-(C_{2-3})alkoxy; (C_{1-3})alkyl which is mono-substituted with $-NR^7R^8$; (C_{2-3})alkoxy which is mono-substituted with $-NR^7R^8$; heterocyclyl, wherein the heterocyclyl is a 4- to 6-membered mono-cyclic saturated ring containing one or two heteroatoms independently selected from nitrogen and oxygen and wherein said heterocyclyl is unsubstituted or mono-substituted with (C_{1-2})alkyl; or heterocyclyloxy, wherein the heterocyclyl is a 4- to 6-membered mono-cyclic saturated ring containing one oxygen atom;

R^2 represents hydrogen, (C_{1-4})alkoxy or fluoro;

R^3 represents hydrogen or (C_{1-4})alkyl;

R^4 represents (C_{1-4})alkyl, (C_{1-4})alkyl which is mono-substituted with hydroxy, or (C_{1-2})alkyl which is mono-substituted with $-NR^7R^8$;

R^5 represents (C_{1-4})alkyl or (C_{1-4})alkyl which is mono-substituted with hydroxy;

R^6 represents hydrogen, (C_{1-4})alkyl or fluoro; or R^4 and R^6 form, together with the carbon atoms to which they are attached, a 5- or 6-membered heterocyclic ring, wherein the moiety needed to complete said heterocyclic ring is selected from $-OCH_2CH_2-*$, $-OCH_2O-*$, $-OCH_2CH_2CH_2-*$ and $-OCH_2CH_2O-*$, wherein the asterisks indicate the bond which is linked to the R^6 bearing carbon atom;

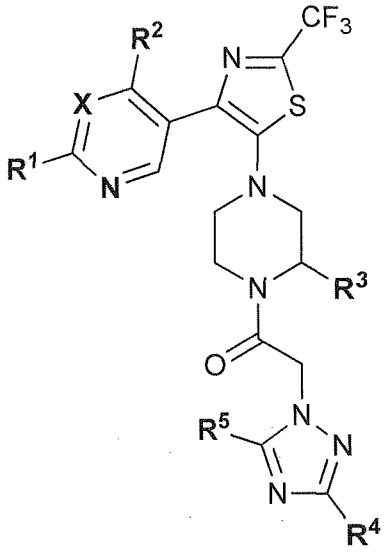
R^7 represents (C_{1-2})alkyl; and

~~R^8 represents (C_{1-2})alkyl;~~

~~or a salt thereof.~~

2. A compound according to claim 1, wherein R^1 represents ethyl; *n*-propyl; cyclopropyl; ethoxy; *iso*-propoxy; cyclobutyloxy; trifluoromethyl; trifluoromethoxy; or 2,2,2-trifluoroethoxy; or a pharmaceutically acceptable salt thereof.

3. A compound according to claim 1, which is also a compound of Formula (II)



Formula (II)

wherein

X represents N or CH;

R^1 represents (C_{1-4})alkyl; (C_{3-6})cycloalkyl; (C_{1-4})alkoxy; (C_{3-6})cycloalkoxy; (C_{1-3})fluoroalkyl; (C_{1-3})fluoroalkoxy; (C_{1-2})alkoxy-(C_{2-3})alkoxy; (C_{1-3})alkyl which is mono-substituted with $-NR^7R^8$; (C_{2-3})alkoxy which is mono-substituted with $-NR^7R^8$; heterocyclyl, wherein the heterocyclyl is a 4- to 6-membered mono-cyclic saturated ring containing one or two heteroatoms independently selected from nitrogen and oxygen and wherein said heterocyclyl is unsubstituted or mono-substituted with (C_{1-2})alkyl; or heterocyclyloxy, wherein the heterocyclyl is a 4- to 6-membered mono-cyclic saturated ring containing one oxygen atom;

R^2 represents hydrogen or (C_{1-4})alkoxy;

R^3 represents hydrogen or methyl;

R^4 represents (C_{1-4})alkyl, or (C_{1-2})alkyl which is mono-substituted with $-NR^7R^8$;

R^5 represents (C_{1-4})alkyl;

R^7 represents (C_{1-2})alkyl; and

R^8 represents (C_{1-2})alkyl;

or a pharmaceutically acceptable salt thereof.

4. A compound according to claim 3, wherein

X represents N or CH;

$\mathbf{R^1}$ represents (C_{1-4})alkyl; (C_{3-6})cycloalkyl; (C_{1-4})alkoxy; (C_{3-6})cycloalkoxy; (C_{1-2})fluoroalkyl; or (C_{1-2})fluoroalkoxy;

$\mathbf{R^2}$ represents hydrogen or ethoxy;

$\mathbf{R^3}$ represents hydrogen or methyl;

$\mathbf{R^4}$ represents methyl or ethyl; and

$\mathbf{R^5}$ represents methyl or ethyl;

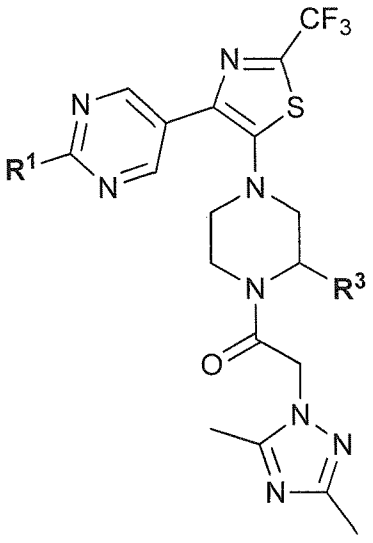
or a pharmaceutically acceptable salt thereof.

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

X represents N;

or a pharmaceutically acceptable salt thereof.

6. A compound according to claim 1, which is also a compound of Formula (III)



Formula (III)

wherein

$\mathbf{R^1}$ represents (C_{1-4})alkyl; (C_{3-6})cycloalkyl; (C_{1-4})alkoxy; (C_{3-6})cycloalkoxy; (C_{1-2})fluoroalkyl; or (C_{1-2})fluoroalkoxy; and

$\mathbf{R^3}$ represents hydrogen or methyl;

or a pharmaceutically acceptable salt thereof.

7. A compound according to claim 6, wherein

$\mathbf{R^1}$ represents ethyl; *n*-propyl; cyclopropyl; ethoxy; *iso*-propoxy; cyclobutyloxy; trifluoromethyl; or 2,2,2-trifluoroethoxy;

or a pharmaceutically acceptable salt thereof.

8. A compound according to claim 6, wherein

R^1 represents (C_{1-4})alkoxy; or (C_{1-2})fluoroalkyl;

or a pharmaceutically acceptable salt thereof.

9. A compound according to any one of claims 6 to 8, wherein

R^3 represents methyl;

or a pharmaceutically acceptable salt thereof.

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

2-(3,5-Dimethyl-[1,2,4]triazol-1-yl)-1-{(R)-4-[4-(4-methoxy-phenyl)-2-trifluoromethyl-thiazol-5-yl]-2-methyl-piperazin-1-yl}-ethanone;

2-(3,5-Dimethyl-[1,2,4]triazol-1-yl)-1-{(R)-4-[4-(4-isopropoxy-phenyl)-2-trifluoromethyl-thiazol-5-yl]-2-methyl-piperazin-1-yl}-ethanone;

2-(3,5-Dimethyl-[1,2,4]triazol-1-yl)-1-{(R)-2-methyl-4-[4-(4-trifluoromethoxy-phenyl)-2-trifluoromethyl-thiazol-5-yl]-piperazin-1-yl}-ethanone;

2-(3,5-Dimethyl-[1,2,4]triazol-1-yl)-1-((R)-2-methyl-4-{4-[4-(2,2,2-trifluoro-ethoxy)-phenyl]-2-trifluoromethyl-thiazol-5-yl}-piperazin-1-yl)-ethanone;

4-(5-{(R)-4-[2-(3,5-Dimethyl-[1,2,4]triazol-1-yl)-acetyl]-3-methyl-piperazin-1-yl}-2-trifluoromethyl-thiazol-4-yl)-benzonitrile;

2-(3,5-Dimethyl-[1,2,4]triazol-1-yl)-1-{(R)-4-[4-(4-fluoro-phenyl)-2-trifluoromethyl-thiazol-5-yl]-2-methyl-piperazin-1-yl}-ethanone;

1-{(R)-4-[4-(4-Chloro-phenyl)-2-trifluoromethyl-thiazol-5-yl]-2-methyl-piperazin-1-yl}-2-(3,5-dimethyl-[1,2,4]triazol-1-yl)-ethanone;

2-(3,5-Dimethyl-[1,2,4]triazol-1-yl)-1-[(R)-2-methyl-4-(4-p-tolyl-2-trifluoromethyl-thiazol-5-yl)-piperazin-1-yl]-ethanone;

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

2-(3,5-Dimethyl-[1,2,4]triazol-1-yl)-1-{(R)-4-[4-(3-fluoro-4-methoxy-phenyl)-2-trifluoromethyl-thiazol-5-yl]-2-methyl-piperazin-1-yl}-ethanone;

2-(3,5-Dimethyl-[1,2,4]triazol-1-yl)-1-{(R)-4-[4-(2-fluoro-4-methoxy-phenyl)-2-trifluoromethyl-thiazol-5-yl]-2-methyl-piperazin-1-yl}-ethanone;

2-(3,5-Dimethyl-[1,2,4]triazol-1-yl)-1-{(R)-4-[4-(4-methoxy-3-methyl-phenyl)-2-trifluoromethyl-thiazol-5-yl]-2-methyl-piperazin-1-yl}-ethanone;

1-[(R)-4-(4-Benzo[1,3]dioxol-5-yl-2-trifluoromethyl-thiazol-5-yl)-2-methyl-piperazin-1-yl]-2-(3,5-dimethyl-[1,2,4]triazol-1-yl)-ethanone;

1-{(R)-4-[4-(2,3-Dihydro-benzo[1,4]dioxin-6-yl)-2-trifluoromethyl-thiazol-5-yl]-2-methyl-piperazin-1-yl}-2-(3,5-dimethyl-[1,2,4]triazol-1-yl)-ethanone;

2-(3,5-Dimethyl-[1,2,4]triazol-1-yl)-1-{(R)-4-[4-(6-ethoxy-pyridin-3-yl)-2-trifluoromethyl-thiazol-5-yl]-2-methyl-piperazin-1-yl}-ethanone;

2-(3,5-Dimethyl-[1,2,4]triazol-1-yl)-1-{(R)-4-[4-(6-methoxy-pyridin-3-yl)-2-trifluoromethyl-thiazol-5-yl]-2-methyl-piperazin-1-yl}-ethanone;

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

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

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

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

1-[(R)-4-(4-Chroman-6-yl-2-trifluoromethyl-thiazol-5-yl)-2-methyl-piperazin-1-yl]-2-(3,5-dimethyl-[1,2,4]triazol-1-yl)-ethanone;

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

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

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

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

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

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

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

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

2-(3,5-Dimethyl-[1,2,4]triazol-1-yl)-1-{(R)-4-[4-(4-ethoxy-phenyl)-2-trifluoromethyl-thiazol-5-yl]-2-methyl-piperazin-1-yl}-ethanone;

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

1-{(R)-4-[4-(2-Cyclopropyl-pyrimidin-5-yl)-2-trifluoromethyl-thiazol-5-yl]-2-methyl-piperazin-1-yl}-2-(3,5-dimethyl-[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-methyl-piperazin-1-yl}-ethanone;
2-(3,5-Dimethyl-[1,2,4]triazol-1-yl)-1-{4-[4-(2-ethoxy-pyrimidin-5-yl)-2-trifluoromethyl-thiazol-5-yl]-piperazin-1-yl}-ethanone;
2-(3,5-Dimethyl-[1,2,4]triazol-1-yl)-1-{(R)-2-methyl-4-[4-(2-pyrrolidin-1-yl-pyrimidin-5-yl)-2-trifluoromethyl-thiazol-5-yl]-piperazin-1-yl}-ethanone;
2-(3,5-Dimethyl-[1,2,4]triazol-1-yl)-1-((R)-2-methyl-4-{4-[2-(4-methyl-piperazin-1-yl)-pyrimidin-5-yl]-2-trifluoromethyl-thiazol-5-yl}-piperazin-1-yl)-ethanone;
1-{(R)-4-[4-(2-Cyclobutoxy-pyrimidin-5-yl)-2-trifluoromethyl-thiazol-5-yl]-2-methyl-piperazin-1-yl}-2-(3,5-dimethyl-[1,2,4]triazol-1-yl)-ethanone;
1-{(R)-4-[4-(3,4-Dihydro-2H-pyrano[2,3-b]pyridin-6-yl)-2-trifluoromethyl-thiazol-5-yl]-2-methyl-piperazin-1-yl}-2-(3,5-dimethyl-[1,2,4]triazol-1-yl)-ethanone;
1-{(R)-4-[4-(2,3-Dihydro-benzofuran-5-yl)-2-trifluoromethyl-thiazol-5-yl]-2-methyl-piperazin-1-yl}-2-(3,5-dimethyl-[1,2,4]triazol-1-yl)-ethanone;
2-(3,5-Dimethyl-[1,2,4]triazol-1-yl)-1-{(R)-4-[4-(2-ethoxy-pyrimidin-5-yl)-2-trifluoromethyl-thiazol-5-yl]-2-methyl-piperazin-1-yl}-2,2-dideuterium-ethanone;
1-((R)-4-{4-[2-(2-Dimethylamino-ethyl)-pyrimidin-5-yl]-2-trifluoromethyl-thiazol-5-yl}-2-methyl-piperazin-1-yl)-2-(3,5-dimethyl-[1,2,4]triazol-1-yl)-ethanone; and
2-(3,5-Dimethyl-[1,2,4]triazol-1-yl)-1-{(R)-4-[4-(2-ethyl-pyrimidin-5-yl)-2-trifluoromethyl-thiazol-5-yl]-2-methyl-piperazin-1-yl}-ethanone;
or a pharmaceutically acceptable salt thereof.

~~11. A compound according to claim 1 selected from the group consisting of:~~
~~2-(3-Hydroxymethyl-5-methyl-[1,2,4]triazol-1-yl)-1-{(R)-2-methyl-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl}-ethanone;~~
~~2-(5-Hydroxymethyl-3-methyl-[1,2,4]triazol-1-yl)-1-{(R)-2-methyl-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl}-ethanone;~~
~~2-(3-Ethyl-5-methyl-[1,2,4]triazol-1-yl)-1-{(R)-2-methyl-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-methyl-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl}-ethanone;~~
~~2-[3-(1-Hydroxy-1-methyl-ethyl)-5-methyl-[1,2,4]triazol-1-yl]-1-{(R)-2-methyl-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-{(R)-2-methyl-4-[2-trifluoromethyl-4-(6-trifluoromethyl-pyridin-3-yl)-thiazol-5-yl]-piperazin-1-yl}-ethanone;~~
~~2-(3,5-Dimethyl-[1,2,4]triazol-1-yl)-1-{(S)-2-methyl-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-{(R)-2-ethyl-4-[2-trifluoromethyl-4-(2-trifluoromethyl-pyrimidin-5-yl)-thiazol-5-yl]-piperazin-1-yl}-ethanone; and~~

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

~~or a salt thereof.~~

~~12~~11. A pharmaceutical composition comprising, as active principle, a compound according to any one of claims 1 to ~~11~~10, or a pharmaceutically acceptable salt thereof, and at least one therapeutically inert excipient.

~~13~~12. A compound according to any one of claims 1 to ~~11~~10, or a pharmaceutically acceptable salt thereof, for use as a medicament.

~~14~~13. A compound according to any one of claims 1 to ~~11~~10, or a pharmaceutically acceptable salt thereof, for use in the ~~prevention or~~ treatment of a disease selected from the group consisting of autoimmune 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, or metastatic spread of those cancers~~disorders, inflammatory diseases, infectious diseases, transplant rejection, fibrosis, neurodegenerative disorders and cancer~~.

~~15~~14. Use of a compound according to any one of claims 1 to ~~11~~10, 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 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, or metastatic spread of those cancers~~autoimmune disorders, inflammatory diseases, infectious diseases, transplant rejection, fibrosis, neurodegenerative disorders and cancer~~.