We claim:

1. A pharmaceutical formulation, comprising:
a) a polyethylene glycol having a freezing point of at least about 30 °C;
b) an active pharmaceutical ingredient that is soluble in molten polyethylene glycol wherein the polyethylene glycol is as defined in a); and
c) a crystallisation rate inhibitor.

2. The pharmaceutical formulation of claim 1, wherein the pharmaceutical formulation is a solid formulation.

3. The pharmaceutical formulation of claim 1 or 2, wherein the polyethylene glycol has a freezing point of from about 35 °C to about 70 °C.

4. The pharmaceutical formulation of any one of claims 1 to 3, wherein the polyethylene glycol has an average molecular weight of at least about 900 g/mol or at least about 1000 g/mol.

5. The pharmaceutical formulation of claim 4, wherein the polyethylene glycol has an average molecular weight of from about 1000 to about 20000 g/mol.

6. The pharmaceutical formulation of any one of claims 1 to 5, wherein the polyethylene glycol is PEG1500, PEG2000, PEG3000, PEG3350 or PEG4000.

7. The pharmaceutical formulation of any one of claims 1 to 6, wherein the crystallisation rate inhibitor is selected from polyvinylpyrrolidone (PVP), a polyvinylpyrrolidone-vinyl acetate copolymer (PVPVA), a poly(meth)acrylate polymer, a cyclodextrin and a derivative thereof, hydroxypropylcellulose, methylcellulose, hydroxypropyl methylcellulose (HPMC), hydroxypropyl methylcellulose acetate succinate (HPMCAS), a poloxamer, and combinations thereof.

8. The pharmaceutical formulation of claim 7, wherein the crystallisation rate inhibitor is selected from polyvinylpyrrolidone (PVP) and a polyvinylpyrrolidone-vinyl acetate copolymer (PVPVA), and a combination thereof.

9. The pharmaceutical formulation of claim 8, wherein the crystallisation rate inhibitor is polyvinylpyrrolidone-vinyl acetate copolymer (PVPVA).

10. The pharmaceutical formulation of claim 9, wherein the PVPVA is a copolymer of 1-vinyl-2-pyrrolidone and vinyl acetate in a ratio of 6:4 by mass (PVPVA64).

11. The pharmaceutical formulation of any one of claims 1 to 10, wherein the formulation comprises from about 1 w/w% to about 15 w/w% of the crystallisation rate inhibitor relative to the total weight of the formulation.

12. The pharmaceutical formulation of claim 11, wherein the formulation comprises about 1 w/w%, about 5 w/w% or about 10 w/w% of the crystallisation rate inhibitor.

13. The pharmaceutical formulation of any one of claims 1 to 12, wherein the formulation further comprises an antioxidant.

14. The pharmaceutical formulation of claim 13, wherein the antioxidant is selected from tocopherol (vitamin E), thiodipropionic acid, lipoic acid, hydroquinone, phytic acid, monothioglycerol, sodium thioglycolate, thioglycol, beta carotene, butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), cysteine, cysteine hydrochloride, propyl gallate (PG), sodium metabisulfite, ascorbyl palmitate, ascorbyl stearate, potassium metabisulfite, disodium EDTA (ethylenediamine tetraacetic acid; also known as disodium edentate), EDTA, erythorbic acid, ethoxyquin, glutathione, gum guaiac, lecithin, propyl gallate, TBHQ (tert butyl hydroxyquinone), tartaric acid, citric acid, citric acid monohydrate, methane sulfonic acid, methionine, sodium metabisulfite, sodium thiosulfate, sodium sulphite, and combinations thereof.

15. The pharmaceutical formulation of claim 14, wherein the antioxidant is selected from tocopherol (vitamin E), lipoic acid, hydroquinone, monothioglycerol, thioglycol, beta

carotene, butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), propyl gallate (PG), ascorbyl palmitate, ascorbyl stearate, ethoxyquin, propyl gallate, TBHQ (tert butyl hydroxyquinone), and combinations thereof.

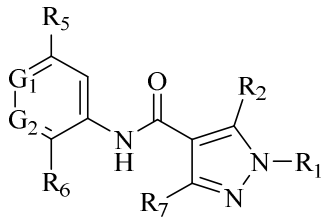
16. The pharmaceutical formulation of claim 15, wherein the antioxidant is all-rac-alpha tocopherol.

17. The pharmaceutical formulation of any one of claims 1 to 16, wherein the formulation comprises from about 0.1 w/w% to about 40 w/w%, from about 1 w/w% to about 30 w/w%, or from about 5 w/w% to about 25 w/w% of the active pharmaceutical ingredient relative to the total weight of the formulation.

18. The pharmaceutical formulation of claim 17, wherein the formulation comprises from about 20 w/w% to about 25 w/w% of the active pharmaceutical ingredient relative to the total weight of the formulation.

19. The pharmaceutical formulation of any one of claims 1 to 18, wherein the active pharmaceutical ingredient is a MALT1 inhibitor.

20. The pharmaceutical formulation of any one of claims 1 to 19, wherein the active pharmaceutical ingredient is a compound of Formula (I)



Formula (I)

wherein

R_1 is selected from the group consisting of

i) naphthalen-1-yl, optionally substituted with a fluoro or amino substituent; and

ii) a heteroaryl of nine to ten members containing one to four heteroatoms selected from the group consisting of O, N, and S; such that no more than one heteroatom is O or S; wherein said heteroaryl of ii) is optionally

independently substituted with one or two substituents selected from deuterium, methyl, ethyl, propyl, isopropyl, trifluoromethyl, cyclopropyl, methoxymethyl, difluoromethyl, 1,1-difluoroethyl, hydroxymethyl, 1-hydroxyethyl, 1-ethoxyethyl, hydroxy, methoxy, ethoxy, fluoro, chloro, bromo, methylthio, cyano, amino, methylamino, dimethylamino, 4-oxotetrahydrofuran-2-yl, 5-oxopyrrolidin-2-yl, 1,4-dioxanyl, aminocarbonyl, methylcarbonyl, methylaminocarbonyl, oxo, 1-(t-butoxycarbonyl)azetidin-2-yl, *N*-(methyl)formamidomethyl, tetrahydrofuran-2-yl, 3-hydroxy-pyrrolidin-1-yl, pyrrolidin-2-yl, 3-hydroxyazetidinyl, azetidin-3-yl, or azetidin-2-yl;

R_2 is selected from the group consisting of C_{1-4}alkyl, 1-methoxy-ethyl, difluoromethyl, fluoro, chloro, bromo, cyano, and trifluoromethyl;

G_1 is N or C(R_4);

G_2 is N or C(R_3); such that only one of G_1 and G_2 are N in any instance;

R_3 is independently selected from the group consisting of trifluoromethyl, cyano, C_{1-4}alkyl, fluoro, chloro, bromo, methylcarbonyl, methylthio, methylsulfinyl, and methanesulfonyl; or, when G_1 is N, R_3 is further selected from C_{1-4}alkoxycarbonyl;

R_4 is selected from the group consisting of

i) hydrogen, when G_2 is N;

ii) C_{1-4}alkoxy;

iii) cyano;

iv) cyclopropyloxy;

v) a heteroaryl selected from the group consisting of triazolyl, oxazolyl, isoxazolyl, pyrazolyl, pyrrolyl, thiazolyl, tetrazolyl, oxadiazolyl, imidazolyl, 2-amino-pyrimidin-4-yl, 2H-[1,2,3]triazolo[4,5-c]pyridin-2-yl, 2H-[1,2,3]triazolo[4,5-b]pyridin-2-yl, 3H-[1,2,3]triazolo[4,5-b]pyridin-3-yl, *1H*-[1,2,3]triazolo[4,5-c]pyridin-1-yl, wherein the heteroaryl is optionally substituted with one or two substituents independently selected from oxo, C_{1-4}alkyl, carboxy, methoxycarbonyl, aminocarbonyl, hydroxymethyl, aminomethyl, (dimethylamino)methyl, amino, methoxymethyl, trifluoromethyl, amino(C_{2-4}alkyl)amino, or cyano;

vi) 1-methyl-piperidin-4-yloxy;

vii) 4-methyl-piperazin-1-ylcarbonyl;

viii) (4-aminobutyl)aminocarbonyl;

ix) (4-amino)butoxy;

x) 4-(4-aminobutyl)-piperazin-1-ylcarbonyl;

xi) methoxycarbonyl;

xii) 5-chloro-6-(methoxycarbonyl)pyridin-3-ylaminocarbonyl;

xiii) 1,1-dioxo-isothiazolidin-2-yl;

xiv) 3-methyl-2-oxo-2,3-dihydro-*1H*-imidazol-1-yl;

xv) 2-oxopyrrolidin-1-yl;

xvi) (*E*)- (4-aminobut-1-en-1-yl-aminocarbonyl;

xvii) difluoromethoxy;

and

xviii) morpholin-4-ylcarbonyl;

R_5 is independently selected from the group consisting of hydrogen, chloro, fluoro, bromo, methoxy, methylsulfonyl, cyano, C_{1-4}alkyl, ethynyl, morpholin-4-yl, trifluoromethyl, hydroxyethyl, methylcarbonyl, methylsulfinyl, 3-hydroxy-pyrrolidin-1-yl, pyrrolidin-2-yl, 3-hydroxyazetidinyl, azetidin-3-yl, azetidin-2-yl, methylthio, and 1,1-difluoroethyl;

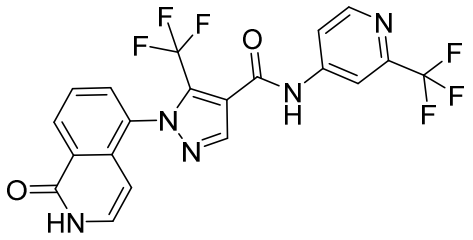
or R_4 and R_5 may be taken together to form 8-chloro-4-methyl-3-oxo-3,4-dihydro-*2H*-benzo[*b*][1,4]oxazin-6-yl, 8-chloro-3-oxo-3,4-dihydro-*2H*-benzo[*b*][1,4]oxazin-6-yl, 2-methyl-1-oxo-1,2,3,4-tetrahydroisoquinolin-7-yl, 4-methyl-3-oxo-3,4-dihydro-2H-benzo[b][1,4]oxazin-6-yl, 3-oxo-3,4-dihydro-2H-benzo[b][1,4]oxazin-6-yl, 1-methyl-*1H*-pyrazolo[3,4-b]pyridin-5-yl, *1H*-pyrazolo[3,4-b]pyridin-5-yl, 2,3-dihydro-[1,4]dioxino[2,3-b]pyridin-5-yl, 1,3-dioxolo[4,5]pyridine-5-yl, 1-oxo-1,3-dihydroisobenzofuran-5-yl, 2,2-dimethylbenzo[d][1,3]dioxol-5-yl, 2,3-dihydrobenzo[b][1,4]dioxin-6-yl, 1-oxoisoindolin-5-yl, or 2-methyl-1-oxoisoindolin-5-yl, 1*H*-indazol-5-yl;

R_6 is hydrogen, C_{1-4}alkyl, fluoro, 2-methoxy-ethoxy, chloro, cyano, or trifluoromethyl; and

R_7 is hydrogen or fluoro;

or an enantiomer, diastereomer, solvate, or pharmaceutically acceptable salt form thereof.

21. The pharmaceutical formulation according to claim 20, wherein the compound of Formula (I) is 1-(1-oxo-1,2-dihydroisoquinolin-5-yl)-5-(trifluoromethyl)-*N*-(2-(trifluoromethyl)pyridin-4-yl)-1*H*-pyrazole-4-carboxamide:



or a solvate or pharmaceutically acceptable salt thereof.

22. A solid dosage form comprising the pharmaceutical formulation of any one of claims 1 to 21.

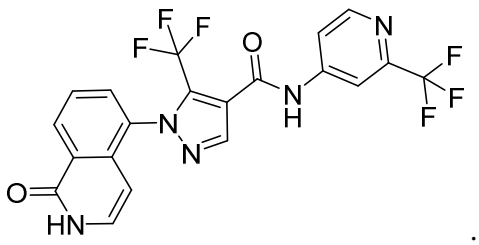
23. The solid dosage form of claim 22, wherein the dosage form is an oral dosage form.

24. The solid dosage form of claim 22 or 23, wherein the dosage form comprises a capsule encapsulating the pharmaceutical formulation.

25. The solid dosage form of claim 24, wherein the capsule is a hard gelatin capsule.

26. The solid dosage form of any one of claims 22 to 25, wherein the formulation comprises about 2 to about 1000 mg of the active pharmaceutical ingredient.

27. The solid dosage form of claim 26, wherein the formulation comprises 2, 10, 50 or 200 mg of 1-(1-oxo-1,2-dihydroisoquinolin-5-yl)-5-(trifluoromethyl)-*N*-(2-(trifluoromethyl)pyridin-4-yl)-1*H*-pyrazole-4-carboxamide:



.

28. The use of a pharmaceutical formulation of any one of claims 19 to 21 for the preparation of a medicament for treating a disease, syndrome, disorder or condition in a subject in need thereof, wherein said disease, syndrome, condition, or disorder is affected by the inhibition of MALT1.

29. The use of a pharmaceutical formulation of claim 28 wherein said disease, syndrome, condition, or disorder is selected from cancer and immunological diseases.

30. A pharmaceutical formulation of any one of claims 19 to 21 for use in the treatment of a disease, syndrome, disorder or condition in a subject in need thereof, wherein said disease, syndrome, condition, or disorder is affected by the inhibition of MALT1.

31. The pharmaceutical formulation for use of claim 30 wherein said disease, syndrome, condition, or disorder is selected from cancer and immunological diseases.

32. A process for preparing a pharmaceutical formulation according to any one of claims 1 to 21, comprising the steps of:

a) forming a melt comprising polyethylene glycol having a freezing point of at least about 30 °C, an active pharmaceutical ingredient, and a crystallisation rate inhibitor, wherein the forming a melt step comprises heating polyethylene glycol to a temperature above its freezing point; and

b) cooling the melt below the freezing point of the polyethylene glycol;

to provide a pharmaceutical formulation according to any one of claims 1 to 21.

33. A process for preparing a solid dosage form according to claim 24, the process comprising the steps of:

a) forming a melt comprising polyethylene glycol having a freezing point of at least about 30 °C, an active pharmaceutical ingredient, and a crystallisation rate inhibitor, wherein the forming a melt step comprises heating polyethylene glycol to a temperature above its freezing point;

b) filling a hard capsule with the melt; and

c) cooling the filled capsule below the freezing point of the polyethylene glycol;

to provide a solid dosage form according to claim 24.

34. The process of claim 32 or 33, wherein the polyethylene glycol is heated to a temperature of at least about 5 °C above its freezing point.

35. The process of claim 32 or 33, wherein the polyethylene glycol is heated to a temperature of at least about 10 °C above its freezing point.

36. The process of any one of claims 32-35, wherein the API used as starting material in step b) of the process is a crystalline form of Compound A monohydrate producing an X-ray powder diffraction pattern comprising peaks at 16.4, 23.7 and 25.7 degrees two theta ± 0.2 degrees two theta.

37. A solid dosage form comprising

a) a polyethylene glycol having a freezing point of at least about 30 °C; and

b) an active pharmaceutical ingredient that is soluble in molten polyethylene glycol wherein the polyethylene glycol is as defined in a);

wherein the solid dosage form is a capsule acting as crystallisation rate inhibitor, e.g. a HPMC capsule.