

the disease has been confirmed in one child, the sibling can be diagnosed with NPC by genetic testing before the onset of any visible signs or symptoms.

[008] At the terminal stage, patients are bedridden with complete ophthalmoplegia and loss of volitional movements caused by severe encephalopathy with uncontrolled seizures. At this stage, therapy consist primarily of palliative care.

[009] While Miglustat is authorized in the European Union (EU) for the treatment of progressive neurological manifestations in patients with NPC, at present there are no cure or disease-modifying therapies for NPC. Consequently there is a high unmet medical need for new treatment options (Geberhiwot et al. 2018). Given the progressive, debilitating, life limiting, and fatal nature of the NPC disease (i.e., high morbidity), there is an urgent need for treatments that delay disease progression, as patients continuing to have progressive neurodegeneration with fatal outcome. In a recent paper over an observation period of 50 years, 338 deaths caused by NPC with a mean age of 13 years were described and it was concluded that there was no significant change in survival over the last 20 years (Bianconi et al. 2019).

[010] Since at present there are no cure or disease-modifying therapies for NPC, and consequently there is a high unmet medical need for new treatment options (Geberhiwot et al. 2018). Given the progressive, debilitating, life limiting, and fatal nature of the NPC disease (i.e., high morbidity), there is an urgent need for treatments that delay disease progression, such as the present disclosure monotherapy treatment of arimoclomol citrate or in combination therapy with miglustat. There is also a present need to provide improved delivery and administration of arimoclomol medicaments, to enhance patient compliance with such administration, especially with patients aged 2 years or less.

BRIEF SUMMARY

[010a] In one aspect, there is provided the use of a sufficient amount of a pharmaceutical composition or formulation of arimoclomol or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating Niemann Pick disease, type C (NPC), in a human patient in need thereof,

wherein the composition or formulation of arimoclomol is to be provided in a capsular dosage form; and

wherein the sufficient amount of the pharmaceutical composition or formulation of arimoclomol, or the pharmaceutically acceptable salt thereof, is selected from the group consisting of 31 mg, 47mg, 62mg, 93mg, and 124mg of arimoclomol (base form);

the capsular dosage form is to be opened and the pharmaceutical composition or formulation of arimoclomol or the pharmaceutically acceptable salt thereof is to be dispersed in at least one liquid or at least one solid medium to form at least one dispersion; wherein the liquid medium is at least one member selected from the group consisting of water and apple juice;

wherein the solid medium is at least one soft food; and

the dispersion is to be administered to the patient within a twenty-four period of time after the pharmaceutical composition or formulation, or the pharmaceutically acceptable salt thereof, is dispersed or suspended within the at least one liquid or solid medium.

[011] The present disclosure further relates to one or more methods of treating NPC in a human patient, comprising a pharmaceutical composition or formulation of arimoclomol citrate or a pharmaceutically acceptable salt thereof, either in monotherapy or in combination treatment therapy with miglustat. The present disclosure additionally relates to methods of treating NPC in a human patient via

dispersion or suspension of a pharmaceutical composition comprising a formulation of arimoclomol, specifically arimoclomol citrate, in at least one liquid or at least one solid medium prior to administration to the patient. The present disclosure further relates to the biomarkers and metabolites of arimoclomol.

[012] MIPLYFFA®, a arimoclomol citrate formulation, is indicated for the treatment of Niemann-Pick disease type C (NPC) in patients aged 2 years and older, in combination with miglustat and as monotherapy in patients not suitable for therapy with miglustat.

[013] In at least one example of the disclosure, this disclosure provides a method of treating Niemann Pick disease, type C (NPC), in a human patient in need thereof, the method comprising the steps of: providing to the patient a sufficient amount of a pharmaceutical composition or formulation of arimoclomol or a pharmaceutically acceptable salt thereof; wherein the composition or formulation of arimoclomol is provided in a capsular dosage form; and wherein the sufficient amount of the pharmaceutical composition or formulation of arimoclomol, or the pharmaceutically acceptable salt thereof, is selected from the group consisting of 31 mg, 47mg, 62mg, 93mg, and 124mg of arimoclomol (base form); opening the capsular dosage form and dispersing the pharmaceutical composition or formulation of arimoclomol or the pharmaceutically acceptable salt thereof in at least one liquid or at least one solid medium to form at least one dispersion; wherein the liquid medium is at least one member selected from the group consisting of water and apple juice; wherein the solid medium is selected from the group consisting of at least one soft food; and administering the dispersion to the patient within a twenty-four period of time after the pharmaceutical composition or formulation, or the pharmaceutically acceptable salt thereof, is dispersed within the at least one liquid or solid medium.

BRIEF DESCRIPTION OF SEVERAL VIEWS OF THE DRAWINGS

[014] FIG. 1 are chemical drawings that show the metabolization of arimoclomol.

[015] FIG. 2 is Table 41, entitled Comparison of test data obtained from vessel 1-6 vs. vessel 7-12.

Claims

1. Use of a sufficient amount of a pharmaceutical composition or formulation of arimoclomol or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating Niemann Pick disease, type C (NPC), in a human patient in need thereof,

wherein the composition or formulation of arimoclomol is to be provided in a capsular dosage form; and

wherein the sufficient amount of the pharmaceutical composition or formulation of arimoclomol, or the pharmaceutically acceptable salt thereof, is selected from the group consisting of 31 mg, 47mg, 62mg, 93mg, and 124mg of arimoclomol (base form);

the capsular dosage form is to be opened and the pharmaceutical composition or formulation of arimoclomol or the pharmaceutically acceptable salt thereof is to be dispersed in at least one liquid or at least one solid medium to form at least one dispersion; wherein the liquid medium is at least one member selected from the group consisting of water and apple juice;

wherein the solid medium is at least one soft food; and

the dispersion is to be administered to the patient within a twenty-four period of time after the pharmaceutical composition or formulation, or the pharmaceutically acceptable salt thereof, is dispersed or suspended within the at least one liquid or solid medium.

2. The use of claim 1, wherein the medicament is to be administered orally, via a nasogastric tube, via a gastric tube, or via a non-gastric feeding tube.

3. The use of claim 1, wherein the pharmaceutically acceptable salt of arimoclomol is arimoclomol citrate.

4. The use of any of claims 1-3, wherein the patient is under the age of two years.

5. The use of claim 1, wherein the soft food is applesauce.
6. The use of claim 1, the liquid medium is apple juice.
7. The use according to either claims 1 or 2, wherein the liquid medium is water;
and
wherein the dispersion is to be administered to the patient via at least one gastric or non-gastric feeding tube.
8. The use according to any one of claims 1-7, wherein the Niemann Pick disease, type C is either sub-type NPC1 or sub-type NPC2.
9. The use according to any of claim 1-8, further comprising a sufficient amount of miglustat to be administered to the patient.
10. The use according to any one of claims 1-8, wherein the treatment is a monotherapy with arimoclomol, or pharmaceutically acceptable salt thereof.
11. The use according to any one of claims 1-10, where in the pharmaceutical composition or formulation of arimoclomol, or a pharmaceutically acceptable salt thereof, is metabolized by the patient into at least one metabolite of arimoclomol.
12. The use of claim 11, wherein the at least one metabolite is a member selected from the group consisting of M1, M2, M3, M4, M5, M7, M39, M104, M105 and M 107.
13. The use of claim 12, wherein the metabolite is M2, M5, or M105.
14. The use of claim 1, wherein at least 80% of the pharmaceutical composition or formulation of the arimoclomol, or the pharmaceutically acceptable salt thereof, is to be dissolved in the liquid medium within 15 minutes following dispersion.

15. The use of claim 3, wherein at least 80% the arimoclomol citrate is to be dissolved in the liquid medium within 15 minutes following dispersion.

16. The use according to either claims 14 or 15, wherein the liquid medium has a pH range of about 1.2 to about 6.8.

17. The use of claim 16, wherein the liquid medium has a pH range of about 1.2 to about 4.5.