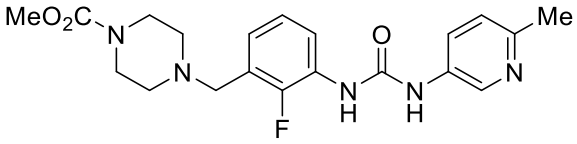
[0005] U.S. Patent No. 7,507,735, herein incorporated by reference, discloses a genus of compounds, including omecamtiv mecarbil (AMG 423, CK-1827452), having the structure:



[0006] Omecamtiv mecarbil is a first in class direct activator of cardiac myosin, the motor protein that causes cardiac contraction. It is being evaluated as a potential treatment of heart failure in both intravenous and oral formulations with the goal of establishing a new continuum of care for patients in both the in-hospital and outpatient settings.

[0007] Clinical trials providing an I.V. delivery of omecamtiv mecarbil have shown that plasma levels of the drug can be delivered safely and effectively. However, standard release formulations and some extended release formulations gave peak to trough ratios that may be too great to provide a safe and effective amount of omecamtiv mecarbil to patients who need the drug in a chronic or preventative setting (See, Figure 4). Accordingly, an effective sustained release formulation would be desirable for increased patient safety and effectiveness.

SUMMARY

[0007a] In one aspect, the present disclosure refers to a dihydrochloride monohydrate salt of omecamtiv mecarbil.

[0007b] In another aspect, the present disclosure refers to a pharmaceutical formulation comprising the salt as disclosed herein and a pharmaceutically acceptable excipient.

[0007c] In another aspect, the present disclosure refers to a use of the pharmaceutical formulation as disclosed herein in the manufacture of a medicament for the treatment of heart failure.

[0008] Provided is a pharmaceutical formulation comprising:

omecamtiv mecarbil, or a pharmaceutically acceptable salt, a pharmaceutically acceptable hydrate, or a pharmaceutically acceptable hydrate of a pharmaceutically acceptable salt thereof;

a control release agent;

a pH modifying agent; a filler; and

a lubricant.

What is Claimed:

1. A dihydrochloride monohydrate salt of omecamtiv mecarbil.

2. The salt of claim 1, wherein the salt is crystalline.

3. The salt of claim 1 or 2, wherein the salt is characterized by an X-ray powder diffraction pattern comprising peaks at about 6.6, 14.9, 20.1, 21.4, and 26.8 ± 0.2° 2θ using Cu Kα radiation.

4. The salt of claim 3, wherein the X-ray powder diffraction pattern further comprises peaks at about 8.4, 24.2, 26.0, and 33.3± 0.2° 2θ using Cu Kα radiation.

5. The salt of claim 3 or 4, wherein the X-ray powder diffraction pattern further comprises peaks at about 6.2, 9.7, 13.2, 14.3, 15.4, 16.3, 16.9, 18.9, 19.5, 20.7, 21.8, 22.8, 23.6, 25.1, 27.3, 27.7, 28.4, 29.4, 30.2, 31.2, 31.5, 31.9, 33.9, 34.5, 34.9, 36.1, 36.8, 37.7, 38.5, and 39.7± 0.2° 2θ using Cu Kα radiation.

6. The salt of any one of claims 1 to 5, having an X-ray powder diffraction pattern substantially as shown in Figure 7.

7. A pharmaceutical formulation comprising the salt of any one of claims 1-6 and a pharmaceutically acceptable excipient.

8. Use of the pharmaceutical formulation of claim 7 in the manufacture of a medicament for the treatment of heart failure.