hepatitis, autoimmune disease, heredity, or metabolism, or can be idiopathic. Liver damage is generally irreversible, and treatment consists of prevention of progression and treatment of symptoms. In severe cases, liver transplant is the only option. Hepatic impairment can exhibit no significant symptoms, or may be characterized by such symptoms as reduced ability for the blood to clot (coagulopathy) and brain dysfunction (encephalopathy), fluid retention in the abdominal cavity, increased infection risk, hypogonadism, change in liver size, jaundice, and increased sensitivity to medication.

[0007] The changes in systemic drug exposures, as quantified by pharmacokinetic parameters such as AUC, C_{max}, and $t_{1/2}$ of a drug and/or its metabolites, in patients with hepatic impairment can lead to many problems, including need for adjusting dose, need for liver function tests, complications for physicians in prescribing due to lack of availability of suitable doses and/or lack of availability of certain medications to those with hepatic impairment, and unintended overdosing.

[0008] There is a significant, unmet need for methods for administering a SST2 agonist, such as paltusotine, or a pharmaceutically acceptable salt thereof, to a patient in need thereof, wherein the patient has hepatic impairment. The present disclosure fulfills these and other needs, evident in reference to the following disclosure.

BRIEF SUMMARY

[0009] Provided is a method of administering paltusotine, or a pharmaceutically acceptable salt thereof, to a patient, wherein the patient has hepatic impairment.

[0009a] In one aspect, the present disclosure provides a use of paltusotine, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treatment of hepatic impairment in a patient in need thereof.

[0010] Also provided is method of administering a therapeutically effective amount of paltusotine, or a pharmaceutically acceptable salt thereof, to a patient, wherein the patient has hepatic impairment, and wherein the therapeutically effective amount of paltusotine, or a pharmaceutically acceptable salt thereof, is the same amount that would be administered to a patient who does not have hepatic impairment.

[0010a] In another aspect, the present disclosure provides a use of paltusotine, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treatment of hepatic impairment in a patient in need thereof, wherein a therapeutically effective amount of

[0011] paltusotine, or a pharmaceutically acceptable salt thereof, is the same amount that would be administered to a patient who does not have hepatic impairment.Also provided is a method of administering to a patient a therapeutically effective amount of paltusotine, or a pharmaceutically acceptable salt thereof; subsequently determining that the patient has hepatic impairment; and administering the same therapeutically effective amount of paltusotine, or a pharmaceutically acceptable salt thereof, to the patient.

[0011a] In yet another aspect, the present disclosure provides a use of paltusotine, or a pharmaceutically effective salt thereof in the manufacture of a medicament for treatment of hepatic impairment, wherein the same therapeutically effective amount of paltusotine, or a pharmaceutically acceptable salt thereof is to be administered before, and after determination that the patient has hepatic impairment.

[0012] Also provided is a pharmaceutical composition for use in treating a patient with paltusotine, wherein the patient has hepatic impairment, wherein the composition includes paltusotine, or a pharmaceutically acceptable salt thereof.

[0012a] In a further aspect, there is provided a use of a pharmaceutical composition comprising a therapeutically effective amount of paltusotine, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating acromegaly, carcinoid syndrome and/or neuroendocrine tumors (NETs), wherein the patient has hepatic impairment.

[0013] Also provided is a pharmaceutical composition for use in treating a patient with paltusotine, wherein the patient has hepatic impairment, wherein the composition includes a therapeutically effective amount of paltusotine, or a pharmaceutically acceptable salt thereof, wherein the composition includes the same amount of paltusotine, or a pharmaceutically acceptable salt thereof, for use in treating a patient with paltusotine who does not have hepatic impairment.

[0013a] In another aspect, there is provided a use of a pharmaceutical composition comprising a therapeutically effective amount of paltusotine, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a patient with acromegaly, carcinoid syndrome and/or neuroendocrine tumors (NETs), wherein the patient has hepatic impairment, and wherein the composition comprises the same amount of paltusotine, or a pharmaceutically acceptable salt thereof, for use in treating a patient who does not have hepatic impairment.

[0014] Also included is a use of paltusotine, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a patient with hepatic impairment.

[0014a] In yet another aspect, there is provided a use of paltusotine, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a patient with acromegaly, carcinoid syndrome and/or neuroendocrine tumors (NETs), wherein the patient has hepatic impairment.

[0015] Also included is paltusotine, or a pharmaceutically acceptable salt thereof, for use in a method of treating a patient, said method comprises administering a therapeutically effective amount of paltusotine, or a pharmaceutically acceptable salt thereof, to the patient; subsequently determining that the patient has hepatic impairment; and administering the same therapeutically effective amount of paltusotine, or a pharmaceutically acceptable salt thereof, to the patient.

[0015a] In a further aspect, the present disclosure provides a use of paltusotine, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating acromegaly, carcinoid syndrome and/or neuroendocrine tumors (NETs) in a patient, wherein the same therapeutically effective amount of paltusotine is to be administered to the patient before, and after determination that the patient has hepatic impairment.

BRIEF DESCRIPTION OF THE DRAWINGS

[0016] FIG. 1 depicts paltusotine metabolites detected in human excreta after administration of [^{14}C]paltusotine.

[0017] FIG. 2 depicts a summary of % recovery of paltusotine and excretory metabolites in humans following oral administration of a single dose of [^{14}C]paltusotine.

[0018] FIG. 3A-FIG. 3D depict the mean plasma concentrations of paltusotine versus time of patients; FIG. 3A depicts the mean plasma concentration of paltusotine versus time of patients with mild hepatic impairment; FIG. 3B depicts the mean plasma concentration of paltusotine versus time of patients with moderate hepatic impairment; Fig. 3C depicts the mean plasma concentration of paltusotine versus time of patients with severe hepatic impairment; and Fig. 3D depicts the mean plasma concentration of paltusotine versus time of patients without hepatic impairment (i.e. normal patients).

[0019] FIG. 4 depicts the mean plasma concentrations of paltusotine versus time semi-log of patients; (A) depicts the mean plasma concentration of paltusotine versus time semi-log of patients with mild hepatic impairment; (B) depicts the mean plasma concentration of

CLAIMS

What is claimed is:

1. Use of paltusotine, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treatment of hepatic impairment in a patient in need thereof.

2. Use of paltusotine, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treatment of hepatic impairment in a patient in need thereof, wherein a therapeutically effective amount of paltusotine, or a pharmaceutically acceptable salt thereof, is the same amount that would be administered to a patient who does not have hepatic impairment.

3. Use of paltusotine, or a pharmaceutically effective salt thereof in the manufacture of a medicament for treatment of hepatic impairment, wherein the same therapeutically effective amount of paltusotine, or a pharmaceutically acceptable salt thereof is to be administered before, and after determination that the patient has hepatic impairment.

4. The use of any one of claims 1-3, wherein the patient has mild, moderate, or severe hepatic impairment.

5. The use of claim 4, wherein the patient has mild hepatic impairment.

6. The use of claim 4, wherein the patient has moderate hepatic impairment.

7. The use of claim 4, wherein the patient has severe hepatic impairment.

8. The use of any one of claims 1-4, wherein the patient has a Child-Pugh Score of 5-6, 7-9, or 10-15.

9. The use of claim 8, wherein the patient has a Child-Pugh Score of 5-6.

10. The use of claim 8, wherein the patient has a Child-Pugh Score of 7-9.

11. The use of claim 8, wherein the patient has a Child-Pugh Score of 10-15.

12. The use of any one of claims 1-11, wherein the patient has acromegaly, carcinoid syndrome and/or neuroendocrine tumors (NETs).

13. The use of any one of claims 1-12, wherein the patient has acromegaly.

14. The use of claim 13, wherein the paltusotine, or a pharmaceutically acceptable salt thereof, is to be administered in an amount equivalent to about 40 mg of paltusotine free base.

15. The use of claim 13, wherein the paltusotine, or a pharmaceutically acceptable salt thereof, is to be administered in an amount equivalent to about 60 mg of paltusotine free base.

16. The use of any one of claims 1-15, wherein the paltusotine, or a pharmaceutically acceptable salt thereof, is to be administered to the patient to treat acromegaly.

17. The use of any one of claims 1-12, wherein the patient has carcinoid syndrome and/or NETs.

18. The use of claim 17, wherein the paltusotine, or a pharmaceutically acceptable salt thereof, is to be administered in an amount equivalent to about 40 mg of paltusotine free base.

19. The use of claim 17, wherein the paltusotine, or a pharmaceutically acceptable salt thereof, is to be administered in an amount equivalent to about 80 mg of paltusotine free base.

20. The use of claim 17, wherein the paltusotine, or a pharmaceutically acceptable salt thereof, is to be administered in an amount equivalent to about 120 mg of paltusotine free base.

21. The use of any one of claims 1-12 and 17-20, wherein the paltusotine, or a pharmaceutically acceptable salt thereof, is to be administered to the patient to treat carcinoid syndrome and/or NETs.

22. The use of any one of claims 1-21, wherein the paltusotine, or a pharmaceutically acceptable salt thereof, is to be administered daily.

23. The use of any one of claims 1-22, wherein the paltusotine, or a pharmaceutically acceptable salt thereof, is to be administered once daily.

24. The use of any one of claims 1-23, wherein the paltusotine, or a pharmaceutically acceptable salt thereof, is to be administered orally.

25. The use of any one of claims 1-24, wherein the paltusotine, or a pharmaceutically acceptable salt thereof, is to be administered in one or more oral dosage forms.

26. The use of claim 25, wherein the oral dosage form is a tablet.

27. The use of any of one claims 1-25, wherein the paltusotine, or a pharmaceutically acceptable salt thereof, is a hydrochloride salt of paltusotine.

28. The use of claim 27, wherein the hydrochloride salt of paltusotine is amorphous.

29. The use of any one of claims 1-28, wherein the patient with hepatic impairment has equivalent exposure of paltusotine free base as in a patient with normal hepatic function who is administered the same amount of paltusotine, or a pharmaceutically acceptable salt thereof.

30. Use of a pharmaceutical composition comprising a therapeutically effective amount of paltusotine, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating acromegaly, carcinoid syndrome and/or neuroendocrine tumors (NETs), wherein the patient has hepatic impairment.

31. Use of a pharmaceutical composition comprising a therapeutically effective amount of paltusotine, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a patient with acromegaly, carcinoid syndrome and/or neuroendocrine tumors (NETs), wherein the patient has hepatic impairment, and wherein the composition comprises the same amount of paltusotine, or a pharmaceutically acceptable salt thereof, for use in treating a patient who does not have hepatic impairment.

32. Use of paltusotine, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a patient with acromegaly, carcinoid syndrome and/or neuroendocrine tumors (NETs), wherein the patient has hepatic impairment.

33. Use of paltusotine, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating acromegaly, carcinoid syndrome and/or neuroendocrine tumors (NETs) in a patient, wherein the same therapeutically effective amount of paltusotine is to be administered to the patient before, and after determination that the patient has hepatic impairment.