

CLAIMS

1. A pharmaceutical aerosol solution composition intended for use in a pressurized metered dose inhaler comprising:

5 (a) glycopyrronium bromide at a dosage in the range of from 5 to 26 µg per actuation;

(b) formoterol, or a salt thereof or a solvate of said salt, at a dosage in the range of from 1 to 25 µg per actuation;

(c) a HFA propellant;

10 (d) a co-solvent;

(e) a stabilising amount of a mineral acid;

said composition being contained in an aerosol can internally coated by a resin comprising a fluorinated ethylene propylene (FEP) polymer.

15 2. A pharmaceutical aerosol solution composition according to claim 1 characterised in that the amount of the degradation product N-(3-bromo)-[2-hydroxy-5-[1-hydroxy-2-[1-(4-methoxyphenyl)propan-2-ylamino]ethyl] phenyl]formamide (DP3), is lower than 0.10% w/w with respect to the theoretical formoterol fumarate content of 6 µg/actuation, when stored in accelerated conditions at 25°C and 60% relative humidity
20 for at least 6 months.

3. A pharmaceutical aerosol solution composition according to claim 1 or 2 wherein the stabilising amount of a mineral acid is an amount of acid equivalent to 1M hydrochloric acid in the range from 0.15 to 0.28 µg/µl.

25

4. A pharmaceutical aerosol solution composition according to claim 3 wherein the stabilising amount of a mineral acid is an amount of acid equivalent to 1M hydrochloric acid in the range from 0.200 to 0.240 µg/µl.

30 5. A pharmaceutical aerosol solution composition according to claim 4 wherein the stabilising amount of a mineral acid is an amount of acid equivalent to 1M hydrochloric acid in the range from 0.200 to 0.227 µg/µl.

6. A pharmaceutical aerosol solution composition according to any one of claims 1 to 5 wherein the co-solvent is ethanol.

5 7. A pharmaceutical aerosol solution composition according to claim 1 wherein the formoterol salt is formoterol fumarate.

8. A pharmaceutical aerosol solution composition according to claim 1 wherein the solvate form of the formoterol salt is formoterol fumarate dihydrate.

10

9. A pharmaceutical aerosol solution composition according to claim 1 further comprising one or more pharmaceutically active ingredient selected from the group consisting of beta-2 agonists, inhalation corticosteroids, antimuscarinic agents, and phosphodiesterase-4 inhibitors.

15

10. A pharmaceutical aerosol solution composition according to claim 9 wherein the inhalation corticosteroid is selected from the group of beclometasone dipropionate, budesonide or its 22R-epimer, ciclesonide, flunisolide, fluticasone propionate, fluticasone furoate, mometasone furoate, butixocort, triamcinolone
20 acetonide, triamcinolone, methylprednisolone, prednisone, loteprednol and rofleponide.

25

11. A pharmaceutical aerosol solution composition according to claim 10 wherein the inhalation corticosteroid beclometasone dipropionate is present in an amount in the range from 50 to 250 µg per actuation.

12. A pharmaceutical aerosol solution composition according to claim 10 wherein the inhalation corticosteroid budesonide is present in an amount in the range from 50 to 250 µg per actuation.

30

13. A pharmaceutical aerosol solution composition according to claim 1 wherein the overall formoterol degradation products level is lower than 10% w/w with

respect to the theoretical formoterol fumarate content of 6µg/actuation and the residual level of formoterol fumarate is higher than 90% w/w with respect to its initial content.

14. A pharmaceutical aerosol solution composition according to claim 13 wherein the overall formoterol degradation products level is lower than 2% w/w with respect to the theoretical formoterol fumarate content of 6µg/actuation and the residual level of the formoterol fumarate is higher than 95% w/w with respect to its initial content.

15. A pressurised metered dose inhaler including an aerosol can internally coated by a resin comprising a fluorinated ethylene propylene (FEP) polymer, said can containing a pharmaceutical aerosol solution composition comprising:

- (a) glycopyrronium bromide at a dosage in the range of from 5 to 26 µg per actuation;
- (b) formoterol, or a salt thereof or a solvate of said salt, at a dosage in the range of from 1 to 25 µg per actuation;
- (c) a HFA propellant;
- (d) a co-solvent;
- (e) a stabilising amount of a mineral acid; and, optionally,
- (f) an inhalation corticosteroid.

16. A method to lower the amount of degradation product N-(3-bromo)-[2-hydroxy-5-[1-hydroxy-2-[1-(4-methoxyphenyl)propan-2-ylamino]ethyl]phenyl]formamide (DP3) during the shelf-life of a pharmaceutical aerosol solution composition intended for use in a pressurised metered dose inhaler comprising:

- (a) glycopyrronium bromide at a dosage in the range from 5 to 26 µg per actuation;
- (b) formoterol, or a salt thereof or a solvate of said salt, at a dosage in the range from 1 to 25 µg per actuation;
- (c) a HFA propellant;
- (d) a co-solvent;
- (e) a stabilising amount of a mineral acid; and, optionally,

(f) an inhalation corticosteroid

characterised in that said method comprises containing the above composition in an aerosol can internally coated by a resin comprising a fluorinated ethylene propylene (FEP) polymer.

5

17. A method according to claim 16 further characterised by the fact that the overall formoterol degradation products level lower than 10% w/w with respect to the theoretical formoterol fumarate content of 6 µg/actuation and the residual level of formoterol fumarate is higher than 90 w/w with respect to its initial content.

10

18. A method according to claim 16 or 17 further characterised by the fact that the overall formoterol degradation products level is lower than 2% w/w with respect to the theoretical formoterol fumarate content of 6µg/actuation and the residual level of the formoterol fumarate is higher than 95% w/w with respect to its initial content.

15

19. A pharmaceutical aerosol solution composition as defined in any one of claims 1 to 14 for use in the prevention and/or treatment of an obstructive respiratory disorder selected from asthma and COPD.

20

20. Use of a pharmaceutical aerosol solution composition as defined in any one of claims 1 to 14 in the manufacture of a medicament for the prevention and/or treatment of an obstructive respiratory disorder selected from asthma and COPD.