Pharmaceutical Compositions

TECHNICAL FIELD

[001] The present disclosure relates to crystal forms of pharmaceutical compounds, formulations including, methods of forming, and methods of using these crystal forms.

SUMMARY

[002] Described herein are new crystal forms of pharmaceutical compounds. In one embodiment, the pharmaceutical compounds are included in a pharmaceutical composition useful for treating a disease or condition. In one embodiment, the disease or condition is cancer.

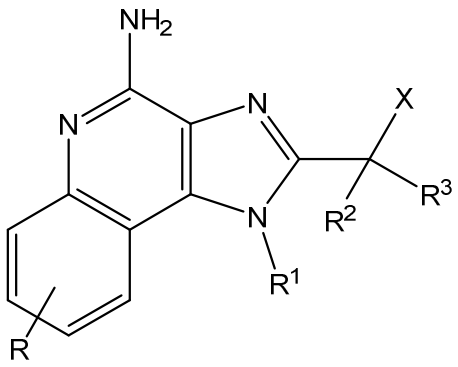
[003] In some embodiments, pharmaceutical compositions are described including resiquimod in the form of a sulfate salt in crystal form A. The sulfate salt can be a monosulfate salt and/or an anhydrate. This crystal form can be prepared in an appropriate dosage from.

[003a] In one aspect, there is provided a dosage form comprising the composition described herein.

[004] In one embodiment, the sulfate salt in crystal form A is characterized by x-ray powder diffraction spectrum that comprises peaks at about 7 to about 8 degrees 2θ, about 13.5 to about 14.5 degrees 2θ, about 18 to about 19 degrees 2θ, and/or about 15 to about 16 degrees 2θ.

[005] The sulfate salt in crystal form A can be stable at room temperature for at least about 2 days or at least about 1 week.

[006] Other embodiments describe pharmaceutical compositions comprising a crystal form of a compound of Formula I:

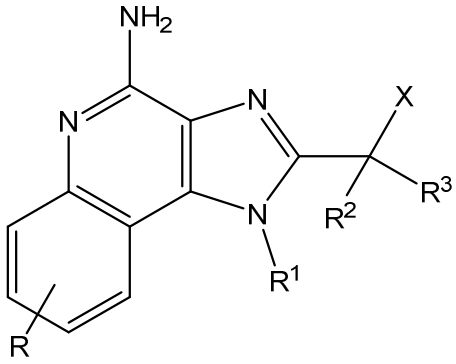


(I).

[007] Formula I can be a compound having a formula 4-amino-α-butyl-1-(2-methylpropyl)-1H-imidazo-[4,5-c]-quinoline-2-methanol hemihydrate, 4-amino-α,α-dimethyl-2-ethoxymethyl-1H-imidazo-[4,5-c]-quinoline-1-ethanol, 2-ethoxymethyl-1-(2-methylpropyl)-1H-imidazo-[4,5-c]-quinolin-4-amine, or 4-amino-1-phenylmethyl-1H-imidazo-[4,5-c]-quinoline-2-methanol. In one embodiment, Formula I is resiquimod.

[008] In some embodiments, the crystal form of a compound of Formula I can be in form A and/or be a sulfate salt. In one embodiment, a sulfate salt is a monosulfate salt and/or an anhydrate.

[009] Other embodiments provide methods of treating diseases or conditions. In one embodiment, methods of treating cancer are described. The methods can comprise: administering a pharmaceutical composition including a crystal form of a compound having a Formula I:



(I).

[009a] In another aspect, there is provided a use of a composition including a crystal form of a compound as described herein in the preparation of a medicament for the treatment of cancer in a subject in need thereof.

[009b] In yet another aspect, there is provided a use of a composition including a crystal form of a compound as described herein in the preparation of a medicament for the treatment of a tumor in a subject in need thereof.

BRIEF DESCRIPTION OF THE DRAWINGS

[0010] FIG. 1 illustrates XRPD patterns of mono-HCl salt crystal form Type A batches.

[0011] FIG. 2 illustrates a PLM image of mono-HCl salt crystal form Type A (807919-16-A).

[0012] FIG. 3 illustrates TGA/DSC curves of mono-HCl salt crystal form Type A (807919-16-A).

[0013] FIG. 4 illustrates an XRPD pattern of di-HCl salt crystal form Type A (807919-14-A).

[0014] FIG. 5 illustrates a PLM image of di-HCl salt crystal form Type A (807919-14-A).

We claim:

1. A composition comprising resiquimod in the form of a sulfate salt in crystal form A.

2. The composition of claim 1, wherein the sulfate salt is a monosulfate salt.

3. The composition of claim 1, wherein the sulfate salt is an anhydrate.

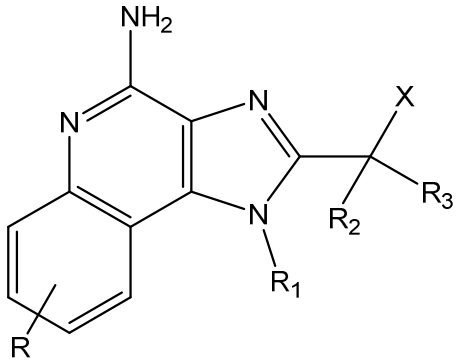
4. The composition of claim 1, wherein crystal form A is characterized by x-ray powder diffraction spectrum that comprises peaks at about 7 to about 8 degrees 2θ, about 13.5 to about 14.5 degrees 2θ, about 19 to about 20 degrees 2θ, and about 19.5 to about 20.5 degrees 2θ.

5. The composition of claim 1, wherein the crystal form A is stable at room temperature at least about 2 days.

6. The composition of claim 1, wherein the crystal form A is stable at room temperature at least about 1 week.

7. A dosage form comprising the composition of claim 1.

8. A composition comprising a crystal form of a compound of Formula I:



(I),

wherein R^1 is hydrogen; C_1-C_{10} straight chain or branched chain substituted or unsubstituted alkyl, wherein the substituent is C_3-C_6 cycloalkyl or C_3-C_6 cycloalkyl substituted by straight chain or branched chain C_1-C_4 alkyl; straight chain or branched chain C_2-C_{10} alkenyl; or substituted straight chain or branched chain C_2-C_{10} alkenyl, wherein the substituent is C_3-C_6 cycloalkyl or C_3-C_6 cycloalkyl substituted by straight chain or branched chain C_1-C_4 alkyl; C_1-C_6 hydroxyalkyl; alkoxyalkyl wherein the alkoxy moiety contains one to

about four carbon atoms and the alkyl moiety contains one to about six carbon atoms; acyloxyalkyl wherein the acyloxy moiety is alkanoyloxy of two to about four carbon atoms or benzoyloxy, and the alkyl moiety contains one to about six carbon atoms; benzyl; (phenyl)ethyl; or phenyl; the benzyl, (phenyl)ethyl, or phenyl substituent being optionally substituted on the benzene ring by one or two moieties independently selected from C_1-C_4 alkyl, C_1-C_4 alkoxy, or halogen, with the proviso that if the benzene ring is substituted by two moieties, then the moieties together contain no more than six carbon atoms;

R^2 and R^3 are independently selected from hydrogen, C_1-C_4 alkyl, phenyl, or substituted phenyl, wherein the substituent is C_1-C_4 alkyl, C_1-C_4 alkoxy, or halogen;

X is C_1-C_4 alkoxy, alkoxyalkyl wherein the alkoxy moiety contains one to about four carbon atoms and the alkyl moiety contains one to about four carbon atoms, C_1-C_4 hydroxyalkyl, C_1-C_4 haloalkyl, alkylamido wherein the alkyl group contains one to about four carbon atoms, amino, substituted amino wherein the substituent is C_1-C_4 alkyl or C_1-C_4 hydroxyalkyl, azide, chloro, hydroxy, 1-morpholino, 1-pyrrolidino, or C_1-C_4 alkylthio; and

R is hydrogen, straight chain or branched chain C_1-C_4 alkoxy, halogen, or straight chain or branched chain C_1-C_4 alkyl; and

wherein the crystal form is a hydrochloric acid salt, a sulfate salt, a phosphate salt, a maleate salt, a malate salt, an adipate salt, a glycolate salt, a hippurate salt, a tartrate salt, a fumarate salt, a citrate salt, a lactate salt, a succinate salt, a tosylate salt, mesylate salt, an oxalate salt, a gentisate salt, a benzoate salt, or a nitrate salt in crystalline form A, B, C, D, E, F or G.

9. The composition of claim 8, wherein R_1 is 2-methylpropyl or benzyl.

10. The composition of claim 8, wherein X is azido, hydroxy, ethoxy, methoxy, 1-morpholino, or methylthio.

11. The composition of claim 8, wherein R is hydrogen.

12. The composition of claim 8, wherein the compound is 4-amino-a-butyl-1-(2-methylpropyl)-1H-imidazo-[4,5-c]-quinoline-2-methanol hemihydrate, 4-amino-α, α-dimethyl-2-ethoxymethyl-1H-imidazo-[4,5-c]-quinoline-1-ethanol, 2-ethoxymethyl-1-(2-methylpropyl)-1H-imidazo-[4,5-c]-quinolin-4-amine, or 4-amino-1-phenylmethyl-1H-imidazo-[4,5-c]-quinoline-2-methanol.

13. The composition of claim 8, wherein the compound is resiquimod.

14. The composition of claim 8, wherein the crystal form is form A.

15. The composition of claim 8, wherein the crystal form is in a sulfate salt.

16. The composition of claim 15, wherein the sulfate salt is a monosulfate salt.

17. The pharmaceutical composition of claim 15, wherein the sulfate salt is an anhydrate.

18. Use of a composition including a crystal form of a compound having a Formula of claim 8 in the preparation of a medicament for the treatment of cancer in a subject in need thereof.

19. Use of a composition including a crystal form of a compound having a Formula of claim 8 in the preparation of a medicament for the treatment of a tumor in a subject in need thereof.

20. The use of claim 19, wherein the tumor is a carcinoma, a sarcoma, or a blastoma.