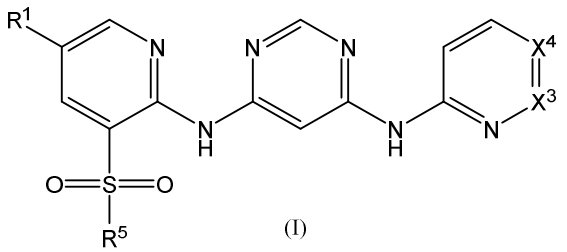
Claims

1. A compound of Formula I:



(I)

wherein

R^1 is a member selected from H, halogen, substituted or unsubstituted straight- or branched-chain C_1-C_6 alkyl, and substituted or unsubstituted straight- or branched-chain C_1-C_6 alkoxy;

R^5 is C_1-C_6 alkyl; and

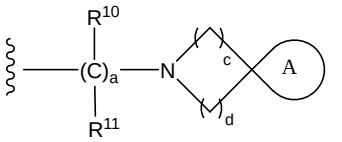
X^3 is selected from N and CR^7;

X^4 is selected from and CR^8,

wherein

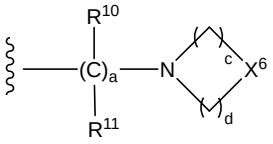
R^7 is selected from H, substituted or unsubstituted C_1-C_6 alkyl, and substituted or unsubstituted C_1-C_6 aminoalkyl, wherein R^7 and R^8, together with the carbon atoms to which they are joined, are optionally joined to form a ring selected from substituted or unsubstituted cycloalkyl and substituted or unsubstituted heterocycloalkyl,

R^8 is selected from substituted or unsubstituted C_1-C_6 alkyl,



(II)

; and



(III)

wherein

one or more carbon atom of a ring in Formula II or Formula III is optionally substituted with a member independently selected from halogen, and substituted or unsubstituted alkyl;

a is selected from the integers 0 and 1;

R^{10} and R^{11} are independently selected from H, halogen and substituted or unsubstituted C_1-C_6 alkyl;

c and d are independently selected from the integers 0, 1, 2, 3 and 4 with the proviso that the sum c+d is selected from the integers 3, 4, 5, and 6;

A is a ring system selected from substituted or unsubstituted cycloalkyl and substituted or unsubstituted heterocylcoalkyl; and

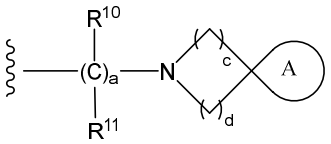
X^6 is selected from O, NR^{12}, and $CR^{12}R^{13}$ in which

R^{12} and R^{13} are independently selected from H, halogen, and substituted or unsubstituted alkyl,

or a pharmaceutically acceptable salt, tautomer, solvate or hydrate thereof.

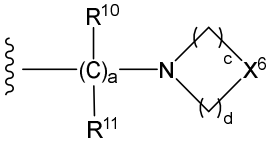
2. The compound according to claim 1, wherein the ring system includes an oxygen and a nitrogen.

3. The compound according to claim 1, wherein R^8 is selected from:



(II)

; and



(III)

wherein

A is a ring system selected from substituted or unsubstituted cycloalkyl and substituted or unsubstituted heterocycloalkyl, wherein one or more carbon atom is substituted with halogen;

R^{10} and R^{11} are independently selected from H, halogen and substituted or unsubstituted C_1-C_6 alkyl;

a is selected from the integers 0 and 1;

c and d are independently selected from the integers 0, 1, 2, 3 and 4 with the proviso that the sum c+d is selected from the integers 3, 4, 5, and 6; and

X^6 is selected from O, NR^{12}, and $CR^{12}R^{13}$

in which

R^{12} and R^{13} are independently selected from H, halogen, and substituted or unsubstituted alkyl.

4. The compound according to claim 3, wherein R^{13} is selected from H and halogen.

5. The compound according to claim 1, wherein X^3 is CR^7.

6. The compound according to claim 3, wherein one of R^{10} or R^{11} is CF_3.

7. The compound according to claim 1 in which R^1 is F.

8. A pharmaceutical formulation comprising the compound the pharmaceutically acceptable salt, tautomer, solvate or hydrate thereof according to claim 1, and a pharmaceutically acceptable carrier.

9. The pharmaceutical formulation of claim 8, formulated for parenteral or oral administration.

10. The pharmaceutical formulation of claim 8, formulated for intravenous, subcutaneous or intraperitoneal injection.

11. Use of the compound, pharmaceutically acceptable salt, tautomer, solvate or hydrate thereof according to claim 1 in the manufacture of a medicament for the treatment of a TYK2-mediated disease in a subject in need thereof, wherein a therapeutically effective amount of the compound, pharmaceutically acceptable salt, tautomer, solvate or hydrate is to be administered to the subject and wherein the TYK2-mediated disease is susceptible to treatment with a TYK2 inhibitor.

12. The use according to claim 11, wherein the compound, salt, tautomer, hydrate or solvate is to be administered to the subject as a pharmaceutically acceptable formulation.

13. The use according to claim 12, wherein the pharmaceutically acceptable formulation is formulated for intravenous, subcutaneous, intrathecal, intracerebral ventricular or intraperitoneal injection.

14. Use of the compound, pharmaceutically acceptable salt, tautomer, solvate or hydrate thereof according to claim 1 in the manufacture of a medicament for the treatment of an autoimmune or inflammatory disease in a subject in need thereof, wherein a therapeutically effective amount of the compound, pharmaceutically acceptable salt, tautomer, solvate or hydrate is to be administered to the subject to inhibit TYK2 kinase in the subject and wherein the autoimmune/autoinflammatory disease is susceptible to treatment with a TYK2 inhibitor.

15. The use according to claim 14, wherein the disease is a member selected from Plaque Psoriasis, Psoriatic Arthritis, Lupus, and Inflammatory Bowel Disease.

16. An *in vitro* method of inhibiting TYK2, the method comprising bringing into contact with the TYK2 an effective TYK2 - inhibiting amount of the compound according to claim 1, tautomer, solvate, hydrate, or a salt thereof.

17. The use according to claim 15, wherein the Inflammatory Bowel Disease is a member selected from Crohn’s, Ulcerative Colitis and a combination thereof.

18. The compound, pharmaceutically acceptable salt, tautomer, solvate or hydrate thereof according to claim 1 for use in therapy.