PHARMACEUTICAL FORMULATIONS

CROSS-REFERENCE

[0001] This application claims benefit of U.S. Provisional Application No. 62/423,124, filed on November 16, 2016, and U.S. Provisional Application No. 62/545,857, filed on August 15, 2017, which are herein incorporated by reference in their entirety.

BACKGROUND OF THE INVENTION

[0002] Monoacylglycerol lipase (MAGL) is an enzyme responsible for hydrolyzing endocannabinoids such as 2-AG (2-arachidonoylglycerol), an arachidonate based lipid, in the nervous system. 1,1,1,3,3,3-Hexafluoropropan-2-yl 4-(2-(pyrrolidin-1-yl)-4-(trifluoromethyl)benzyl)piperazine-1-carboxylate is a MAGL inhibitor.

SUMMARY

[0003] Provided herein are pharmaceutical formulations in solid dosage form comprising 1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-(pyrrolidin-1-yl)-4-(trifluoromethyl)benzyl)piperazine-1-carboxylate, or a pharmaceutically acceptable salt thereof. In one example, described herein is a pharmaceutical formulation in a solid dosage form comprising:

(a) about 1 mg to about 60 mg of 1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-(pyrrolidin-1-yl)-4-(trifluoromethyl)benzyl)piperazine-1-carboxylate, or a pharmaceutically acceptable salt thereof;

(b) about 5 mg to about 425 mg of a polymeric carrier;

(c) about 0.2 mg to about 10 mg of a surfactant; and

(d) 0.2 mg to about 10 mg of a glidant.

[0003a] In one aspect, provided herein is a pharmaceutical formulation in a solid dosage form comprising:

(a) 1 mg to 60 mg of crystalline 1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-(pyrrolidin-1-yl)-4-(trifluoromethyl)benzyl)piperazine-1-carboxylate, or a pharmaceutically acceptable salt thereof;

(b) 50 mg to 175 mg of microcrystalline cellulose;

(c) 6 mg to 15 mg of croscarmellose sodium; and

(d) 0.5 mg to 2.5 mg of magnesium stearate

[0004] In some examples, the pharmaceutical formulation comprises about 10 mg to about 150 mg of the polymeric carrier. In some examples, the pharmaceutical formulation comprises about 14 mg to about 85 mg of the polymeric carrier. In some

CLAIMS

What is claimed is:

1. A pharmaceutical formulation in a solid dosage form comprising:
   (a) 1 mg to 60 mg of crystalline 1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-(pyrrolidin-1-yl)-4-(trifluoromethyl)benzyl)piperazine-1-carboxylate, or a pharmaceutically acceptable salt thereof;
   (b) 50 mg to 175 mg of microcrystalline cellulose;
   (c) 6 mg to 15 mg of croscarmellose sodium; and
   (d) 0.5 mg to 2.5 mg of magnesium stearate.

2. The pharmaceutical formulation according to claim 1, wherein the 1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-(pyrrolidin-1-yl)-4-(trifluoromethyl)benzyl)piperazine-1-carboxylate is a hydrochloride salt.

3. The pharmaceutical formulation in a solid dosage form according to claim 1 comprising:
   (a) 2.1 mg of crystalline 1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-(pyrrolidin-1-yl)-4-(trifluoromethyl)benzyl)piperazine-1-carboxylate hydrochloride salt;
   (b) 156 mg of microcrystalline cellulose;
   (c) 10 mg of croscarmellose sodium; and
   (d) 1.7 mg of magnesium stearate.
4. The pharmaceutical formulation in a solid dosage form according to claim 1 comprising:
   (a) 10.7 mg of crystalline 1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-(pyrrolidin-1-yl)-4-(trifluoromethyl)benzyl)piperazine-1-carboxylate hydrochloride salt;
   (b) 147 mg of microcrystalline cellulose;
   (c) 10.2 mg of croscarmellose sodium; and
   (d) 1.7 mg of magnesium stearate.
5. The pharmaceutical formulation in a solid dosage form according to claim 1 comprising:
   (a) 53.6 mg of crystalline 1,1,1,3,3,3-hexafluoropropan-2-yl 4-(2-(pyrrolidin-1-yl)-4-(trifluoromethyl)benzyl)piperazine-1-carboxylate hydrochloride salt;
   (b) 104 mg of microcrystalline cellulose;
   (c) 10 mg of croscarmellose sodium; and
   (d) 1.7 mg of magnesium stearate.

6. The pharmaceutical formulation of any one of claims 1-5, wherein the solid dosage form is a tablet.

7. The pharmaceutical formulation of any one of claims 1-5, wherein the solid dosage form is a capsule.