

CLAIMS

1. An inhalable fixed dose dry powder composition comprising:
 - (a) 5 µg to about 50 µg of glycopyrronium bromide,
 - (b) 5 µg to 25 µg of formoterol fumarate dihydrate,
 - (c) 50 µg to about 500 µg of fluticasone propionate, and
 - (d) a pharmaceutically acceptable carrier consisting of: (i) about 0.1 to about 10 % w/w of fine particles of lactose having a particle size D₉₀ less than about 50 µm; and (ii) about 90 to 99.9 % w/w of coarse particles of lactose having a particle size D₉₀ more than about 150 µm;

wherein the weight ratio of fine lactose particles to coarse lactose particles ranges from about 1:100 to about 1:7 and wherein the composition is free from a hydrophobic excipient.
2. The dry powder composition according to claim 1, wherein the composition is free from a hydrophobic excipient selected from magnesium stearate, calcium stearate, amino acids, fatty acid, peptides and phospholipids.
3. The dry powder composition according to either one of claims 1 or 2, wherein the pharmaceutically acceptable carrier is an admixture of (i) fine lactose particles having a particle size D₅₀ less than about 30µm and (ii) coarse lactose particles having a particle size D₅₀ more than 80 µm.
4. The dry powder composition according to any one of claims 1-3, where the composition is filled into a capsule or into a blister for use in a dry powder inhaler.
5. The dry powder composition according to claim 4, wherein the dry powder inhaler is selected from a single dose capsule inhaler device and a multiple dose capsule inhaler device.
6. The dry powder composition according to claim 5, wherein the composition is filled into a capsule for use in the single dose capsule inhaler device.

7. The dry powder composition according to any one of claims 1-6, wherein the composition has D_{50} values of less than 120 μm or less than 100 μm .

8. The dry powder composition according to any one of claims 1-6, wherein the composition has D_{90} values of about 120 μm to about 200 μm or about 150 μm to about 180 μm .

9. The dry powder composition according to any one of claims 1-6, wherein the composition has fine particle mass having particle size less than about 50 μm in the range of about 5% to about 30% and/or coarse particle mass having particle size more than 80 μm in the range of about 20% to about 90% w/w.

10. The dry powder composition according to claim 6, wherein the capsule comprises gelatin or HPMC having a reduced moisture content less than 15% w/w or less than 10% w/w.

11. The dry powder composition according to any one of claims 1-6, wherein the composition has a bulk density in the range of about 0.3 g/ml to about 1 g/ml and/or a tapped density in the range of about 0.5 g/ml to about 1.25 g/ml.

12. The composition according to any one of claims 4-11, wherein the inhaler is capable of delivering 12.5 μg or 25 μg of glycopyrronium, 12 μg of formoterol fumarate dihydrate and 250 μg of fluticasone propionate upon each actuation.

13. The dry powder composition according to claim 6, wherein the single dose inhaler device comprises a single medicament chamber for holding the capsule, a rotatable mouthpiece and a piercing means for perforating the said capsule, contained in said capsule.

14. A process for preparing an inhalable fixed dose dry powder composition according to claim 1, the process comprising:

(i) mixing glycopyrronium bromide, formoterol fumarate dihydrate and fluticasone propionate with fine particles of lactose having an average particle size less than about 30 μm ;

(ii) blending the mixture obtained in step (i) with coarse lactose having average particle size of about more than 80 μm ; and

(iii) filling the blend of step (ii) in a capsule or a blister.

15. The process according to claim 14, wherein about 1% w/w to about 10% w/w of the fine lactose particles have a D_{90} particle size less than about 50 μm and about 90% to about 99% w/w of the coarse lactose particles have a D_{90} particle size more than about 150 μm .

16. The process according to either one of claims 14 or 15, wherein the process does not include any step of co-micronization.

17. The process according to any one of claims 14-16, where the glycopyrronium bromide, formoterol fumarate dihydrate and fluticasone propionate are in micronized form having D_{50} value of each drug not more than 5 μm or not more than 4 μm and/or D_{90} of each drug not more than 10 μm or not more than 6 μm .

18. An inhalable fixed dose dry powder composition comprising:

(a) glycopyrronium bromide,

(b) formoterol fumarate,

(c) fluticasone propionate, and

(d) an admixture of fine lactose monohydrate particles and coarse lactose monohydrate, wherein

(i) the ratio of (a) glycopyrronium or its salt, (b) formoterol or its salt, and (c) fluticasone propionate ranges from 0.8-2.5:1:15-25,

(ii) the fine lactose particles have a D_{50} of from about 2 μm to about 20 μm and/or a D_{90} from about 4 μm to about 50 μm ,

(iii) the coarse lactose particles have a D_{50} of from about 80 μm to about 130 μm and/or a D_{90} from about 150 μm to about 200 μm , and

(iv) the composition is free or substantially free of hydrophobic excipients and/or propellants.

19. The composition of claim 18, wherein the composition is encapsulated in a capsule, wherein (i) the capsule comprises hydroxypropyl methylcellulose and (ii) the composition, when tested for aerodynamic particle size distribution, results in a fine particle mass for (a) glycopyrronium bromide of from about 2 µg to about 5 µg, (b) formoterol fumarate of from about 2 µg to about 5 µg, and (c) fluticasone propionate of from about 45 µg to about 70 µg.

20. The composition of claim 18 or 19, wherein the fine lactose particles have a D₅₀ of from about 2 µm to about 10 µm and/or a D₉₀ of from about 5 µm to about 20 µm.

21. The composition of any one of claims 18-20, wherein the fine lactose particles have a D₅₀ of no more than 5 µm and/or a D₉₀ of no more than 10 µm.

22. The composition of any one of claims 18-21, wherein the coarse lactose particles have a D₅₀ of from about 95 µm to about 125 µm and/or a D₉₀ from about 160 µm to about 190 µm.

23. The composition of any one of claims 18-22, wherein the weight ratio of fine lactose particles to coarse lactose particles ranges from about 1:100 to about 1:7.

24. The composition of claim 23, wherein the weight ratio of fine lactose particles to coarse lactose particles ranges from about 1:15 to about 1:40.

25. The composition of claim 1 or 18, wherein the composition is administered for the treatment of respiratory disease at least once or at least twice daily.

26. The composition according to claim 25, wherein the respiratory disease is COPD and /or asthma.