ensifentrine and lactose. WO 2014/140647 A1 describes a dry powder composition comprising an ensifentrine/beta-adrenergic receptor antagonist combination and a blended lactose comprising at least 15 % of lactose particles having a mass median diameter (MMD) of less than 15 µm.

There is a need to develop a dry powder formulation which delivers ensifentrine effectively. It is also desirable to prepare a dry powder formulation which is capable of delivering a wide range of different ensifentrine doses.

SUMMARY ~~OF THE INVENTION~~

It is a surprising finding of the present ~~invention~~ disclosure that a dry powder composition comprising ensifentrine and a specific blend of lactose comprising a low proportion of fine lactose with a specific particle size, delivers an improved fine particle fraction. This composition provides an improved way in which to administer ensifentrine by inhalation.

In an aspect of the present disclosure, there is provided a dry powder pharmaceutical composition suitable for administration by inhalation comprising:

(i) ensifentrine particles;

(ii) coarse lactose particles having a Dv50 of from 40 µm to 80 µm ; and

(iii) fine lactose particles having a Dv50 of from 5 µm to 10 µm,

wherein:

the fine lactose particles are present in an amount of from 0.1 wt% to 6.0 wt% relative to the total weight of the dry powder pharmaceutical composition.

In another aspect of the present disclosure, there is provided a dry powder inhaler comprising a dry powder pharmaceutical composition disclosed herein.

In a further aspect of the present disclosure, there is provided a dry powder pharmaceutical composition disclosed herein for use in therapy.

In another aspect of the present disclosure, there is provided a use of a dry powder pharmaceutical composition disclosed herein in the manufacture of a medicament for the treatment or prevention of a disease or condition selected from asthma, allergic asthma, hay fever, allergic rhinitis, bronchitis, emphysema, bronchiectasis, chronic

obstructive pulmonary disease (COPD), adult respiratory distress syndrome (ARDS), steroid resistant asthma, severe asthma, paediatric asthma, cystic fibrosis, lung fibrosis, pulmonary fibrosis, interstitial lung disease, skin disorders, atopic dermatitis, psoriasis, ocular inflammation, cerebral ischaemia, inflammatory diseases and auto-immune disease.

In a further aspect of the present disclosure, there is provided a use of a dry powder pharmaceutical composition disclosed herein in the manufacture of a medicament for treating a disease or condition disclosed herein, wherein a dry powder inhaler comprising the dry powder pharmaceutical composition is to be inhaled, wherein the fine particle fraction of the ensifentrine particles following inhalation is at least 20%.

The present disclosure ~~invention~~ provides a dry powder pharmaceutical composition suitable for administration by inhalation comprising: (i) ensifentrine particles; (ii) coarse lactose particles having a Dv50 of from 40 µm to 80 µm; and (iii) fine lactose particles having a Dv50 of from 5 µm to 10 µm, wherein the fine lactose particles are present in an amount of from 0.1 wt% to 6.0 wt% relative to the total weight to the dry powder pharmaceutical composition.

The present disclosure ~~invention~~ also provides a dry powder inhaler comprising a dry powder pharmaceutical composition according to the present disclosure~~invention~~.

Further provided by the present disclosure ~~invention~~ is a dry powder pharmaceutical composition according to the present disclosure ~~invention~~ for use in the treatment of the human or animal body.

DETAILED DESCRIPTION OF THE INVENTION

The dry powder pharmaceutical composition comprises the fine lactose particles in an amount of from 0.1 wt% to 6.0 wt% relative to the total weight to the dry powder pharmaceutical composition. Typically, the amount of the fine lactose particles is from 0.5 wt% to 5.0 wt% or from 1.0 wt% to 5.0 wt% relative to the total weight of the dry powder pharmaceutical composition. The amount of fine lactose may be from

CLAIMS

1. A dry powder pharmaceutical composition suitable for administration by inhalation comprising:

(i) ensifentrine particles;

(ii) coarse lactose particles having a Dv50 of from ~~50~~40 µm to ~~70~~80 µm ~~as measured by laser diffraction using a dry powder dispersion system~~; and

(iii) fine lactose particles having a Dv50 of from 5 µm to 10 µm ~~as measured by laser diffraction using a dry powder dispersion system~~,

wherein:

the fine lactose particles are present in an amount of from ~~2.0~~0.1 wt% to ~~4.5~~6.0 wt% relative to the total weight of the dry powder pharmaceutical composition~~; and~~

~~the ensifentrine particles are present in an amount of from 0.2 wt% to 6.0 wt% relative to the total weight of the dry powder pharmaceutical composition~~.

2. A dry powder pharmaceutical composition according to claim 1, wherein the amount of fine lactose particles is from ~~0~~3.5 wt% to ~~5~~4.0 wt% relative to the total weight of the dry powder pharmaceutical composition, preferably from 3.5 wt% to 4.0 wt%.

3. A dry powder pharmaceutical composition according to claim 1 or 2, wherein the coarse lactose particles are present in an amount of from 80.0 wt% to 99.0 wt % relative to the total weight of the dry powder pharmaceutical composition~~.~~

~~4. A dry powder pharmaceutical composition according to claim 3, wherein the coarse lactose particles are present in an amount of~~, preferably from 90.0 wt% to 96.0 wt%.

4. A dry powder pharmaceutical composition according to any one of the preceding claims, wherein the coarse lactose particles have a Dv50 of from 50 µm to 70 µm, preferably from 55 µm to 65 µm.

5. A dry powder pharmaceutical composition according to any one of the preceding claims, wherein the ensifentrine particles are present in an amount of from 0.1 wt% to 10 wt% relative to the total weight of the dry powder pharmaceutical composition, preferably from 0.2 wt% to 6.0 wt%.

~~5~~6. A dry powder pharmaceutical composition according to any one of the preceding claims, wherein the ensifentrine particles comprise at least 90 wt% ensifentrine or a pharmaceutically acceptable salt thereof relative to the total weight of the ensifentrine particles~~.~~

~~6. A dry powder pharmaceutical composition according to claim 5, wherein the ensifentrine particles comprise~~, preferably at least 95.0 wt%~~ relative to the total weight of the ensifentrine particles~~.

7. A dry powder pharmaceutical composition according to any one of the preceding claims, wherein the ensifentrine particles have a Dv50 of from 0.5 µm to 5.0 µm~~ as measured by laser diffraction using a wet powder dispersion system~~, preferably from 1.0 µm to 2.0 µm.

8. A dry powder pharmaceutical composition according to any one of the preceding claims, wherein the total amount of the ensifentrine particles, the coarse lactose particles and the fine lactose particles is at least 90.0 wt% relative to the total weight of the dry powder pharmaceutical composition, preferably at least 95.0 wt%.

9. A dry powder pharmaceutical composition according to any one of the preceding claims, which dry powder pharmaceutical composition is suitable for administration by a dry powder inhaler.

10. A dry powder inhaler comprising a dry powder pharmaceutical composition according to any one of the preceding claims.

11. A dry powder pharmaceutical composition according to any one of claims 1 to 9 for use in therapy~~ the treatment of the human or animal body~~.

12. ~~A~~Use of a dry powder pharmaceutical composition ~~according to~~ as defined in any one of claims 1 to 9 in the manufacture of a medicament for ~~use in~~ the treatment or prevention of a disease or condition selected from asthma, allergic asthma, hay fever, allergic rhinitis, bronchitis, emphysema, bronchiectasis, chronic obstructive pulmonary disease (COPD), adult respiratory distress syndrome (ARDS), steroid resistant asthma, severe asthma, paediatric asthma, cystic fibrosis, lung fibrosis, pulmonary fibrosis, interstitial lung disease, skin disorders, atopic dermatitis, psoriasis, ocular inflammation, cerebral ischaemia, inflammatory diseases and auto-immune disease.

13. ~~A dry powder pharmaceutical composition for~~ The use according to claim 12 wherein the disease or condition is chronic obstructive pulmonary disease (COPD).

14. ~~A~~Use of a dry powder pharmaceutical composition ~~according to~~as defined in any one of claims 1 to 9 in the manufacture of a medicament for ~~use in a method of~~ treating a disease or condition as defined in claim 12 or claim 13, ~~which method comprises inhalation of~~ wherein a dry powder inhaler comprising the dry powder pharmaceutical composition is to be inhaled,

wherein the fine particle fraction of the ensifentrine particles following inhalation is at least 20%.

15. ~~A dry powder pharmaceutical composition for~~ The use according to claim 14, wherein the fine particle fraction of the ensifentrine particles following inhalation is at least 30%, preferably at least 35%.

~~16. A method of treating or preventing a disease or condition as defined in claim 12 or claim 13 in a subject, which method comprises administering to said subject an effective amount of a dry powder pharmaceutical composition according to any one of claims 1 to 9.~~