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(54) **INHALATION COMPOSITIONS COMPRISING GLUCOSE ANHYDROUS**

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(58) **Field of Classification Search**

None

See application file for complete search history.

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(57) **ABSTRACT**

The invention relates to pharmaceutical powder compositions administered by means of inhalers. More particularly, it relates to pharmaceutical powder compositions having the content uniformity and the desired stability used in inhaler devices.

34 Claims, No Drawings

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INHALATION COMPOSITIONS COMPRISING GLUCOSE ANHYDROUS

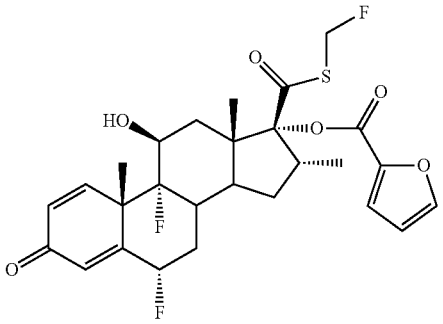
TECHNICAL FIELD

The invention relates to pharmaceutical powder compositions administered by means of inhaler devices. More particularly, it relates to pharmaceutical powder compositions having the content uniformity and the desired stability used in inhaler devices.

BACKGROUND OF THE INVENTION

Fluticasone is an intermediate potency synthetic corticosteroid. Chemical name thereof is 6alpha,9-Difluoro-17{[(fluoromethyl)sulphonyl]carbonyl}-11beta-hydroxy-16alpha-methyl-3-oxoandrosta-1,4-diene-17alpha-yl furane-2-carboxylate and its chemical formula is as shown in formula I:

Formula 1



Fluticasone molecules are used in the treatment of allergic rhinitis, asthma and chronic obstructive pulmonary disease. It is launched onto the market under the trade name of Flixotide® with an inhaler of 60 blisters, each of which comprises 100 mcg of fluticasone propionate.

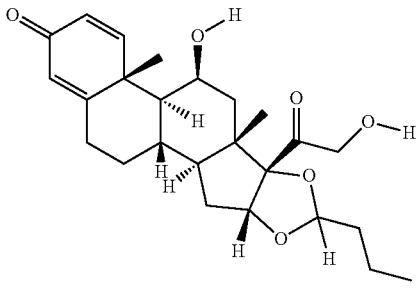
Fluticasone molecule was first disclosed in the U.S. Pat. No. 4,335,121.

WO9531964 patent application discloses a formulation comprising fluticasone propionate suitable for nebulization. Size of fluticasone particles in the formulation is smaller than 12 mm, and it further comprises one or more surfactant, one or more buffering agent and water.

WO2004069225 patent application mentions a formulation comprising fluticasone having a mean particle size smaller than 2000 nm, and at least a surface stabilizer.

This corticosteroid is administered via intranasal and oral route by inhalation for the treatment of budesonide allergic rhinitis and asthma, and via oral route for the treatment of Crohn's disease. Budesonide exhibits strong glucocorticoid and weak mineralocorticoid activity. Its chemical name is 16alpha,17alpha-butylydienedioxy-11beta,21-dihydroxy pregna-1,4-diene-3,20-dione. Chemical structure thereof is as shown in formula 2.

Formula 2



Budesonide is used in the treatment of allergic rhinitis, asthma and Crohn's disease. It is present in the market in the form reference dose inhaler under the name of Pulmicort®.

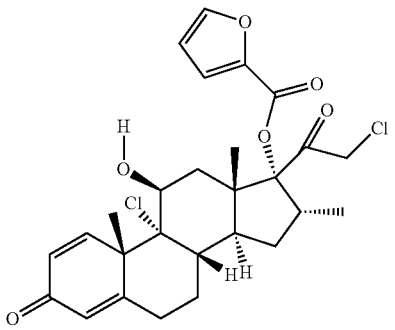
U.S. Pat. No. 3,929,768 is the first patent to disclose Budesonide molecule.

U.S. Pat. No. 6,598,603 patent describes a method of treatment for respiratory disorder by applying nebulized budesonide no more than once a day.

EP1124544B1 patent discloses a solid formulation applicable to nose, comprising an excipient of fine particles and medicament particles. Mass median diameter of the medicament particles is larger than that of the excipient particles. Budesonide is addressed as the active ingredient.

Mometasone is an intermediate potency corticosteroid having anti-inflammatory, anti-pruritic and vasoconstrictor properties. Its chemical name is 9alpha,21-Dichloro-11beta, 17-dihydroxy-16alpha-methyl pregna-1,4-diene-3,20-dione 17-(2-furoate). Chemical structure thereof is as shown in formula 3.

Formula 3



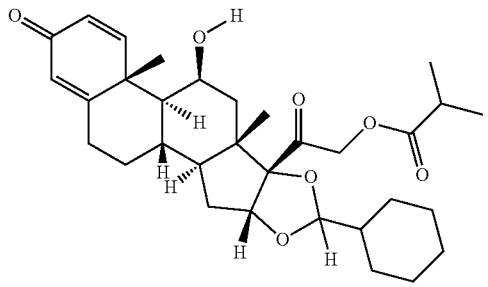
It has been launched onto the market under the trade name of ASMANEX®.

Mometasone molecule was first disclosed in the European patent EP0057401. European patent application

EP1968548 discloses mometasone furoate particles, particle size of which is less than 200 nm and at least one surface stabilizer.

Ciclesonide is a halogen free glucocorticoid used in the treatment of inflammatory diseases such as allergic rhinitis and asthma. Chemical name thereof is {16alpha,17-[(R)-cyclohexylmethylenedioxy]-11beta-hydroxy-3,20-dioxoo-pregna-1,4-diene-21-il}isobutyrate. Chemical structure thereof is as shown in formula 4.

Formula 4



It has been launched onto the market under the trade name of ALVESCO®.

Ciclesonide molecule was first disclosed in the U.S. Pat. No. 5,482,934.

European patent application EP1611150 discloses a process regarding the preparation of ciclesonide particles, 50% of the total particle size of which are 1.8-2.0 μm.

Inhalation compositions show activity by reaching directly to the respiratory system. Contriving the compositions is based on containing the active ingredient along with the carrier and the extender having the particle sizes capable of carrying said active ingredient to the respiratory system. On the other hand, carrier particle size enabling conveying the active ingredient to the respiratory system in the desired levels is also critical. Flowing and filling of the components constituting the composition also depend on the particle size and the ratios in-between are determined accordingly. Said ratio to be in desired levels is substantially critical and the filling process rate and the amount of the formulation to be filled depend on this. Achieving the homogeneous mixture and carrying out filling of said mixture economically and in an advantageous manner in terms of process rate is a preferred condition.

It is a pre-condition for the medicament to possess content uniformity, in terms of user safety and effectiveness of the treatment. Difference of the particle sizes between the carrier and the extender used is important in order to ensure the content uniformity. This difference to be beyond measure hampers to achieve the desired content uniformity. Another potential problem is to be unable to achieve the dosage accuracy present in each cavity or capsule. And this is of vital importance in terms of effectiveness of the treatment.

In order to meet all these requirements, dry powder inhalers (DPI) should meet a series of criteria taking particularly into account the following circumstances:

Content Uniformity of the Active Drug:

Each capsule or blister should contain same amount of drug in the single dose system. Whereas in a multi-dose system, same amount of drug must be released in each application in order to ensure that the patient administers the same dosage in each time. Presence of the carrier should support the content uniformity even in a low dose drug.

Fluidity:

Design of the device, characteristics of the active ingredient and the filling platform to be used define the required properties of the carrier needed. Formulation flow characteristics have importance in terms of ensuring that the device carries out all the functions properly and provides a continuous performance. Choosing the carrier is of high importance in that it ensures that the device functions properly and carries accurate amount of active ingredient to the patient. Therefore it is quite important to employ glucose anhydrous as the carrier, in two different particle sizes (fine and coarse).

Dose Consistency:

In order that all of the doses coming out of the device contain accurate amount of active ingredient, dry powder inhaler (DPI) devices should exhibit consistent dose uniformity. Irrespective of the inhalation capability of a patient, it is of substantial importance that the dose released from the dry powder inhaler device to be same in each time. For this reason, employing glucose anhydrous as a carrier possessing proper characteristics in the formulation assists the dose to be administered consistently.

Small drug particles are likely to agglomerate. Said coagulation can be prevented by employing suitable carrier or carrier mixtures. It also assists in controlling the fluidity of the drug coming out of the carrier device and ensuring that the active ingredient reaching to lungs is accurate and consistent.

In addition to this, the mixture of the drug particles adhered to the carrier should be homogeneous. Adhesion should be quite strong as the drug could not detach from the carrier particle. Moreover, lower doses of powder should also be filled into the device and the drug should always be released in the same way. One of the main parameters for the formulation is the particle size. Therefore, it has been found to be very important to employ the fine (small) and coarse (large) particles of the selected carrier in the formulations of the present invention in an accurate ratio.

In order to meet all these requirements, dry powder inhaler (DPI) formulations should be adapted especially by carefully choosing the employed carriers. In order to meet these requirements, the inhalable, fine or micro-fine particles of the active compounds are mixed with carriers. By means of mixing process, particle size of the carrier can be changed in order that a certain amount thereof to become inhalable. Particle size of employed carrier depends on the requirements and specifications of the powder inhaler used for application of the formulation. In this mixture, no dissociation should occur during all of the required procedures, transportation, and storage and dosing, i.e., active compound should not dissociate from its carrying particles. However, during the dissociation in the inhaler induced by inhalation of the patient, active compound particles should dissociate as effective as possible, i.e., as much as possible.

Furthermore, in the active ingredients administered via inhalation, one encounters certain stability related problems due to environmental and physical conditions. Mentioned active substances are influenced substantially by the temperature, air and humidity conditions. Exposure to air and moisture causes structural destruction of said active substances and leads them to build up a change in chemical behavior. Stability of the developed products is not in desired levels and shelf-life thereof are getting shorter. In addition, these active substances may react with auxiliary substances used along with them in the step of developing formulation. This, on the other hand, leads to impurities in the formulations and undesired compositions to get involved in the formulations. It is of critical importance for the formulation, to employ auxiliary substances and method not bringing along to mentioned problems. Moisture and air content of the active ingredients kept in the blister or capsule may be determinative for the stability. That is, the air and the moisture content within the closed blister and capsule, is quite important for these kinds of pharmaceutical forms.

For this reason, there is still a need for the carriers capable of overcoming aforementioned problems, problems related to interaction between active ingredient and carrier and

moreover, problems related to pulmonary application of the drugs. Present inventions makes it possible as well, to obtain different compositions and compositions of combinations having satisfactory characteristics in a safe and effective manner, in terms of increasing the drug storing for pulmonary application or increasing the drug release rates.

As a result, there is a need for a novelty in the field relating to the compositions administrable by the patients suffering from chronic obstructive pulmonary disease or asthma.

Object and Brief Description of the Invention

Present invention relates to easily applicable inhalation compositions overcoming all of the aforementioned problems and bringing further advantages to the technical field.

Starting out from the state of the art, main object of the invention is to obtain effective and stable composition applicable in chronic obstructive pulmonary disease and asthma.

Another object of the invention is to enable a composition in which the desired filling rate and content uniformity is achieved.

Still other object of the invention is to obtain inhalation compositions having appropriate particle size and ratios ensuring to facilitate filling process into the blister package or the capsule, and enabling on the other hand to realize a homogeneous mixture.

Dry powder inhalation compositions are developed with the intent of achieving aforementioned purposes and all of the objectives that might come up from the detailed description below.

In a preferred embodiment of the invention, novelty is achieved by,

- at least one corticosteroid or a pharmaceutically acceptable salt thereof,
- fine particle lactose in the ratio of 1-20% by weight of said composition and having (d50) particle size in the range of 4-10 μm and coarse particle glucose anhydrous in the ratio of 80-99% by weight of said composition and having (d50) particle size in the range of 50-120 μm.

In a preferred embodiment of the invention, (d50) particle size of said fine particle lactose is preferably 4-7 μm.

In a preferred embodiment of the invention, particle size of said fine particle lactose (d10) is 1-5 μm, preferably 1-4 μm.

In a preferred embodiment of the invention, particle size of said fine particle lactose (d90) is 7-20 μm, preferably 7-15 μm.

In a preferred embodiment of the invention, (d50) particle size of said coarse particle glucose anhydrous is preferably 50-75 μm.

In a preferred embodiment of the invention, particle size of said coarse particle glucose anhydrous (d10) is preferably 10-50 μm.

In a preferred embodiment of the invention, particle size of said coarse particle glucose anhydrous (d90) is 120-300 μm, preferably 75-250 μm.

A preferred embodiment of the invention further comprises coarse particle lactose of (d50) particle size of 50-80 μm, preferably of 50-75 μm.

A preferred embodiment of the invention further comprises coarse particle lactose (d10) having particle size of 10-50 μm.

A preferred embodiment of the invention further comprises coarse particle lactose (d90) having particle size of 120-300 μm, preferably of 75-250 μm.

A preferred embodiment of the invention further comprises fine particle glucose anhydrous of (d50) particle size of 4-7 μm.

A preferred embodiment of the invention further comprises fine particle glucose anhydrous (d10) having particle size of 1-5 μm, preferably of 1-4 μm.

A preferred embodiment of the invention further comprises fine particle glucose anhydrous (d90) having particle size of 10-20 μm, preferably of 7-10 μm.

In a preferred embodiment of the invention, said lactose amount is preferably in the range of 1-15%, more preferably 1-10% by weight.

In a preferred embodiment of the invention, said glucose anhydrous amount is preferably in the range of 85-99%, more preferably 90-99% by weight of the composition.

In a preferred embodiment of the invention, said corticosteroid is is selected from the group consisting of at least one or a mixture of ciclesonide, budesonide, fluticasone, aldosterone, beklometazone, betametazone, chioprednol, cortisone, cortivasole, deoxycortone, desonide, desoxymetasone, dexametasone, difluorocortolone, fluchiorolone, flumetasone, flunisolide, fluquinolone, fluquinonide, flurocortisone, fluorocortolone, flurometolone, flurandrenolone, halcynonide, hydrocortisone, icometasone, meprednisone, methylprednisolone, mometasone, paramethasone, prednisolone, prednisone, tixocortole, triamcynolondane, or is a combination thereof.

In a preferred embodiment of the invention, said corticosteroid is ciclesonide.

In another preferred embodiment of the invention, said corticosteroid is budesonide.

In another preferred embodiment of the invention, said corticosteroid is fluticasone.

In another preferred embodiment of the invention, said corticosteroid is mometasone.

Another preferred embodiment of the invention further comprises one or a combination of two or more selected from β2-adrenergic agonist and muscarinic receptor antagonist.

In another preferred embodiment of the invention, said composition comprises corticosteroid and β2-adrenergic agonist.

In another preferred embodiment of the invention, said composition comprises corticosteroid and muscarinic antagonist.

In another preferred embodiment of the invention, said composition comprises corticosteroid, β2-adrenergic agonist and muscarinic receptor antagonist.

In another preferred embodiment of the invention, said muscarinic receptor antagonist is selected from the group consisting of at least one or a mixture of tiotropium, glycopyrronium, aclidinium, darotropium and ipratropium.

In a preferred embodiment of the invention, said beta-2 adrenergic agonist is selected from the group consisting of at least one or a mixture of salmeterol, ormoterol, arformoterol, salbutamol, indacaterol, terbutaline, metaproterenol, vilanterol, carmoterol, olodaterol, bambuterol, clenbuterol.

In another preferred embodiment of the invention, said retard muscarinic receptor antagonist is tiotropium.

In another preferred embodiment of the invention, said retard muscarinic receptor antagonist is glycopyrronium.

In another preferred embodiment of the invention, said retard muscarinic receptor antagonist is aclinidium.

In another preferred embodiment of the invention, said retard muscarinic receptor antagonist is darotropium.

In another preferred embodiment of the invention, said beta-2 adrenergic agonist is salmeterol.

In another preferred embodiment of the invention, said beta-2 adrenergic agonist is formoterol.

In another preferred embodiment of the invention, said beta-2 adrenergic agonist is arfomoterol.

In another preferred embodiment of the invention, said beta-2 adrenergic agonist is salbutomol.

In another preferred embodiment of the invention, said beta-2 adrenergic agonist is carmoterol.

In another preferred embodiment of the invention, said beta-2 adrenergic agonist is olodaterol.

In another preferred embodiment of the invention, said beta-2 adrenergic agonist is vilanterol.

In another preferred embodiment of the invention, said beta-2 adrenergic agonist is indacaterol.

Another preferred embodiment of the invention further comprises one of or a mixture of the excipients from glucose, mannitol, sorbitol, trehalose, cellobiose.

In another preferred embodiment of the invention, said composition comprises one of the following therapeutically active combinations:

i. Budesonide and indacaterol,
ii. Budesonide and oladaterol,
iii. Budesonide and vilanterol,
iv. Budesonide and salmeterol,
v. Budesonide and formoterol,
vi. Budesonide and carmoterol,
vii. Budesonide and arformoterol

In another preferred embodiment of the invention, said composition comprises one of the following therapeutically active combinations:

i. fluticasone ve formoterol,
ii. fluticasone ve salmeterol,
iii. fluticasone ve vilanterol,
iv. fluticasone ve indacaterol
v. fluticasone ve olodaterol,
vi. fluticasone ve carmoterol,
vii. fluticasone ve arformoterol,
viii. fluticasone ve salbutamol

In another preferred embodiment of the invention, said composition comprises one of the following therapeutically active combinations:

i. mometasone ve formoterol,
ii. mometasone ve indacaterol
iii. mometasone ve vilanterol,
iv. mometasone ve olodaterol,
v. mometasone ve carmoterol,
vi. mometasone ve arformoterol,
vii. mometasone ve salmeterol.

In another preferred embodiment of the invention, said composition comprises one of the following therapeutically active combinations:

i. ciclesonide ve formoterol,
ii. ciclesonide ve vilanterol,
iii. ciclesonide ve indacaterol
iv. ciclesonide ve olodaterol,
v. ciclesonide ve carmoterol,
vi. ciclesonide ve arformoterol,
vii. ciclesonide ve salmeterol.

In another preferred embodiment of the invention, said composition comprises one of the following therapeutically active combinations:

i. budesonide ve tiotropium,
ii. fluticasone ve tiotropium,
iii. mometason ve tiotropium,
iv. ciclesonide ve tiotropium.

In another preferred embodiment of the invention, said composition comprises one of the following therapeutically active combinations:

i. budesonide, formoterol ve tiotropium,
ii. budesonide, salmeterol ve tiotropium,
iii. budesonide, arformoterol ve tiotropium,
iv. budesonide, carmoterol ve tiotropium.

In another preferred embodiment of the invention, said composition comprises one of the following therapeutically active combinations:

i. ciclesonide, formoterol ve tiotropium,
ii. ciclesonide, salmeterol ve tiotropium,
iii. ciclesonide, carmoterol ve tiotropium,
iv. ciclesonide, arformoterol ve tiotropium,
v. ciclesonide, indacaterol ve tiotropium,
vi. ciclesonide, olodaterol ve tiotropium,
vii. ciclesonide, vilanterol ve tiotropium.

In another preferred embodiment of the invention, said composition comprises one of the following therapeutically active combinations:

i. fluticasone, salmeterol ve tiotropium,
ii. fluticasone, formoterol ve tiotropium,
iii. fluticasone, arfomoterol ve tiotropium,
iv. fluticasone, carmoterol ve tiotropium,
v. fluticasone, vilanterol ve tiotropium,
vi. fluticasone, olodaterol ve tiotropium,
vii. fluticasone, indacaterol ve tiotropium.

In another preferred embodiment of the invention, said composition comprises one of the following therapeutically active combinations:

i. budesonide, indacaterol ve tiotropium,
ii. budesonide, olodaterol ve tiotropium,
iii. budesonide, vilanterol ve tiotropium.

In another preferred embodiment of the invention, said composition comprises one of the following therapeutically active combinations:

i. mometasone, salmeterol ve tiotropium
ii. mometasone, formoterol ve tiotropium,
iii. mometasone, indacaterol ve tiotropium,
iv. mometasone, vilanterol ve tiotropium,
v. mometasone, oladaterol ve tiotropium,
vi. mometasone, arformoterol ve tiotropium.

In another preferred embodiment of the invention, said composition comprises one of the following therapeutically active combinations:

i. mometasone, indacaterol ve glycopyrronium,
ii. mometasone, salmeterol ve glycopyrronium,
iii. mometasone, formoterol ve glycopyrronium,
iv. mometasone, carmoterol ve glycopyrronium,
v. mometasone, olodaterol ve glycopyrronium,
vi. mometasone, vilanterol ve glycopyrronium.

In another preferred embodiment of the invention, said composition comprises one of the following therapeutically active combinations:

i. fluticasone, salmeterol ve salbutamol,
ii. fluticasone, arformeterol ve salbutamol.

Said compositions are used for the prevention or treatment of chronic obstructive pulmonary disease and asthma in mammals, especially in humans.

In another preferred embodiment of the invention, said composition comprises a blister having air and moisture barrier property, enabling simultaneous, respective and synchronic application.

In another preferred embodiment of the invention, said composition comprises a dry powder inhaler device suitable for simultaneous, respective and synchronic application in a blister and having at least one locking mechanism ensuring the device to be maintained locked in both of the positions

in which it is ready for inhalation and its lid is closed and ensuring the device to be automatically re-set once the lid is closed.

In another preferred embodiment of the invention, said composition comprises a dry powder inhaler device suitable for simultaneous, respective and synchronic application in a blister.

In another preferred embodiment of the invention, pharmaceutically acceptable amount of said composition is administered one a day.

In another preferred embodiment of the invention, pharmaceutically acceptable amount of said composition is administered twice a day.

DETAILED DESCRIPTION OF INVENTION

Examples—A

Content	% Weight (a/a)
1-	
Corticosteroid	0.1-12
Lactose (fine particle)	4.3-5.3
Glucose anhydrous (coarse particle)	84-96
2-	
Corticosteroid	0.1-12
Glucose anhydrous (fine particle)	4.3-5.3
Lactose (coarse particle)	84-96
3-	
Corticosteroid	0.1-12
Glucose anhydrous + Lactose (fine particle)	4.3-5.3
Lactose + Glucose anhydrous (coarse particle)	84-96

	Weight and percentage amount			
Content	25 mg	%	5 mg	%
4-				
Ciclesonide	0.16	0.64	0.16	3.2
Lactose	1.242	4.968	0.242	4.84
Glucose anhydrous	23.598	94.392	4.598	91.96
TOTAL	25	100	5	100
5-				
Ciclesonide	0.16	0.64	0.16	3.2
Glucose anhydrous	1.242	4.968	0.242	4.84
Lactose	23.598	94.392	4.598	91.96
TOTAL	25	100	5	100
6-				
ciclesonide	0.2	0.8	0.2	4
Lactose	1.24	4.96	0.24	4.8
Glucose anhydrous	23.56	94.24	4.56	91.2
TOTAL	25	100	5	100
7-				
ciclesonide	0.2	0.8	0.2	4
Glucose anhydrous	1.24	4.96	0.24	4.8
Lactose	23.56	94.24	4.56	91.2
TOTAL	25	100	5	100

-continued

8-				
budesonide	0.2	0.8	0.2	4
Lactose	1.24	4.96	0.24	4.8
Glucose anhydrous	23.56	94.24	4.56	91.2
TOTAL	25	100	5	100
9-				
budesonide	0.2	0.8	0.2	4
Glucose anhydrous	1.24	4.96	0.24	4.8
Lactose	23.56	94.24	4.56	91.2
TOTAL	25	100	5	100
10-				
Budesonide	0.4	1.6	0.4	8
Lactose	1.23	4.92	0.23	4.6
Glucose anhydrous	23.37	93.48	4.37	87.4
TOTAL	25	100	5	100
11-				
Budesonide	0.4	1.6	0.4	8
Glucose anhydrous	1.23	4.92	0.23	4.6
Lactose	23.37	93.48	4.37	87.4
TOTAL	25	100	5	100
12-				
Mometasone	0.1	0.4	0.1	2
Lactose	1.245	4.98	0.245	4.9
Glucose anhydrous	23.655	94.62	4.655	93.1
TOTAL	25	100	5	100
13-				
Mometasone	0.1	0.4	0.1	2
Glucose anhydrous	1.245	4.98	0.245	4.9
Lactose	23.655	94.62	4.655	93.1
TOTAL	25	100	5	100
14-				
Mometasone	0.2	0.8	0.2	
Lactose	1.24	4.96	0.24	4.8
Glucose anhydrous	23.56	94.24	4.56	91.2
TOTAL	25	100	5	100
15-				
Mometasone	0.2	0.8	0.2	4
Glucose anhydrous	1.24	4.96	0.24	4.8
Lactose	23.56	94.24	4.56	91.2
TOTAL	25	100	5	100
16-				
Fluticasone	0.05	0.2	0.05	1
Lactose	1.2475	4.99	0.2475	4.95
Glucose anhydrous	23.7025	94.81	4.7025	94.05
TOTAL	25	100	5	100

-continued

		17-		
Fluticasone	0.05	0.2	0.05	1
Glucose anhydrous	1.2475	4.99	0.2475	4.95
Lactose	23.7025	94.81	4.7025	94.05
TOTAL	25	100	5	100
		18-		
Fluticasone	0.1	0.4	0.1	2
Lactose	1.245	4.98	0.245	4.9
Glucose anhydrous	23.655	94.62	4.655	93.1
TOTAL	25	100	5	100
		19-		
Fluticasone	0.1	0.4	0.1	2
Glucose anhydrous	1.245	4.98	0.245	4.9
Lactose	23.655	94.62	4.655	93.1
TOTAL	25	100	5	100
		20-		
Fluticasone	0.125	0.5	0.125	2.5
Lactose	1.24375	4.975	0.24375	4.875
Glucose anhydrous	23.63125	94.525	4.63125	92.625
TOTAL	25	100	5	100
		21-		
Fluticasone	0.125	0.5	0.125	2.5
Glucose anhydrous	1.24375	4.975	0.24375	4.875
Lactose	23.63125	94.525	4.63125	92.625
TOTAL	25	100	5	100
		22-		
Fluticasone	0.25	1	0.25	5
Lactose	1.2375	4.95	0.2375	4.75
Glucose anhydrous	23.5125	94.05	4.5125	90.25
TOTAL	25	100	5	100
		23-		
Fluticasone	0.25	1	0.25	5
Glucose anhydrous	1.2375	4.95	0.2375	4.75
Lactose	23.5125	94.05	4.5125	90.25
TOTAL	25	100	5	100
		24-		
Fluticasone	0.5	2	0.5	10
Lactose	1.225	4.9	0.225	4.5
Glucose anhydrous	23.275	93.1	4.275	85.5
TOTAL	25	100	5	100
		25-		
Fluticasone	0.5	2	0.5	10
Glucose anhydrous	1.225	4.9	0.225	4.5
Lactose	23.275	93.1	4.275	85.5
TOTAL	25	100	5	100

Examples—B

Content	% Weight (a/a)			
Corticosteroid β2-adrenergic agonist Lactose Glucose anhydrous excipient				
	Weight and percentage amount			
Content	25 mg	%	5 mg	%
		1-		
Indacaterol	0.15	0.6	0.15	3
Budesonide	0.2	0.8	0.2	4
Lactose	1.2325	4.93	0.2325	4.65
Glucose anhydrous	23.4175	93.67	4.4175	88.35
TOTAL	25		5	
		2-		
Indacaterol	0.15	0.6	0.15	3
Budesonide	0.2	0.8	0.2	4
Glucose anhydrous	1.2325	4.93	0.2325	4.65
Lactose	23.4175	93.67	4.4175	88.35
TOTAL	25		5	
		3-		
Indacaterol	0.15	0.6	0.15	3
Budesonide	0.4	1.6	0.4	8
Lactose	1.2225	4.89	0.2225	4.45
Glucose anhydrous	23.2275	92.91	4.2275	84.55
TOTAL	25		5	
		4-		
Indacaterol	0.15	0.6	0.15	3
Budesonide	0.4	1.6	0.4	8
Glucose anhydrous	1.2225	4.89	0.2225	4.45
Lactose	23.2275	92.91	4.2275	84.55
TOTAL	25		5	
		5-		
Oladetarol	0.005	0.02	0.005	0.1
Budesonide	0.2	0.8	0.2	4
Lactose	1.23975	4.959	0.23975	4.795
Glucose anhydrous	23.55525	94.221	4.55525	91.105
TOTAL	25		5	
		6-		
Oladetarol	0.005	0.02	0.005	0.1
Budesonide	0.2	0.8	0.2	4
Glucose anhydrous	1.23975	4.959	0.23975	4.795
Lactose	23.55525	94.221	4.55525	91.105
TOTAL	25		5	
		7-		
Oladetarol	0.005	0.02	0.005	0.1
Budesonide	0.4	1.6	0.4	8
Lactose	1.22975	4.919	0.22975	4.595
Glucose anhydrous	23.36525	93.461	4.36525	87.305
TOTAL	25		5	
		8-		
Oladetarol	0.005	0.02	0.005	0.1
Budesonide	0.4	1.6	0.4	8
Glucose anhydrous	1.22975	4.919	0.22975	4.595
Lactose	23.36525	93.461	4.36525	87.305
TOTAL	25		5	
		9-		
Vilanterol	0.025	0.1	0.025	0.5
Budesonide	0.2	0.8	0.2	4

-continued

Lactose	1.23875	4.955	0.23875	4.775
Glucose anhydrous	23.53625	94.145	4.53625	90.725
TOTAL	25		5	

10-

Vilanterol	0.025	0.1	0.025	0.5
Budesonide	0.2	0.8	0.2	4
Glucose anhydrous	1.23875	4.955	0.23875	4.775
Lactose	23.53625	94.145	4.53625	90.725
TOTAL	25		5	

	Weight and percentage amount			
Content	mg	%	mg	%

11-

Vilanterol	0.025	0.1	0.025	0.5
Budesonide	0.4	1.6	0.4	8
Lactose	1.22875	4.915	0.22875	4.575
Glucose anhydrous	23.34625	93.385	4.34625	86.925
TOTAL	25		5	

12-

Vilanterol	0.025	0.1	0.025	0.5
Budesonide	0.4	1.6	0.4	8
Glucose anhydrous	1.22875	4.915	0.22875	4.575
Lactose	23.34625	93.385	4.34625	86.925
TOTAL	25		5	

	Weight and percentage amount			
Content	25 mg	25 mg	25 mg	25 mg

13-

Formoterol	0.005	0.02	0.005	0.1
Mometasone	0.1	0.4	0.1	2
Lactose	1.24475	4.979	0.24475	4.895
Glucose anhydrous	23.65025	94.601	4.65025	93.005
TOTAL	25		5	

14-

Formoterol	0.005	0.02	0.005	0.1
Mometasone	0.1	0.4	0.1	2
Glucose anhydrous	1.24475	4.979	0.24475	4.895
Lactose	23.65025	94.601	4.65025	93.005
TOTAL	25		5	

15-

Formoterol	0.005	0.02	0.005	0.1
Mometasone	0.2	0.8	0.2	4
Lactose	1.23975	4.959	0.23975	4.795
Glucose anhydrous	23.55525	94.221	4.55525	91.105
TOTAL	25		5	

16-

Formoterol	0.005	0.02	0.005	0.1
Mometasone	0.2	0.8	0.2	
Glucose anhydrous	1.23975	4.959	0.23975	4.795
Lactose	23.55525	94.221	4.55525	91.105
TOTAL	25		5	

17-

Indacaterol	0.15	0.6	0.15	3
Mometasone	0.1	0.4	0.1	2
Lactose	1.2375	4.95	0.2375	4.75
Glucose anhydrous	23.5125	94.05	4.5125	90.25
TOTAL	25		5	

18-

Indacaterol	0.15	0.6	0.15	3
Mometasone	0.1	0.4	0.1	2
Glucose anhydrous	1.2375	4.95	0.2375	4.75
Lactose	23.5125	94.05	4.5125	90.25
TOTAL	25		5	

19-

Indacaterol	0.15	0.6	0.15	3
Mometasone	0.2	0.8	0.2	4
Lactose	1.2325	4.93	0.2325	4.65
Glucose anhydrous	23.4175	93.67	4.4175	88.35
TOTAL	25		5	

20-

Indacaterol	0.15	0.6	0.15	3
Mometasone	0.2	0.8	0.2	4
Glucose anhydrous	1.2325	4.93	0.2325	4.65
Lactose	23.4175	93.67	4.4175	88.35
TOTAL	25		5	

21-

Vilanterol	0.025	0.1	0.025	0.5
Flutikasone	0.1	0.4	0.1	2
Lactose	1.24375	4.975	0.24375	4.875
Glucose anhydrous	23.63125	94.525	4.63125	92.625
TOTAL	25		5	

22-

Vilanterol	0.025	0.1	0.025	0.5
Flutikasone	0.1	0.4	0.1	2
Glucose anhydrous	1.24375	4.975	0.24375	4.875
Lactose	23.63125	94.525	4.63125	92.625
TOTAL	25		5	

23-

Salbutamol	0.1	0.4	0.1	2
Fluticasone	0.5	2	0.5	10
Lactose	1.22	4.88	0.22	4.4
Glucose anhydrous	23.18	92.72	4.18	83.6
TOTAL	25		5	

24-

Salbutamol	0.1	0.4	0.1	2
Fluticasone	0.5	2	0.5	10
Glucose anhydrous	1.22	4.88	0.22	4.4
Lactose	23.18	92.72	4.18	83.6
TOTAL	25		5	

25-

Salbutamol	0.1	0.4	0.1	2
Fluticasone	0.1	0.4	0.1	2
Lactose	1.24	4.96	0.24	4.8
Glucose anhydrous	23.56	94.24	4.56	91.2
TOTAL	25		5	

26-

Salbutamol	0.1	0.4	0.1	2
Fluticasone	0.1	0.4	0.1	2
Glucose anhydrous	1.24	4.96	0.24	4.8
Lactose	23.56	94.24	4.56	91.2
TOTAL	25		5	

27-

Salbutamol	0.1	0.4	0.1	2
Fluticasone	0.25	1	0.25	5

-continued

Lactose	1.2325	4.93	0.2325	4.65
Glucose anhydrous	23.4175	93.67	4.4175	88.35
TOTAL	25		5	

28-

Salbutamol	0.1	0.4	0.1	2
Fluticasone	0.25	1	0.25	5
Glucose anhydrous	1.2325	4.93	0.2325	4.65
Lactose	23.4175	93.67	4.4175	88.35
TOTAL	25		5	

29-

Formoterol	0.012	0.048	0.012	0.24
Fluticasone	0.1	0.4	0.1	2
Lactose	1.2444	4.9776	0.2444	4.888
Glucose anhydrous	23.6436	94.5744	4.6436	92.872
TOTAL	25		5	

30-

Formoterol	0.012	0.048	0.012	0.24
Fluticasone	0.1	0.4	0.1	2
Glucose anhydrous	1.2444	4.9776	0.2444	4.888
Lactose	23.6436	94.5744	4.6436	92.872
TOTAL	25		5	

31-

Formoterol	0.006	0.024	0.006	0.12
Fluticasone	0.125	0.5	0.125	2.5
Lactose	1.24345	4.9738	0.24345	4.869
Glucose anhydrous	23.62555	94.5022	4.62555	92.511
TOTAL	25		5	

32-

Formoterol	0.006	0.024	0.006	0.12
Fluticasone	0.125	0.5	0.125	2.5
Glucose anhydrous	1.24345	4.9738	0.24345	4.869
Lactose	23.62555	94.5022	4.62555	92.511
TOTAL	25		5	

33-

Formoterol	0.006	0.024	0.006	0.12
Fluticasone	0.25	1	0.25	5
Lactose	1.2372	4.9488	0.2372	4.744
Glucose anhydrous	23.5068	94.0272	4.5068	90.136
TOTAL	25		5	

34-

Formoterol	0.006	0.024	0.006	0.12
Fluticasone	0.25	1	0.25	5
Glucose anhydrous	1.2372	4.9488	0.2372	4.744
Lactose	23.5068	94.0272	4.5068	90.136
TOTAL	25		5	

35-

Formoterol	0.006	0.024	0.006	0.12
Fluticasone	0.25	1	0.25	5
Glucose anhydrous	1.2372	4.9488	0.2372	4.744
Lactose	23.5068	94.0272	4.5068	90.136
TOTAL	25		5	

36-

Formoterol	0.012	0.048	0.012	0.24
Fluticasone	0.25	1	0.25	5
Lactose	1.2369	4.9476	0.2369	4.738
Glucose anhydrous	23.5011	94.0044	4.5011	90.022
TOTAL	25		5	

-continued

37-

Formoterol	0.012	0.048	0.012	0.24
Fluticasone	0.25	1	0.25	5
Glucose anhydrous	1.2369	4.9476	0.2369	4.738
Lactose	23.5011	94.0044	4.5011	90.022
TOTAL	25		5	

38-

Formoterol	0.0045	0.018	0.0045	0.09
Ciclesonide	0.16	0.64	0.16	3.2
Lactose	1.241775	4.9671	0.241775	4.8355
Glucose anhydrous	23.593725	94.3749	4.593725	91.8745
TOTAL	25		5	

39-

Formoterol	0.0045	0.018	0.0045	0.09
Ciclesonide	0.16	0.64	0.16	3.2
Glucose anhydrous	1.241775	4.9671	0.241775	4.8355
Lactose	23.593725	94.3749	4.593725	91.8745
TOTAL	25		5	

	Weight and percentage amount			
Content	mg	%	mg	%

40-

Budesonide	0.2	0.8	0.2	4
Salmeterol	0.05	0.2	0.05	1
Lactose	1.2375	4.95	0.2375	4.75
Glucose anhydrous	23.5125	94.05	4.5125	90.25
TOTAL	25	100	5	100

41-

Budesonide	0.4	1.6	0.4	8
Salmeterol	0.05	0.2	0.05	1
Lactose	1.2275	4.91	0.2275	4.55
Glucose anhydrous	23.3225	93.29	4.3225	86.45
TOTAL	25		5	

42-

Budesonide	0.2	0.8	0.2	4
Salmeterol	0.05	0.2	0.05	1
Glucose anhydrous	1.2375	4.95	0.2375	4.75
Lactose	23.5125	94.05	4.5125	90.25
TOTAL	25		5	

43-

Budesonide	0.4	1.6	0.4	8
Salmeterol	0.05	0.2	0.05	1
Glucose anhydrous	1.2275	4.91	0.2275	4.55
Lactose	23.3225	93.29	4.3225	86.45
TOTAL	25		5	

44-

Budesonide	0.2	0.8	0.2	4
Formoterol	0.012	0.048	0.012	0.24
Lactose	1.2394	4.9576	0.2394	4.788
Glucose anhydrous	23.5486	94.1944	4.5486	90.972
TOTAL	25		5	

45-

Budesonide	0.4	1.6	0.4	8
Formoterol	0.012	0.048	0.012	0.24
Lactose	1.2294	4.9176	0.2294	4.588
Glucose anhydrous	23.3586	93.4344	4.3586	87.172
TOTAL	25		5	

-continued

46-				
Budesonide	0.2	0.8	0.2	4
Formoterol	0.012	0.048	0.012	0.24
Glucose anhydrous	1.2394	4.9576	0.2394	4.788
Lactose	23.5486	94.1944	4.5486	90.972
TOTAL	25		5	

47-				
Budesonide	0.4	1.6	0.4	8
Formoterol	0.012	0.048	0.012	0.24
Lactose	1.2294	4.9176	0.2294	4.588
Glucose anhydrous	23.3586	93.4344	4.3586	87.172
TOTAL	25		5	

48-				
Budesonide	0.4	1.6	0.4	8
Formoterol	0.012	0.048	0.012	0.24
Glucose anhydrous	1.2294	4.9176	0.2294	4.588
Lactose	23.3586	93.4344	4.3586	87.172
TOTAL	25		5	

49-				
Mometasone furoate	0.1	0.4	0.1	2
Oladaterol	0.005	0.02	0.005	0.1
Lactose	1.24475	4.979	0.24475	4.895
Glucose anhydrous	23.65025	94.601	4.65025	93.005
TOTAL	25		5	

50-				
Mometasone furoate	0.2	0.8	0.2	4
Oladaterol	0.005	0.02	0.005	0.1
Lactose	1.23975	4.959	0.23975	4.795
Glucose anhydrous	23.55525	94.221	4.55525	91.105
TOTAL	25		5	

51-				
Mometasone furoate	0.1	0.4	0.1	2
Oladaterol	0.005	0.02	0.005	0.1
Glucose anhydrous	1.24475	4.979	0.24475	4.895
Lactose	23.65025	94.601	4.65025	93.005
TOTAL	25		5	

52-				
Mometasone furoate	0.2	0.8	0.2	4
Oladaterol	0.005	0.02	0.005	0.1
Glucose anhydrous	1.23975	4.959	0.23975	4.795
Lactose	23.55525	94.221	4.55525	91.105
TOTAL	25		5	

53-				
Mometasone furcate	0.1	0.4	0.1	2
Arformoterol	0.015	0.06	0.015	0.3
Lactose	1.24425	4.977	0.24425	4.885
Glucose anhydrous	23.64075	94.563	4.64075	92.815
TOTAL	25		5	

54-				
Mometasone furoate	0.2	0.8	0.2	4
Arformoterol	0.015	0.06	0.015	0.3
Lactose	1.23925	4.957	0.23925	4.785
Glucose anhydrous	23.54575	94.183	4.54575	90.915
TOTAL	25		5	

55-				
Mometasone furoate	0.1	0.4	0.1	2
Arformoterol	0.015	0.06	0.015	0.3
Glucose anhydrous	1.24425	4.977	0.24425	4.885
Lactose	23.64075	94.563	4.64075	92.815
TOTAL	25		5	

-continued

56-				
Mometasone furoate	0.2	0.8	0.2	4
Arformoterol	0.015	0.06	0.015	0.3
Glucose anhydrous	1.23925	4.957	0.23925	4.785
Lactose	23.54575	94.183	4.54575	90.915
TOTAL	25		5	

57-				
Mometasone furoate	0.1	0.4	0.1	2
Salmeterol	0.05	0.2	0.05	1
Lactose	1.2425	4.97	0.2425	4.85
Glucose anhydrous	23.6075	94.43	4.6075	92.15
TOTAL	25		5	

58-				
Mometasone furoate	0.2	0.8	0.2	4
Salmeterol	0.05	0.2	0.05	1
Lactose	1.2375	4.95	0.2375	4.75
Glucose anhydrous	23.5125	94.05	4.5125	90.25
TOTAL	25		5	

59-				
Mometasone furoate	0.1	0.4	0.1	2
Salmeterol	0.05	0.2	0.05	1
Glucose anhydrous	1.2425	4.97	0.2425	4.85
Lactose	23.6075	94.43	4.6075	92.15
TOTAL	25		5	

60-				
Mometasone furoate	0.2	0.8	0.2	4
Salmeterol	0.05	0.2	0.05	1
Glucose anhydrous	1.2375	4.95	0.2375	4.75
Lactose	23.5125	94.05	4.5125	90.25
TOTAL	25		5	

61-				
Ciclesonide	0.1	0.4	0.1	2
Vilanterol	0.025	0.1	0.025	0.5
Lactose	1.24375	4.975	0.24375	4.875
Glucose anhydrous	23.63125	94.525	4.63125	92.625
TOTAL	25		5	

62-				
Ciclesonide	0.1	0.4	0.1	
Vilanterol	0.025	0.1	0.025	0.5
Glucose anhydrous	1.24375	4.975	0.24375	4.875
Lactose	23.63125	94.525	4.63125	92.625
TOTAL	25		5	

	Weight and percentage amount			
Content	25 mg	%	5 mg	%
63-				
Tiotropium	0.018	0.072	0.018	0.36
Budesonide	0.2	0.8	0.2	4
Lactose	1.2391	4.9564	0.2391	4.782
Glucose anhydrous	23.5429	94.1716	4.5429	90.858
TOTAL	25		5	
64-				
Tiotropium	0.018	0.072	0.018	0.36
Budesonide	0.2	0.8	0.2	4
Glucose anhydrous	1.2391	4.9564	0.2391	4.782
Lactose	23.5429	94.1716	4.5429	90.858
TOTAL	25		5	

-continued

65-				
Tiotropium	0.018	0.072	0.018	0.36
Budesonide	0.4	1.6	0.4	8
Lactose	1.2291	4.9164	0.2291	4.582
Glucose anhydrous	23.3529	93.4116	4.3529	87.058
TOTAL	25		5	
66-				
Tiotropium	0.018	0.072	0.018	0.36
Budesonide	0.4	1.6	0.4	8
Glucose anhydrous	1.2291	4.9164	0.2291	4.582
Lactose	23.3529	93.4116	4.3529	87.058
TOTAL	25		5	
67-				
Tiotropium	0.018	0.072	0.018	0.36
Fluticasone	0.1	0.4	0.1	2
Lactose	1.2441	4.9764	0.2441	4.882
Glucose anhydrous	23.6379	94.5516	4.6379	92.758
TOTAL	25		5	
68-				
Tiotropium	0.018	0.072	0.018	0.36
Fluticasone	0.1	0.4	0.1	2
Glucose anhydrous	1.2441	4.9764	0.2441	4.882
Lactose	23.6379	94.5516	4.6379	92.758
TOTAL	25		5	
69-				
Tiotropium	0.018	0.072	0.018	0.36
Fluticasone	0.25	1	0.25	5
Lactose	1.2366	4.9464	0.2366	4.732
Glucose anhydrous	23.4954	93.9816	4.4954	89.908
TOTAL	25		5	
70-				
Tiotropium	0.018	0.072	0.018	0.36
Fluticasone	0.25	1	0.25	5
Glucose anhydrous	1.2366	4.9464	0.2366	4.732
Lactose	23.4954	93.9816	4.4954	89.908
TOTAL	25		5	
71-				
Tiotropium	0.018	0.072	0.018	0.36
Fluticasone	0.05	0.2	0.05	1
Lactose	1.2466	4.9864	0.2466	4.932
Glucose anhydrous	23.6854	94.7416	4.6854	93.708
TOTAL	25		5	
72-				
Tiotropium	0.018	0.072	0.018	0.36
Fluticasone	0.05	0.2	0.05	1
Glucose anhydrous	1.2466	4.9864	0.2466	4.932
Lactose	23.6854	94.7416	4.6854	93.708
TOTAL	25		5	

Examples—C

Content	% Weight (a/a)			
Corticosteroid β-adrenergic agonist Anticholinergic Lactose Glucose anhydrous excipient				
	Weight and percentage amount			
Content	mg	%	mg	%
1-				
Budesonide	0.2	0.8	0.2	4
Formoterol	0.012	0.048	0.012	0.24
Tiotropium	0.018	0.072	0.018	0.36
Lactose	1.2385	4.954	0.2385	4.77
Glucose anhydrous	23.5315	94.126	4.5315	90.63
TOTAL	25	100	5	100
2-				
Budesonide	0.2	0.8	0.2	4
Formoterol	0.012	0.048	0.012	0.24
Tiotropium	0.018	0.072	0.018	0.36
Glucose anhydrous	1.2385	4.954	0.2385	4.77
Lactose	23.5315	94.126	4.5315	90.63
TOTAL	25		5	
3-				
Budesonide	0.4	1.6	0.4	8
Formoterol	0.012	0.048	0.012	0.24
Tiotropium	0.018	0.072	0.018	0.36
Lactose	1.2285	4.914	0.2285	4.57
Glucose anhydrous	23.3415	93.366	4.3415	86.83
TOTAL	25	100	5	100
4 -				
Budesonide	0.4	1.6	0.4	8
Formoterol	0.012	0.048	0.012	0.24
Tiotropium	0.018	0.072	0.018	0.36
Glucose anhydrous	1.2285	4.914	0.2285	4.57
Lactose	23.3415	93.366	4.3415	86.83
TOTAL	25		5	
5-				
Ciclesonide	0.2	0.8	0.2	4
Formoterol	0.006	0.024	0.006	0.12
Tiotropium	0.009	0.036	0.009	0.18
Lactose	1.23925	4.957	0.23925	4.785
Glucose anhydrous	23.54575	94.183	4.54575	90.915
TOTAL	25		5	
6-				
Ciclesonide	0.2	0.8	0.2	4
Formoterol	0.006	0.024	0.006	0.12
Tiotropium	0.018	0.072	0.018	0.36
Glucose anhydrous	1.2388	4.9552	0.2388	4.776
Lactose	23.5372	94.1488	4.5372	90.744
TOTAL	25		5	
7-				
Fluticasone	0.1	0.4	0.1	2
salmeterol	0.05	0.2	0.05	1

-continued

Tiotropium	0.018	0.072	0.018	0.36
Lactose	1.2416	4.9664	0.2416	4.832
Glucose anhydrous	23.5904	94.3616	4.5904	91.808
TOTAL	25		5	

8-

Fluticasone	0.1	0.4	0.1	2
salmeterol	0.05	0.2	0.05	1
Tiotropium	0.018	0.072	0.018	0.36
Glucose anhydrous	1.2416	4.9664	0.2416	4.832
Lactose	23.5904	94.3616	4.5904	91.808
TOTAL	25		5	

9-

Fluticasone	0.25	1	0.25	5
salmeterol	0.05	0.2	0.05	1
Tiotropium	0.018	0.072	0.018	0.36
Lactose	1.2341	4.9364	0.2341	4.682
Glucose anhydrous	23.4479	93.7916	4.4479	88.958
TOTAL	25		5	

10-

Fluticasone	0.25	1	0.25	5
salmeterol	0.05	0.2	0.05	1
Tiotropium	0.018	0.072	0.018	0.36
Glucose anhydrous	1.2341	4.9364	0.2341	4.682
Lactose	23.4479	93.7916	4.4479	88.958
TOTAL	25		5	

11-

Fluticasone	0.05	0.2	0.05	1
salmeterol	0.05	0.2	0.05	1
Tiotropium	0.018	0.072	0.018	0.36
Lactose	1.2441	4.9764	0.2441	4.882
Glucose anhydrous	23.6379	94.5516	4.6379	92.758
TOTAL	25		5	

12-

Fluticasone	0.05	0.2	0.05	1
salmeterol	0.05	0.2	0.05	1
Tiotropium	0.018	0.072	0.018	0.36
Glucose anhydrous	1.2441	4.9764	0.2441	4.882
Lactose	23.6379	94.5516	4.6379	92.758
TOTAL	25		5	

13-

Fluticasone	0.1	0.4	0.1	2
Arformeterol	0.015	0.06	0.015	0.3
Tiotropium	0.018	0.072	0.018	0.36
Lactose	1.24335	4.9734	0.24335	4.867
Glucose anhydrous	23.62365	94.4946	4.62365	92.473
TOTAL	25		5	

14-

Fluticasone	0.1	0.4	0.1	
Arformeterol	0.015	0.06	0.015	0.3
Tiotropium	0.018	0.072	0.018	0.36
Glucose anhydrous	1.24335	4.9734	0.24335	4.867
Lactose	23.62365	94.4946	4.62365	92.473
TOTAL	25		5	

15-

Fluticasone	0.25	1	0.25	5
Arformeterol	0.015	0.06	0.015	0.3
Tiotropium	0.018	0.072	0.018	0.36
Lactose	1.23585	4.9434	0.23585	4.717
Glucose anhydrous	23.48115	93.9246	4.48115	89.623
TOTAL	25		5	

16-

Fluticasone	0.25	1	0.25	5
Arformeterol	0.015	0.06	0.015	0.3
Tiotropium	0.018	0.072	0.018	0.36
Glucose anhydrous	1.23585	4.9434	0.23585	4.717
Lactose	23.48115	93.9246	4.48115	89.623
TOTAL	25		5	

17-

Fluticasone	0.05	0.2	0.05	1
Arformeterol	0.015	0.06	0.015	0.3
Tiotropium	0.018	0.072	0.018	0.36
Lactose	1.24585	4.9834	0.24585	4.917
Glucose anhydrous	23.67115	94.6846	4.67115	93.423
TOTAL	25		5	

18-

Fluticasone	0.05	0.2	0.05	1
Arformeterol	0.015	0.06	0.015	0.3
Tiotropium	0.018	0.072	0.018	0.36
Glucose anhydrous	1.24585	4.9834	0.24585	4.917
Lactose	23.67115	94.6846	4.67115	93.423
TOTAL	25		5	

19-

Fluticasone	0.1	0.4	0.1	2
Indacaterol	0.15	0.6	0.15	3
Tiotropium	0.018	0.072	0.018	0.36
Lactose	1.2366	4.9464	0.2366	4.732
Glucose anhydrous	23.4954	93.9816	4.4954	89.908
TOTAL	25		5	

20-

Fluticasone	0.1	0.4	0.1	2
Indacaterol	0.15	0.6	0.15	3
Tiotropium	0.018	0.072	0.018	0.36
Glucose anhydrous	1.2366	4.9464	0.2366	4.732
Lactose	23.4954	93.9816	4.4954	89.908
TOTAL	25		5	

21-

Fluticasone	0.25	1	0.25	5
Indacaterol	0.15	0.6	0.15	3
Tiotropium	0.018	0.072	0.018	0.36
Lactose	1.2291	4.9164	0.2291	4.582
Glucose anhydrous	23.3529	93.4116	4.3529	87.058
TOTAL	25		5	

22-

Fluticasone	0.25	1	0.25	5
Indacaterol	0.15	0.6	0.15	3
Tiotropium	0.018	0.072	0.018	0.36

-continued

Glucose anhydrous	1.2291	4.9164	0.2291	4.582
Lactose	23.3529	93.4116	4.3529	87.058
TOTAL	25		5	

23-

Fluticasone	0.05	0.2	0.05	1
Indacaterol	0.15	0.6	0.15	3
Tiotropium	0.018	0.072	0.018	0.36
Lactose	1.2391	4.9564	0.2391	4.782
Glucose anhydrous	23.5429	94.1716	4.5429	90.858
TOTAL	25		5	

24-

Fluticasone	0.05	0.2	0.05	1
Indacaterol	0.15	0.6	0.15	3
Tiotropium	0.018	0.072	0.018	0.36
Glucose anhydrous	1.2391	4.9564	0.2391	4.782
Lactose	23.5429	94.1716	4.5429	90.858
TOTAL	25		5	

25-

Budesonide	0.2	0.8	0.2	4
Indacaterol	0.15	0.6	0.15	3
Tiotropium	0.018	0.072	0.018	0.36
Lactose	1.2316	4.9264	0.2316	4.632
Glucose anhydrous	23.4004	93.6016	4.4004	88.008
TOTAL	25		5	

26-

Budesonide	0.2	0.8	0.2	4
Indacaterol	0.15	0.6	0.15	3
Tiotropium	0.018	0.072	0.018	0.36
Glucose anhydrous	1.2316	4.9264	0.2316	4.632
Lactose	23.4004	93.6016	4.4004	88.008
TOTAL	25		5	

27-

Budesonide	0.4	1.6	0.4	8
Indacaterol	0.15	0.6	0.15	3
Tiotropium	0.018	0.072	0.018	0.36
Lactose	1.2216	4.8864	0.2216	4.432
Glucose anhydrous	23.2104	92.8416	4.2104	84.208
TOTAL	25		5	

28-

Budesonide	0.4	1.6	0.4	8
Indacaterol	0.15	0.6	0.15	3
Tiotropium	0.018	0.072	0.018	0.36
Glucose anhydrous	1.2216	4.8864	0.2216	4.432
Lactose	23.2104	92.8416	4.2104	84.208
TOTAL	25		5	

29-

Budesonide	0.2	0.8	0.2	4
Olodeterol	0.005	0.02	0.005	0.1
Tiotropium	0.018	0.072	0.018	0.36
Lactose	1.23885	4.9554	0.23885	4.777
Glucose anhydrous	23.53815	94.1526	4.53815	90.763
TOTAL	25		5	

30-

Budesonide	0.2	0.8	0.2	4
Olodeterol	0.005	0.02	0.005	0.1
Tiotropium	0.018	0.072	0.018	0.36
Glucose anhydrous	1.23885	4.9554	0.23885	4.777
Lactose	23.53815	94.1526	4.53815	90.763
TOTAL	25		5	

31-

Budesonide	0.4	1.6	0.4	8
Olodeterol	0.005	0.02	0.005	0.1
Tiotropium	0.018	0.072	0.018	0.36
Lactose	1.22885	4.9154	0.22885	4.577
Glucose anhydrous	23.34815	93.3926	4.34815	86.963
TOTAL	25		5	

32-

Budesonide	0.4	1.6	0.4	8
Olodeterol	0.005	0.02	0.005	0.1
Tiotropium	0.018	0.072	0.018	0.36
Glucose anhydrous	1.22885	4.9154	0.22885	4.577
Lactose	23.34815	93.3926	4.34815	86.963
TOTAL	25		5	

33-

Budesonide	0.2	0.8	0.2	4
Vilanterol	0.025	0.1	0.025	0.5
Tiotropium	0.018	0.072	0.018	0.36
Lactose	1.23785	4.9514	0.23785	4.757
Glucose anhydrous	23.51915	94.0766	4.51915	90.383
TOTAL	25		5	

34-

Budesonide	0.2	0.8	0.2	4
Vilanterol	0.025	0.1	0.025	0.5
Tiotropium	0.018	0.072	0.018	0.36
Glucose anhydrous	1.23785	4.9514	0.23785	4.757
Lactose	23.51915	94.0766	4.51915	90.383
TOTAL	25		5	

35-

Budesonide	0.4	1.6	0.4	8
Vilanterol	0.025	0.1	0.025	0.5
Tiotropium	0.018	0.072	0.018	0.36
Lactose	1.22785	4.9114	0.22785	4.557
Glucose anhydrous	23.32915	93.3166	4.32915	86.583
TOTAL	25		5	

36-

Budesonide	0.4	1.6	0.4	8
Vilanterol	0.025	0.1	0.025	0.5
Tiotropium	0.018	0.072	0.018	0.36
Lactose	1.22785	4.9114	0.22785	4.557
Glucose anhydrous	23.32915	93.3166	4.32915	86.583
TOTAL	25		5	

37-

Mometasone	0.1	0.4	0.1	2
Indacaterol	0.15	0.6	0.15	3
Glikoporonyum	0.1	0.4	0.1	2
Lactose	1.2325	4.93	0.2325	4.65
Glucose anhydrous	23.4175	93.67	4.4175	88.35
TOTAL	25		5	

-continued

38-				
Mometasone	0.1	0.4	0.1	2
Indacaterol	0.15	0.6	0.15	3
Glikoporonyum	0.1	0.4	0.1	2
Glucose anhydrous	1.2325	4.93	0.2325	4.65
Lactose	23.4175	93.67	4.4175	88.35
TOTAL	25		5	
39-				
Mometasone	0.2	0.8	0.2	4
Indacaterol	0.15	0.6	0.15	3
Glikoporonyum	0.1	0.4	0.1	2
Lactose	1.2275	4.91	0.2275	4.55
Glucose anhydrous	23.3225	93.29	4.3225	86.45
TOTAL	25		5	
40-				
Mometasone	0.2	0.8	0.2	4
Indacaterol	0.15	0.6	0.15	3
Glikoporonyum	0.1	0.4	0.1	2
Glucose anhydrous	1.2275	4.91	0.2275	4.55
Lactose	23.3225	93.29	4.3225	86.45
TOTAL	25		5	
41-				
Fluticasone	0.1	0.4	0.1	2
Salmeterol	0.05	0.2	0.05	1
Salbutamol	0.1	0.4	0.1	2
Lactose	1.2375	4.95	0.2375	4.75
Glucose anhydrous	23.5125	94.05	4.5125	90.25
TOTAL	25		5	
42-				
Fluticasone	0.1	0.4	0.1	2
Salmeterol	0.05	0.2	0.05	1
Salbutamol	0.1	0.4	0.1	2
Glucose anhydrous	1.2375	4.95	0.2375	4.75
Lactose	23.5125	94.05	4.5125	90.25
TOTAL	25		5	
43-				
Fluticasone	0.25	1	0.25	5
Salmeterol	0.05	0.2	0.05	1
Salbutamol	0.1	0.4	0.1	2
Lactose	1.23	4.92	0.23	4.6
Glucose anhydrous	23.37	93.48	4.37	87.4
TOTAL	25		5	
44-				
Fluticasone	0.25	1	0.25	5
Salmeterol	0.05	0.2	0.05	1
Salbutamol	0.1	0.4	0.1	2
Glucose anhydrous	1.23	4.92	0.23	4.6
Lactose	23.37	93.48	4.37	87.4
TOTAL	25		5	
45-				
Fluticasone	0.5	2	0.5	10
Salmeterol	0.05	0.2	0.05	1
Salbutamol	0.1	0.4	0.1	2
Lactose	1.2175	4.87	0.2175	4.35
Glucose anhydrous	23.1325	92.53	4.1325	82.65
TOTAL	25		5	
46-				
Fluticasone	0.5	2	0.5	10
Salmeterol	0.05	0.2	0.05	1
Salbutamol	0.1	0.4	0.1	2
Glucose anhydrous	1.2175	4.87	0.2175	4.35
Lactose	23.1325	92.53	4.1325	82.65
TOTAL	25		5	
47 -				
Fluticasone	0.1	0.4	0.1	2
Arformeterol	0.015	0.06	0.015	0.3
Salbutamol	0.1	0.4	0.1	2
Lactose	1.23925	4.957	0.23925	4.785
Glucose anhydrous	23.54575	94.183	4.54575	90.915
TOTAL	25		5	
48-				
Fluticasone	0.1	0.4	0.1	2
Arformeterol	0.015	0.06	0.015	0.3
Salbutamol	0.1	0.4	0.1	2
Glucose anhydrous	1.23925	4.957	0.23925	4.785
Lactose	23.54575	94.183	4.54575	90.915
TOTAL	25		5	
49-				
Fluticasone	0.25	1	0.25	5
Arformeterol	0.015	0.06	0.015	0.3
Salbutamol	0.1	0.4	0.1	2
Lactose	1.23175	4.927	0.23175	4.635
Glucose anhydrous	23.40325	93.613	4.40325	88.065
TOTAL	25		5	
50-				
Fluticasone	0.25	1	0.25	5
Arformeterol	0.015	0.06	0.015	0.3
Salbutamol	0.1	0.4	0.1	2
Glucose anhydrous	1.23175	4.927	0.23175	4.635
Lactose	23.40325	93.613	4.40325	88.065
TOTAL	25		5	
51-				
Fluticasone	0.5	2	0.5	10
Arformeterol	0.015	0.06	0.015	0.3
Salbutamol	0.1	0.4	0.1	2
Lactose	1.21925	4.877	0.21925	4.385
Glucose anhydrous	23.16575	92.663	4.16575	83.315
TOTAL	25		5	
52-				
Fluticasone	0.5	2	0.5	10
Arformeterol	0.015	0.06	0.015	0.3
Salbutamol	0.1	0.4	0.1	2
Glucose anhydrous	1.21925	4.877	0.21925	4.385
Lactose	23.16575	92.663	4.16575	83.315
TOTAL	25		5	

Compositions according to the invention are manufactured by the processes of the state of art in such a way that they include mixtures of fine particle lactose-coarse particle

glucose anhydrous, fine particle glucose anhydrous-coarse particle lactose and the active ingredients.

For fine particle carriers (lactose or glucose anhydrous) might be in the range of:

d10; 1.0-5.0 μm or d10; 1.0-4.0 μm,

d50; 4.0-10.0 μm or d50; 4.0-7.0 μm,

d90; 7.0-20.0 μm or d90; 7.0-15.0 μm.

For coarse particle carriers (lactose or glucose anhydrous) might be in the range of:

d10; 10.0-50.0 μm

d50; 50.0-120.0 μm or d50; 50.0-75.0 μm,

d90; 120.0-300.0 μm or d90; 75.0-250.0 μm.

Said compositions may be formed as:

i. Active ingredient+fine particle lactose+coarse particle glucose anhydrous,

ii. Active ingredient+fine particle lactose+coarse particle lactose,

iii. Active ingredient+fine particle lactose+fine particle glucose anhydrous+coarse particle glucose anhydrous,

iv. Active ingredient+fine particle lactose+fine particle glucose anhydrous+coarse particle lactose,

v. Active ingredient+fine particle lactose+coarse particle glucose anhydrous+coarse particle lactose,

vi. Active ingredient+fine particle lactose+fine particle glucose anhydrous+coarse particle glucose anhydrous+ coarse particle lactose.

Surprisingly, said glucose anhydrous in the invention increases stability by absorbing moisture to it contained in the active ingredients inside the blister having air and moisture barriers or the airtight and moisture-tight capsule. Dehumidification of the active ingredient or ingredients bring the stability values to desired level. Furthermore, by means of ideal lactose and glucose anhydrous ratio and their determined particle sizes, compositions with content uniformity are developed. In addition to this, dosage accuracy present in each cavity or capsule is ensured as well. These preferred values facilitate the flowing and filling of the components as well, during the process. It is ensured that a homogeneous mixture is obtained and this filling is economical and fast.

Coarse carrier particles are used in or order to prevent agglomeration (anew) of the fine particles of the active ingredient. In order to obtain this effect, a carrier, the particle size of which is 10 times that of the active ingredient is used. In general, a single layer composed of the active ingredient particles is formed over the large carrier particles. During inhalation, as the active ingredient and the carrier substance need to be separated from each other, shape and surface roughness of the carrier particles are especially important. Particles of smooth surface will be separated much easier from the active ingredient compared to the particles in the same size but of high porosity.

Fine carrier particles are used so as to assist the active ingredient to reach to the lungs safer and in high doses. Active ingredient will tend to concentrate on the regions having higher energy as the surface energy normally does not dissipate on the carrier particle evenly. This might obstruct the active ingredient to separate from the carrier after pulmonary administration, especially in low dose formulations. As the high-energy regions will be covered by fine carrier particles and thus the active ingredient will tend to bind to low energy regions, usage of small fine carrier particles, size of which are less than 10.0 microns or 5.0 microns will help to prevent this situation. It has been discovered that by increasing the fraction of the fine carrier particles, taking into lungs will also increase. According to this, a decrease in the particle size (having finer particles) increases the fluidizing energy and this, in return, increases the amount of drug reached to the lungs.

Drug particles will adhere then to weak adhesion regions and will be released easier during inhalation. Surface area will significantly increase upon addition of fine particles and carrying capacity will decrease. The fact that the fine carrier particles are slightly coarser than the drug particles is sufficient to eliminate the frictional forces between the drug and the carrier during mixing process.

Another object of the invention is to adjust the fluidity of the formulations accurately in order to ensure that correct amounts of active ingredient are given to the DPIs by suitable devices. In other words, present invention provides freely-flowable formulations by choosing right carriers in order to ensure continuous production of formulations, mechanical filling of the powder inhaler, right dosage and release with powder inhaler.

Another object of the invention is to prevent agglomeration by using a suitable carrier except lactose. Active particles have fine or sometimes micro-fine particles in order to be able to penetrate deep into lungs. For this reason, these small drug particles tend to agglomerate.

In an ideal drug carrier system, binding of the active ingredient to the carrier should be as strong as to prevent decaying of the mixture yet it should be so strong as the active ingredient and the carrier need to separate during inhalation. Accordingly, shape of the carrier particles and surface roughness are of particular importance. Spray-dried glucose anhydrous particles are observed to detach from the active ingredient easier in comparison with the particles of high porosity in same size. Since, spray-dried glucose anhydrous forms more particles of spherical shape and a smooth surface. The characteristic of such particles is that they have a smaller contact area and a smaller and more homogeneous particle size distribution, which leads the inhalable particles to be more, compared to the carriers the diameters of which are diminished mechanically. An advantage of using spray-dried glucose anhydrous is to obtain particles in which the particle size distribution is narrow and the diameters are of a few micrometers. And this ensures the drug embedded in the trachea-bronchial and deep alveoli regions to be stored at maximum ratios by normal inhalation rate, once the suitable particle size is obtained. Furthermore, spray-dried glucose anhydrous exhibits narrow particle size, i.e., the ratio between the particle size (d50) and (d90) is equal to 0.40 or greater. The ratio between the (d50) particle size and d90 is preferably between 0.45 and 0.50, more preferably between 0.50 and 0.70.

In addition to this, this narrow particle size distribution that is equal to 0.40 or greater applies also to glucose anhydrous contained in the compositions of present invention. Preferably, narrow particle size distribution is between 0.45 and 0.50, more preferably between 0.50 and 0.70.

Particle size analysis is performed by MALVERN MASTERSIZER 200™ (a device for determining particle size based on laser diffraction) with laser diffraction technique. According to selected active ingredient may prefer particle characterization techniques that it can be wet dispersion (particles dispersed in a liquid) or dry dispersion (particles dispersed in a gas (usually air)). Particle size distribution measure volume-basis.

According to a preferred embodiment of the invention, therapeutically active amount of said pharmaceutical compositions is administered once a day and/or twice a day.

According to a preferred embodiment, pharmaceutical compositions are used in the treatment of the respiratory diseases selected from asthma and chronic obstructive pul-

monary disease and other obstructive respiratory diseases. Combinations of present invention are particularly useful in the treatment of the respiratory diseases or disorders including asthma, acute respiratory failure, chronic pulmonary inflammatory disease, bronchitis, chronic bronchitis, chronic obstructive pulmonary disease and silicosis or immune diseases and disorders including allergic rhinitis or chronic sinusitis.

According to another application, pharmaceutical compositions are suitable for separate, respective or simultaneous administration with a blister resistant to moisture and encapsulated with a secure barrier or with a capsule.

Blister especially contains aluminum in order to prevent moisture intake and thereby fine particle fraction (FPF) of the dose of the pharmaceutical composition is maintained. Blister is further encapsulated with a secure barrier resistant to moisture. By this means, blister prevents water penetration into the drug dose and moisture intake from outside into the container has been prevented.

In another preferred embodiment of the invention, dry powder is inside a capsule and this capsule may be a gelatin or a natural or synthetic pharmaceutically acceptable polymer such as hydroxypropyl methylcellulose.

Dosage amounts of 25 mg are stored inside air-tight and moisture-tight capsules, whereas dosage amounts of 5 mf are stored inside blisters.

Moreover, as said formulas may contain active ingredient in amounts of 3 or 5 mg alone or else in the amounts that are the multiples of 3 or 5 mg, it is also possible to manufacture combinations of said active ingredient comprising the amounts of 3 or 5 mg or else that are the multiples of 3 or 5 mg.

A pharmaceutically acceptable salt, solvate, polymorph or racemic mixture of said active ingredient may also be used.

Said ciclesonide may contain pharmaceutically acceptable salt, solvate, polymorph or racemic mixture thereof.

Said budesonide may contain pharmaceutically acceptable salt, solvate, polymorph or racemic mixture thereof.

As said fluticasone may contain pharmaceutically acceptable salt, solvate, polymorph or racemic mixture thereof, it is preferably propionate or fluticasone furoate.

As said mometasone may contain pharmaceutically acceptable salt, solvate, polymorph or racemic mixture thereof, it is preferably mometasone furoate or mometasone furoate anhydrate.

As said tiotropium may contain pharmaceutically acceptable salt, solvate, polymorph or racemic mixture thereof, it is preferably tiotropium bromide.

As said glycopyrronium may contain pharmaceutically acceptable salt, solvate, polymorph or racemic mixture thereof, it is preferably glycopyrronium bromide.

Said aclinidium may contain pharmaceutically acceptable salt, solvate, polymorph or racemic mixture thereof.

As said darotropium may contain pharmaceutically acceptable salt, solvate, polymorph or racemic mixture thereof, it is preferably darotropium bromide.

As said salmaterol may contain pharmaceutically acceptable salt, solvate, polymorph or racemic mixture thereof, it is preferably salmeterol xinafoate.

As said formoterol may contain pharmaceutically acceptable salt, solvate, polymorph or racemic mixture thereof, it is preferably formoterol fumarate.

As said arfomoterol may contain pharmaceutically acceptable salt, solvate, polymorph or racemic mixture thereof, it is preferably arfomoterol tartarrate.

As said indacaterol may contain pharmaceutically acceptable salt, solvate, polymorph or racemic mixture thereof, it is preferably indaceterol maleate.

Said salbutamol may contain pharmaceutically acceptable salt, solvate, polymorph or racemic mixture thereof.

Said vilanterol may contain pharmaceutically acceptable salt, solvate, polymorph or racemic mixture thereof.

Said carmoterol may contain pharmaceutically acceptable salt, solvate, polymorph or racemic mixture thereof.

Said olodaterol may contain pharmaceutically acceptable salt, solvate, polymorph or racemic mixture thereof.

Said compositions are inserted in a dry powder inhaler device containing a blister and a cap. Said device has at least one locking mechanism ensuring the device to be maintained locked in both of the positions in which it is ready for inhalation and its cap is closed and ensuring the device to be automatically re-set once the cap is closed.

Subsequent to opening of the device cap, a force is exerted to the device cock by the user. Afterwards, the cock is bolted by being guided by the tracks within the body of the device and the tracks on itself. Mechanism is assured to function via this action. In the end of bolting, cock is locked upon clamping and single dose drug come out of the blister is enabled to be administered. Pushing of the cock by the user completely until the locking position ensures the blister to be completely peeled off and the dosage amount to be accurately administered. As a result of this locking cock is immobilized and is disabled for a short time. This pushing action further causes the spring inside the mechanism to be compressed between the cock and the inner body of the device. Said device becomes ready to re-use following the closing of the cap by the user after the administration of the powder composition, without needing to be set again, thanks to the mechanism involved.

When said compositions are used in a dry powder inhaler comprising capsule, said capsule is put one by one in the device and used by means of exploding the capsule.

The invention claimed is:

1. A dry powder inhalation composition comprising,

at least one corticosteroid or a pharmaceutically acceptable salt thereof,

fine particle lactose in an amount of 1-20% by weight of said composition and having d50 particle size in the range of 4-10 μm and coarse particle anhydrous glucose in an amount of 80-99% by weight of said composition and having a d50 particle size in the range of 50-120 μm.

2. The pharmaceutical composition according to claim **1**, wherein the d50 particle size of said fine particle lactose is 4-7 μm.

3. The pharmaceutical composition according to claim **1**, wherein a d50 particle size of said coarse particle anhydrous glucose is 50-75 μm.

4. The pharmaceutical composition according to claim **1**, further comprising coarse particle lactose with a d50 particle size of 50-80 μm or of 50-75 μm, coarse particle lactose with a d10 particle size of 10-50 μm, and/or coarse particle lactose with a d90 particle size of 120-300 μm or 75-250 μm.

5. The pharmaceutical composition according to claim **1**, further comprising fine particle anhydrous glucose with a d50 particle size of 4-7 μm, fine particle anhydrous glucose with a d10 particle size of 1-5 μm or 1-4 μm; and/or fine particle anhydrous glucose with a d90 particle size of 10-20 μm or 7-10 μm.

6. The pharmaceutical composition according to claim **1**, wherein the amount of said lactose is in the range of 1-15%, or 1-10%, by weight.

7. The pharmaceutical composition according to claim 1, wherein the amount of said anhydrous glucose is in the range of 85-99%, or 90-99%, by weight of the composition.

8. The pharmaceutical composition according to claim 1, wherein, said corticosteroid is selected from the group consisting of at least one or a mixture of ciclesonide, budesonide, fluticasone, aldosterone, beclomethasone, betametazone, chloprednol, cortisone, cortivasol, deoxycortone, desonide, desoxymethasone, dexamethasone, difluocortolone, fluchloralin, flumetasone, flunisolide, fluocinolone, fluocinonide, flurocortisone, fluocortolone, flurometolone, flurandrenolone, halcinonide, hydrocortisone, icometasone, meprednisone, methylprednisolone, mometasone, paramethasone, prednisolone, prednisone, tixocortole, and/or triamcinolone.

9. The pharmaceutical composition according to claim 8, wherein, said corticosteroid is selected from the group consisting of ciclesonide, budesonide, fluticasone, and mometasone.

10. The pharmaceutical composition according to claim 1, further comprising (a) one or more β2-adrenergic agonists; (b) one or more muscarinic receptor antagonists; or (c) one or more β2-adrenergic agonists and one or more muscarinic receptor antagonists.

11. The pharmaceutical composition according to claim 10, wherein, said muscarinic receptor antagonist is selected from the group consisting of at least one or a mixture of tiotropium, glycopyronium, aclidinium, darotropium, and ipratropium.

12. The pharmaceutical composition according to claim 10, wherein, said beta-2 adrenergic agonist is selected from the group consisting of at least one or a mixture of salmeterol, formoterol, arformoterol, salbutamol, indacaterol, terbutaline, metaproterenol, vilanterol, carmoterol, olodaterol, bambuterol, and clenbuterol.

13. The pharmaceutical composition according to claim 1, further comprising at least one excipient selected from the group consisting of glucose, mannitol, sorbitol, trehalose, and cellobiose.

14. The pharmaceutical composition according to claim 1, wherein, said composition comprises one of the following therapeutically active combinations:

i. Budesonide and indacaterol,
ii. Budesonide and oladaterol,
iii. Budesonide and vilanterol,
iv. Budesonide and salmeterol,
v. Budesonide and formoterol,
vi. Budesonide and carmoterol,
vii. Budesonide and arformoterol,
viii. fluticasone and formoterol,
ix. fluticasone and salmeterol,
x. fluticasone and vilanterol,
xi. fluticasone and indacaterol,
xii. fluticasone and olodaterol,
xiii. fluticasone and carmoterol,
xiv. fluticasone and arformoterol,
xv. fluticasone and salbutamol,
xvi. mometasone and formoterol,
xvii. mometasone and indacaterol,
xviii. mometasone and vilanterol,
xix. mometasone and olodaterol,
xx. mometasone and carmoterol,
xxi. mometasone and arformoterol,
xxii. mometasone and salmeterol,
xxiii. ciclesonide and formoterol,
xxiv. ciclesonide and vilanterol,
xxv. ciclesonide and indacaterol,
xxvi. ciclesonide and olodaterol,
xxvii. ciclesonide and carmoterol,
xxviii. ciclesonide and arformoterol,
xxix. ciclesonide and salmeterol,
xxx. budesonide and tiotropium,
xxxi. fluticasone and tiotropium,
xxxii. mometason and tiotropium,
xxxiii. ciclesonide and tiotropium,
xxxiv. budesonide, formoterol and tiotropium,
xxxv. budesonide, salmeterol and tiotropium,
xxxvi. budesonide, arformoterol and tiotropium,
xxxvii. budesonide, carmoterol and tiotropium,
xxxviii. ciclesonide, formoterol and tiotropium,
xxxix. ciclesonide, salmeterol and tiotropium,
xl. ciclesonide, carmoterol and tiotropium,
xli. ciclesonide, arformoterol and tiotropium,
xlii. ciclesonide, indacaterol and tiotropium,
xliii. ciclesonide, olodaterol and tiotropium,
xliv. ciclesonide, vilanterol and tiotropium,
xlv. fluticasone, salmeterol and tiotropium,
xlvi. fluticasone, formoterol and tiotropium,
xlvii. fluticasone, arfomoterol and tiotropium,
xlviii. fluticasone, carmoterol and tiotropium,
xlix. fluticasone, vilanterol and tiotropium,
l. fluticasone, olodaterol and tiotropium,
li. fluticasone, indacaterol and tiotropium,
lii. budesonide, indacaterol and tiotropium,
liii. budesonide, olodaterol and tiotropium,
liv. budesonide, vilanterol and tiotropium,
lv. mometasone, salmeterol and tiotropium,
lvi. mometasone, formoterol and tiotropium,
lvii. mometasone, indacaterol and tiotropium,
lviii. mometasone, vilanterol and tiotropium,
lix. mometasone, oladaterol and tiotropium,
lx. mometasone, arformoterol and tiotropium,
lxi. mometasone, indacaterol and glycopyrronium,
lxii. mometasone, salmeterol and glycopyrronium,
lxiii. mometasone, formoterol and glycopyrronium,
lxiv. mometasone, carmoterol and glycopyrronium,
lxv. mometasone, olodaterol and glycopyrronium,
lxvi. mometasone, vilanterol and glycopyrronium,
lxvii. fluticasone, salmeterol and salbutamol, and
lxviii. fluticasone, arformeterol and salbutamol.

15. The pharmaceutical composition according to claim 1, wherein said composition is in a blister having air and moisture barrier property, enabling simultaneous, respective and synchronic application.

16. The pharmaceutical composition according to claim 1, wherein said composition is in a blister in a dry powder inhaler device suitable for simultaneous, respective and synchronic application, wherein the inhaler device has at least one locking mechanism ensuring the device to be maintained locked in both of the positions in which the inhaler device is ready for inhalation and the lid of the inhaler device is closed and ensuring the device to be automatically re-set once the lid is closed.

17. The pharmaceutical composition according to claim 1, wherein, said composition comprises a dry powder inhaler device suitable for simultaneous, respective and synchronic application in a capsule.

18. The pharmaceutical composition according to claim 1, wherein the coarse particle anhydrous glucose has a ratio of the d50 particle size/d90 particle size equal to 0.40 or greater.

19. The pharmaceutical composition according to claim 1, wherein the coarse particle anhydrous glucose has a ratio of the d50 particle size/d90 particle size between 0.45 and 0.50.

20. The pharmaceutical composition according to claim **1**, wherein the coarse particle anhydrous glucose has a ratio of the d50 particle size/d90 particle size between 0.50 and 0.70.

21. The pharmaceutical composition according to claim **18**, wherein the coarse particle anhydrous glucose comprises spray-dried anhydrous glucose.

22. The pharmaceutical composition according to claim **19**, wherein the coarse particle anhydrous glucose comprises spray-dried anhydrous glucose.

23. The pharmaceutical composition according to claim **20**, wherein the coarse particle anhydrous glucose comprises spray-dried anhydrous glucose.

24. The pharmaceutical composition according to claim **3**, wherein the coarse particle anhydrous glucose has a ratio of the d50 particle size/d90 particle size equal to 0.40 or greater.

25. The pharmaceutical composition according to claim **3**, wherein the coarse particle anhydrous glucose has a ratio of the d50 particle size/d90 particle size between 0.45 and 0.50.

26. The pharmaceutical composition according to claim **3**, wherein the coarse particle anhydrous glucose has a ratio of the d50 particle size/d90 particle size between 0.50 and 0.70.

27. The pharmaceutical composition according to claim **1**, wherein said fine particle lactose has a d10 particle size of 1-5 μm.

28. The pharmaceutical composition according to claim **1**, wherein said fine particle lactose has a d90 particle size of 7-20 μm.

29. The pharmaceutical composition according to claim **1**, wherein said coarse particle anhydrous glucose has a d10 particle size of 10-50 μm.

30. The pharmaceutical composition according to claim **1**, wherein said coarse particle anhydrous glucose has a d90 particle size of 120-300 μm.

31. The pharmaceutical composition according to claim **27**, wherein said fine particle lactose has a d10 particle size of 1-4 μm.

32. The pharmaceutical composition according to claim **28**, wherein said fine particle lactose has a d90 particle size of 7-15 μm.

33. The pharmaceutical composition according to claim **30**, wherein said coarse particle anhydrous glucose has a d90 particle size of 75-250 μm.

34. The pharmaceutical composition according to claim **29**, wherein said coarse particle anhydrous glucose has a d90 particle size of 75-250 μm.

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