3.2.P.1 DESCRIPTION AND COMPOSITION OF THE DRUG PRODUCT

BDP+FORMOTEROL+GLYCOPYRRONIUM 100/6/12.5 µG PRESSURISED INHALATION SOLUTION

3.2.P.1.1 PRODUCT DESCRIPTION

BDP+FORMOTEROL+GLYCOPYRRONIUM 100/6/12.5 µG PRESSURISED INHALATION SOLUTION

The drug product is a pressurised metered dose inhaler (pMDI) containing Beclometasone dipropionate (BDP) 100 µg/actuation plus Formoterol fumarate dihydrate (FF) 6 µg/actuation plus Glycopyrronium bromide (GB) 12.5 µg/actuation in an ethanolic solution, propelled by HFA-134a (norflurane) delivering nominally 60, 120 and 180 actuations/canister.
The primary container for the inhalation solution is an aluminium coated pressurized canister fitted with a 63 µL metering valve and using a polypropylene actuator for inhalation, integrated with a dose counter system (60 and 120 actuations/canister presentations) or dose indicator system (180 actuations/canister presentation).

3.2.P.1.2 COMPOSITION

BDP+FORMOTEROL+GLYCOPYRRONIUM 100/6/12.5 µG PRESSURISED INHALATION SOLUTION

The composition of the drug product ***CHF 5993 pMDI 100+6+12.5 µg/actuation*** (60, 120 and 180 actuations/canister) is given in Table 3.2.P.1/ 1, Table 3.2.P.1/ 2, Table 3.2.P.1/ 3 below.

Table 3.2.P.1/ 1: Composition of drug product *(CHF 5993 pMDI 100+6+12.5 µg/actuation)*, 60 actuations/canister

Ingredients	Unit formula		Function	Ref. standard
	per actuation (mg)	per canister (mg) *		
Beclometasone dipropionate	0.10000	10.0000	Drug substance	3.2.S/3.2.R Ph.Eur. current edition
Formoterol fumarate dihydrate	0.00600	0.6000	Drug substance	3.2.S/3.2.R Ph.Eur. current edition
Glycopyrronium bromide	0.01250	1.2500	Drug substance	3.2.S/3.2.R Ph.Eur. current edition
Ethanol anhydrous	8.85600	885.6000	Co-solvent	Ph.Eur. current edition
Hydrochloric acid 1 M	0.01344	1.3440	pH adjuster	Ph.Eur. current edition
HFA-134a (norflurane)	64.81206	6481.2060	Propellant	3.2.P.4 Ph.Eur. current edition

* includes an over-filling corresponding to solution sufficient for 40 actuations

Table 3.2.P.1/ 2: Composition of drug product (CHF 5993 pMDI 100+6+12.5 µg/actuation), 120 actuations/canister

Ingredients	Unit formula		Function	Ref. standard
	per actuation (mg)	per canister (mg) *		
Beclometasone dipropionate	0.10000	16.0000	Drug substance	3.2.S/3.2.R Ph.Eur. current edition
Formoterol fumarate dihydrate	0.00600	0.9600	Drug substance	3.2.S/3.2.R Ph.Eur. current edition
Glycopyrronium bromide	0.01250	2.0000	Drug substance	3.2.S/3.2.R Ph.Eur. current edition
Ethanol anhydrous	8.85600	1416.9600	Co-solvent	Ph.Eur. current edition
Hydrochloric acid 1 M	0.01344	2.1504	pH adjuster	Ph.Eur. current edition
HFA-134a (norflurane)	64.81206	10369.9296	Propellant	3.2.P.4 Ph.Eur. current edition

* includes an over-filling corresponding to solution sufficient for 40 actuations

Table 3.2.P.1/ 3: Composition of drug product *(CHF 5993 pMDI 100+6+12.5 µg/actuation)*, 180 actuations/canister

Ingredients	Unit formula		Function	Ref. standard
	per actuation (mg)	per canister (mg) *		
Beclometasone dipropionate	0.10000	22.0000	Drug substance	3.2.S/3.2.R Ph.Eur. current edition
Formoterol fumarate dihydrate	0.00600	1.3200	Drug substance	3.2.S/3.2.R Ph.Eur. current edition
Glycopyrronium bromide	0.01250	2.7500	Drug substance	3.2.S/3.2.R Ph.Eur. current edition
Ethanol anhydrous	8.85600	1948.3200	Co-solvent	Ph.Eur. current edition
Hydrochloric acid 1 M	0.01344	2.9568	Formulation stabiliser	Ph.Eur. current edition
HFA-134a (norflurane)	64.81206	14258.6532	Propellant	3.2.P.4 Ph.Eur. current edition

* includes an over-filling corresponding to solution sufficient for 40 actuations

Nominal content per actuation: each nominal metered actuation supplies 100 µg BDP, 6 µg FF and 12.5 µg GB corresponding to 87.4 µg, 5.2 µg and 10.9 µg, as delivered dose, respectively.

Container: the drug product is supplied in aluminium coated canister fitted with a metering valve (metering chamber nominal capacity 63µL) and an actuator integrated in a Dose Counter system (for 60 and 120 actuations/canister presentations) and a Dose Indicator system (for 180 actuations/canister presentation) as detailed in section *3.2.P.7*.

***CHF 5993 pMDI 100+6+12.5 µg/actuation* 60 actuations/canister**
Number of actuations stated on the label: 60 actuations/canister.
Content weight: 7.380 g per canister.
An over-filling of solution corresponding to 40 actuations has been included in the formula of the drug product to ensure delivery of the number of actuations stated on the label throughout the shelf-life of the product.

***CHF 5993 pMDI 100+6+12.5 µg/actuation* 120 actuations/canister**
Number of actuations stated on the label: 120 actuations/canister.
Content weight: 11.808 g per canister.
An over-filling of solution corresponding to 40 actuations has been included in the formula of the drug product to ensure delivery of the number of actuations stated on the label throughout the shelf-life of the product.

***CHF 5993 pMDI 100+6+12.5 µg/actuation* 180 actuations/canister**
Number of actuations stated on the label: 180 actuations/canister.
Content weight: 16.236 g per canister.
An over-filling of solution corresponding to 40 actuations has been included in the formula of the drug product to ensure delivery of the number of actuations stated on the label throughout the shelf-life of the product.

Note to the Reviewer(s):

1) Through the Quality sections of the CTD the following convention was used for the product name: BDP+Formoterol+Glycopyrronium 100/6/12.5 µg Pressurised Inhalation Solution. This is equivalent to "CHF 5993 100 µg/6 µg/12.5 µg per dose pressurised inhalation solution", or "CHF 5993 pMDI 100+6+12.5 µg/actuation" or "CHF 5993" in short, which may be indicated elsewhere in the CTD.