CLAIMS

1. A dry powder formulation for use in a dry powder inhaler (DPI) to deliver by inhalation a combination of micronized particles of an anticholinergic, an inhaled corticosteroid (ICS), and a long-acting β_2-agonist (LABA) as active ingredients in a combined therapeutically effective dose of 100 to 500 μg, comprising:

(a) a fraction of fine particles, comprising a mixture, prepared by co-mixing 90 to 99.5 percent by weight of micronized particles of a physiologically acceptable excipient and 0.5 to 10 percent by weight of magnesium stearate, wherein at least 90% of all said particles have a volume diameter lower than 15 microns and the volume median diameter of said particles is from 3 to 7 microns;

(b) a fraction of coarse particles comprising a physiologically acceptable excipient having a mass median diameter equal to or higher than 175 microns, wherein the ratio between said fine particles (a) and said coarse particles (b) is from 1:99 to 30:70 percent by weight;

(c) micronized particles of an anticholinergic, micronized particles of an inhaled corticosteroid (ICS), and micronized particles of a long-acting β_2-agonist (LABA) as active ingredients, wherein at least 90% of the active ingredient micronized particles have a volume diameter lower than 6.0 μm, wherein, upon actuation of said inhaler, at least 35% of the micronized particles of each of the active ingredients have a diameter equal to or less than 2 μm, and wherein the width of the particle size distribution of said micronized particles of active ingredients, expressed as a span, is from 1.2 to 3.0; and

wherein the active ingredients, upon administration to the respiratory tract by a dry powder inhaler, are capable of reaching the distal tract of the respiratory tree.

2. The dry powder formulation according to claim 1, wherein at least 90% of all said fine particles have a volume diameter lower than 12 microns, and the volume median diameter of said fine particles is from 4 to 6 microns.

3. The dry powder formulation according to claim 1, wherein said LABA is

formoterol fumarate dihydrate, said ICS is beclometasone dipropionate, and said anticholinergic is glycopyrronium bromide.

4. The dry powder formulation according to claim 1, wherein the volume median diameter of the micronized particles of all the active ingredients is from 1.2 to 2.5 microns; and no more than 10% of all said micronized particles have a diameter lower than 0.6 microns.

5. The dry powder formulation according to claim 1, wherein at least 90% of all said micronized particles of said active ingredients (c) have a volume diameter equal to or lower than 5.0 microns, and the volume median diameter of said particles is from 1.3 to 2.2 microns.

6. The dry powder formulation according to claim 1, wherein said magnesium stearate coats the surface of said fine particles (a) in such a way that the extent of the surface coating is at least of 10%.

7. The dry powder formulation according to claim 1, wherein said co-mixing is carried out in a high energy apparatus for a period of less than 20 minutes.

8. The dry powder formulation according to claim 1, wherein the excipient of said fine particles comprises lactose.

9. The dry powder formulation according to claim 1, wherein the excipient of said coarse particles (b) comprises lactose.

10. The dry powder formulation according to claim 1, wherein the excipient of said fine particles (a) comprises lactose, and the excipient of said coarse particles (b) comprises lactose.

11. The dry powder formulation according to claim 7, wherein said high energy apparatus is a mechano-fusion apparatus.

12. The dry powder formulation according to claim 1, wherein said magnesium stearate coats the surface of said fine particles (a) in such a way that the extent of the surface coating is at least of 50%.

13. A dry powder inhaler device, containing a dry powder formulation according to claim 1.

14. A process for preparing a dry powder formulation for use in a dry powder inhaler (DPI) to deliver by inhalation a combination of micronized particles of an anticholinergic, an inhaled corticosteroid (ICS), and a long-acting β_2-agonist (LABA) as active ingredients in a combined therapeutically effective dose of 100 to 500 μg, comprising:

(a) providing a fraction of fine particles, comprising a mixture, prepared by co-mixing 90 to 99.5 percent by weight of micronized particles of a physiologically acceptable excipient and 0.5 to 10 percent by weight of magnesium stearate, wherein at least 90% of all said particles have a volume diameter lower than 15 microns and the volume median diameter of said particles is from 3 to 7 microns;

(b) providing a fraction of coarse particles comprising a physiologically acceptable excipient having a mass median diameter equal to or higher than 175 microns, wherein the ratio between said fine particles (a) and said coarse particles (b) is from 1:99 to 30:70 percent by weight;

(c) providing micronized particles of an anticholinergic, micronized particles of an inhaled corticosteroid (ICS), and micronized particles of a long-acting β_2-agonist (LABA) as active ingredients, wherein at least 90% of the active ingredient micronized particles have a volume diameter lower than 6.0 μm, wherein, upon actuation of said inhaler, at least 35% of the micronized particles of each of the active ingredients have a diameter equal to or less than 2 μm, and wherein the width of the particle size distribution of said micronized particles of active ingredients, expressed as a span, is from 1.2 to 3.0; and

(d) mixing said fraction of fine particles provided in step (a), said fraction of coarse particles provided in step (b), said micronized particles of an anticholinergic provided in step (c), said micronized particles of an ICS provided in step (c), and said micronized particles of a LABA provided in step (c);

wherein the active ingredients, upon administration to the respiratory tract by a dry powder inhaler, are capable of reaching the distal tract of the respiratory tree.