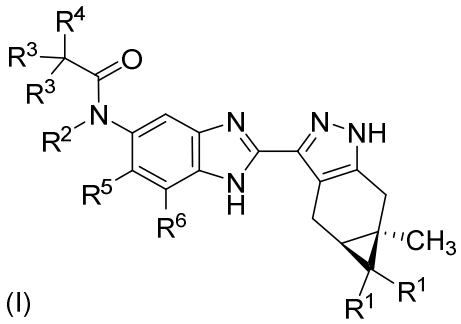
Claims

1. A compound of Formula (I)



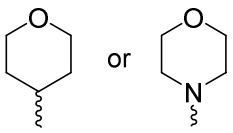
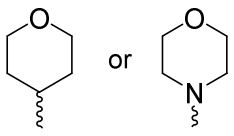
(I)

or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or said pharmaceutically acceptable salt thereof, wherein:

each R^1 is independently H or F;

R^2 is H, (C_1-C_4)alkyl, hydroxy(C_1-C_4)alkyl, (C_1-C_4)alkoxy(C_1-C_4)alkyl or (C_1-C_4)alkyl substituted by one, two or three F;

each R^3 is independently H, F, (C_3-C_5)cycloalkyl, (C_1-C_4)alkyl or (C_1-C_4)alkyl substituted by one, two or three F; or both R^3 taken together with the carbon atom to which they are attached form (C_3-C_5)cycloalkyl;

R^4 is selected from  , wherein each ~~heterocycle~~  is optionally substituted ~~by~~with one or two substituents independently selected from oxo, (C_1-C_4)alkyl, hydroxy(C_1-C_4)alkyl and (C_1-C_4)alkyl substituted by one, two or three F; and

R^5 and R^6 are each independently H; halogen; OH; CN; (C_1-C_6)alkyl; hydroxy(C_1-C_6)alkyl; (C_1-C_4)alkoxy(C_1-C_6)alkyl; (C_1-C_6)alkyl substituted by one, two or three F; (C_1-C_6)alkoxy; or (C_1-C_6)alkoxy substituted by (C_1-C_4)alkoxy.

2. ~~A~~The compound according to claim 1, or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or said pharmaceutically acceptable salt thereof, wherein each R^1 is H.

3. ~~A~~The compound according to claim 1 or claim 2, or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or said pharmaceutically acceptable salt thereof, wherein R^2 is H or (C_1-C_4)alkyl.

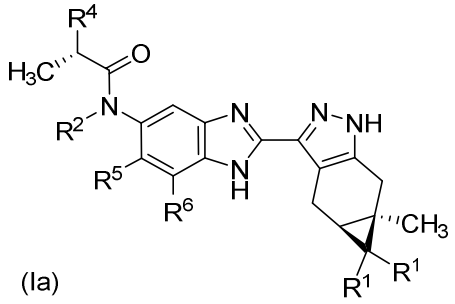
4. ~~A~~The compound according to claim 3, or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or said pharmaceutically acceptable salt thereof, wherein R^2 is methyl.

5. ~~A~~The compound according to any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or said pharmaceutically acceptable salt thereof, wherein each R^3 is independently H, F or (C_1-C_4)alkyl.

6. ~~A~~The compound according to claim 5, or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or said pharmaceutically acceptable salt thereof, wherein each R^3 is independently H, F or methyl.

7. ~~A~~The compound according to claim 6, or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or said pharmaceutically acceptable salt thereof, wherein one R^3 is H and the other R^3 is methyl.

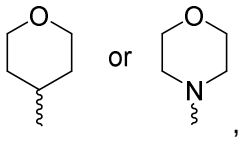
8. ~~A~~The compound according to claim 7 of Formula (Ia)



(Ia)

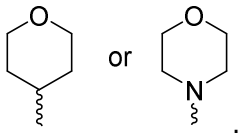
or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or said pharmaceutically acceptable salt thereof.

9. ~~A~~The compound according to any one of claims 1 to 8, or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or said pharmaceutically acceptable salt thereof, wherein R^4 is



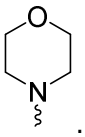
optionally substituted by one or two substituents independently selected from oxo, (C_1-C_4)alkyl and hydroxy(C_1-C_4)alkyl.

10. ~~A~~The compound according to claim 9, or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or said pharmaceutically acceptable salt thereof, wherein R^4 is



.

11. ~~A~~The compound according to claim 10, or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or said pharmaceutically acceptable salt thereof, wherein R^4 is



.

12. ~~A~~The compound according to any one of claims 1 to 11, or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or said pharmaceutically acceptable salt thereof, wherein R^5 and R^6 are each independently H; halogen; OH; CN; (C_1-C_3)alkyl; hydroxy(C_1-C_3)alkyl; (C_1-C_3)alkoxy(C_1-C_3)alkyl; (C_1-C_3)alkyl substituted by one, two or three F; (C_1-C_3)alkoxy; or (C_1-C_3)alkoxy substituted by (C_1-C_3)alkoxy.

13. ~~A~~The compound according to claim 12, or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or said pharmaceutically acceptable salt thereof, wherein R^5 is H, halogen, CN, (C_1-C_3)alkyl, (C_1-C_3)alkoxy or (C_1-C_3)alkoxy substituted by (C_1-C_3)alkoxy.

14. ~~A~~The compound according to claim 12 or claim 13, or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or said pharmaceutically acceptable salt thereof, wherein R^6 is H; halogen; OH; CN; (C_1-C_3)alkyl; hydroxy(C_1-C_3)alkyl; (C_1-C_3)alkoxy(C_1-C_3)alkyl; (C_1-C_3)alkyl substituted by one, two or three F; or (C_1-C_3)alkoxy.

15. ~~A~~The compound according to claim 1, or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or said pharmaceutically acceptable salt thereof, selected from the group consisting of:

(S)-*N*-methyl-*N*-(6-methyl-2-((4aS,5aR)-5a-methyl-1,4,4a,5,5a,6-hexahydrocyclopropa[f]indazol-3-yl)-1*H*-benzo[d]imidazol-5-yl)-2-morpholinopropanamide;

(R)-*N*-methyl-*N*-(2-((4aS,5aR)-5a-methyl-1,4,4a,5,5a,6-hexahydrocyclopropa[f]indazol-3-yl)-1*H*-benzo[d]imidazol-5-yl)-2-(tetrahydro-2*H*-pyran-4-yl)propanamide;

(R)-*N*-(7-fluoro-2-((4aS,5aR)-5a-methyl-1,4,4a,5,5a,6-hexahydrocyclopropa[f]indazol-3-yl)-1*H*-benzo[d]imidazol-5-yl)-*N*-methyl-2-(tetrahydro-2*H*-pyran-4-yl)propanamide;

(S)-*N*-(7-fluoro-2-((4aS,5aR)-5a-methyl-1,4,4a,5,5a,6-hexahydrocyclopropa[f]indazol-3-yl)-1*H*-benzo[d]imidazol-5-yl)-*N*-methyl-2-morpholinopropanamide;

(S)-*N*-ethyl-*N*-(7-fluoro-2-((4aS,5aR)-5a-methyl-1,4,4a,5,5a,6-hexahydrocyclopropa[f]indazol-3-yl)-1*H*-benzo[d]imidazol-5-yl)-2-morpholinopropanamide;

(S)-*N*-(6,7-difluoro-2-((4aS,5aR)-5a-methyl-1,4,4a,5,5a,6-hexahydrocyclopropa[f]indazol-3-yl)-1*H*-benzo[d]imidazol-5-yl)-*N*-methyl-2-morpholinopropanamide;

(S)-*N*-(6.7-difluoro-2-((4aS,5aR)-5a-methyl-1,4,4a,5,5a,6-hexahydrocyclopropa[f]indazol-3-yl)-1*H*-benzo[d]imidazol-5-yl)-*N*-ethyl-2-morpholinopropanamide;

(S)-*N*-(7-fluoro-6-methyl-2-((4a*S*,5a*R*)-5a-methyl-1,4,4a,5,5a,6-hexahydrocyclopropa[*f*]indazol-3-yl)-1*H*-benzo[*d*]imidazol-5-yl)-*N*-methyl-2-morpholinopropanamide; and

(S)-*N*-methyl-*N*-(7-methyl-2-((4a*S*,5a*R*)-5a-methyl-1,4,4a,5,5a,6-hexahydrocyclopropa[*f*]indazol-3-yl)-1*H*-benzo[*d*]imidazol-5-yl)-2-morpholinopropanamide.

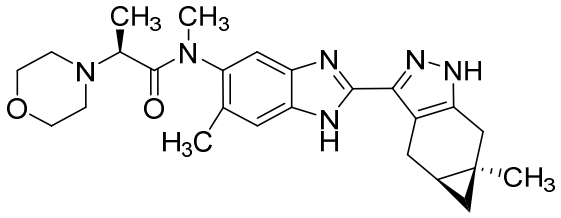
16. The compound according to claim 15 which is (S)-*N*-methyl-*N*-(6-methyl-2-((4aS,5aR)-5a-methyl-1,4,4a,5,5a,6-hexahydrocyclopropa[f]indazol-3-yl)-1*H*-benzo[d]imidazol-5-yl)-2-morpholinopropanamide, or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or said pharmaceutically acceptable salt thereof.

17. The compound according to claim 15 which is (R)-*N*-methyl-*N*-(2-((4aS,5aR)-5a-methyl-1,4,4a,5,5a,6-hexahydrocyclopropa[f]indazol-3-yl)-1*H*-benzo[d]imidazol-5-yl)-2-(tetrahydro-2*H*-pyran-4-yl)propanamide, or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or said pharmaceutically acceptable salt thereof.

18. The compound according to claim 16 which is (S)-*N*-methyl-*N*-(6-methyl-2-((4aS,5aR)-5a-methyl-1,4,4a,5,5a,6-hexahydrocyclopropa[f]indazol-3-yl)-1*H*-benzo[d]imidazol-5-yl)-2-morpholinopropanamide, or a hydrate thereof.

19. The compound according to claim 18 which is (S)-*N*-methyl-*N*-(6-methyl-2-((4aS,5aR)-5a-methyl-1,4,4a,5,5a,6-hexahydrocyclopropa[f]indazol-3-yl)-1*H*-benzo[d]imidazol-5-yl)-2-morpholinopropanamide, dihydrate.

20. The compound according to claim 16 which is



.

21. A pharmaceutical composition comprising a compound according to any one of claims 1 to 20 or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or said pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

22. ~~A~~The pharmaceutical composition according to claim 21 adapted for topical administration.

23. ~~A~~The pharmaceutical composition according to claim 21 or claim 22, further comprising ~~including~~ one or more additional therapeutic agents.

24. ~~A~~The compound according to any one of claims 1 to 20 or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or said pharmaceutically acceptable salt thereof, for use as a medicament.

25. ~~A~~The compound according to any one of claims 1 to 20 or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or said pharmaceutically acceptable salt thereof, for use in the treatment of a disorder for which an ITK inhibitor is indicated.

26. ~~A~~The compound for use according to claim 25 or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or said pharmaceutically acceptable salt thereof, wherein the disorder for which ~~an~~the ITK inhibitor is indicated is a dermatological disorder.

27. ~~A~~The compound for use according to claim 26 or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or said pharmaceutically acceptable salt thereof, wherein the dermatological disorder is dermatitis.

28. ~~A~~The compound for use according to claim 27 or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or said pharmaceutically acceptable salt thereof, wherein the dermatitis is atopic dermatitis.

29. Use of a compound according to any one of claims 1 to 20, or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or said pharmaceutically acceptable salt thereof, ~~for the preparation~~ in the manufacture of a medicament for the treatment of a disorder for which an ITK inhibitor is indicated.

30. Use of a compound according to any one of claims 1-20, or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or said pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of ~~A method of treating a~~ disorder in a human or animal for which an ITK inhibitor is indicated, wherein ~~the use comprising administering to said human or animal a~~ therapeutically effective amount of ~~a~~the compound or the pharmaceutically acceptable salt thereof is to be administered to said human or animal.~~according to any of claims 1 to 20.~~