DEUTERATED DOMPERIDONE FOR TREATING GASTROPARESIS

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Patent Application Nos. 63/333,042, filed April 20, 2022, and 63/333,034, filed April 20, 2022, the disclosures of which are incorporated by reference herein.

TECHNICAL FIELD

[0002] The disclosure relates to methods for increasing gastric emptying in a human having gastroparesis.

BACKGROUND

[0003] Gastroparesis is defined as impaired gastric emptying in the absence of physical gastric outlet obstruction. Symptoms include early satiety, postprandial fullness, nausea, vomiting, and abdominal pain. Gastroparesis affects the patient's nutritional state, especially in diabetics, and severe symptoms of gastroparesis can lead to other complications such as malnutrition, esophagitis, and Mallory-Weiss tears. Gastroparesis negatively impacts a patient's quality of life, causing decreased social interaction, poor work functionality, and development of anxiety or depression.

[0004] The first-line treatment for gastroparesis involves nutritional management and support, including fluid and electrolyte replacement. Currently, metoclopramide, a dopamine D_2 receptor antagonist, is the only United States Food and Drug Administration-approved agent for the treatment of gastroparesis. Unfortunately, this agent readily crosses the blood-brain barrier resulting in central nervous system (CNS) side effects in up to 40% of patients.

[0005] Safe and effective treatments for gastroparesis are needed.

SUMMARY

[0006] In some aspects, the disclosure provides methods for increasing gastric emptying in a human having gastroparesis, comprising orally administering 5 mg to 120 mg of deudomperidone daily to the human.

[0006a] In one aspect, there is provided a use of deudomperidone in the preparation of a medicament for increasing gastric emptying in a human having gastroparesis, wherein the deudomperidone is to be orally administered at a daily amount of 10 mg to 120 mg.

What is claimed:

1. Use of deudomperidone in the preparation of a medicament for increasing gastric emptying in a human having gastroparesis, wherein the deudomperidone is to be orally administered at a daily amount of 10 mg to 120 mg.

2. The use of claim 1, wherein the gastroparesis is idiopathic gastroparesis or diabetic gastroparesis.

3. The use of claim 1 or 2, wherein the human is experiencing an upper gastrointestinal symptom prior to the administration.

4. The use of claim 3, wherein the upper gastrointestinal symptom is postprandial nausea, postprandial vomiting, postprandial fullness, early satiety, bloating, epigastric pain, abdominal pain, or combinations thereof, or wherein the upper gastrointestinal symptom is nausea, vomiting, postprandial fullness, early satiety, bloating, epigastric pain, abdominal pain, or combinations thereof.

5. The use of any one of the preceding claims, wherein the increase in gastric emptying is measured by the gastric emptying breath test (GEBT) about 12 to about 14 days after administering the deudomperidone, as measured by a gastric emptying breath test (GEBT) using ^{13}C-spirulina platensis.

6. The use of any one of the preceding claims, wherein the human has a delayed gastric emptying about 10 days prior to a first dose of deudomperidone, as measured by a gastric emptying breath test (GEBT) using ^{13}C-spirulina platensis.

7. The use of any one of the preceding claims, wherein, prior to administering the deudomperidone, the human has a T½ greater than about 80 minutes, or such as greater than about 200 minutes, as measured by a gastric emptying breath test (GEBT) using ^{13}C-spirulina platensis.

8. The use of any one of the preceding claims, wherein, prior to administering the deudomperidone, the human has an American Neurogastroenterology and Motility Society Gastroparesis Cardinal Symptom Index Daily Diary (ANMS GCSI-DD) average composite score of about 2 or greater and/ or a ANMS GCSI-DD nausea subscale score of about 2 or greater for at least about 4 days.

9. The use of any one of the preceding claims, wherein about 10 mg, or about 20 mg, or about or about 30 mg, or about 60 mg, or about 120 mg of deudomperidone is to be administered to the human.

10. The use of any one of the preceding claims, wherein the deudomperidone is to be administered in divided doses, such as two doses.

11. The use of any one of the preceding claims, wherein the human is an adult.

12. The use of any one of the preceding claims, wherein administration results in a clinically significant improvement in
(i) nausea, early satiety, postprandial fullness, upper abdominal pain, vomiting, and bloating as measured by an ANMS GCSI-DD score after the treatment, and/ or
(ii) an average composite score of the ANMS GCSI-DD score after the treatment; and/ or
(iii) a nausea subscale score of the ANMS GCSI-DD score after the treatment; and/ or
(iv) gastric emptying as measured by GEBT after about 12 to about 16 days after the treatment; and/ or
(v) gastric emptying as measured by ANMS GCSI-DD total scores after the treatment; and/ or
(vi) gastric emptying as measured by ANMS GCSI-DD subscale scores after the treatment.

13. The use of any one of the preceding claims, wherein the human has diabetic neuropathy.

14. The use of any one of the preceding claims, wherein, prior to administration of the deudomperidone, the human has a T½ greater than about 110 minutes.

15. The use of any one of the preceding claims, wherein, prior to administration of the deudomperidone, the human has a T½ less than about 110 minutes.

16. The use of any one of the preceding claims, wherein the deudomperidone administration does not cause a clinically significant QT prolongation; and/ or

the administration does not result in a clinically significant change in the heart rate of the patient; and/ or the cardiac conduction of the patient.

17. The use of any one of the preceding claims, wherein the pulse rate (PR) interval of the patient is about 0.12 to about 0.2 seconds after administration of the deudomperidone; and/ or the QRS interval of the patient is about 0.08 and 0.10 seconds after administration of the deudomperidone.

18. The use of any one of the preceding claims, wherein the administration results in a ΔΔQTcF that is less than about 10 ms.

19. The use of claim 18, wherein the amount of deudomperidone is about 30 mg and the administration results in a ΔΔQTcF of about 1.1 ms or less; or the amount of deudomperidone is about 100 mg and the administration results in a ΔΔQTcF of about 3.5 ms or less.