Medicines & Healthcare products Regulatory Agency

MHRA

# Public Assessment Report

# National Procedure

# Luforbec 100/6 micrograms per actuation pressurised inhalation solution

# (beclometasone dipropionate and formoterol fumarate dihydrate)

# PL 35507/0204

# Lupin Healthcare (UK) Limited

# LAY SUMMARY

## Luforbec 100/6 micrograms per actuation pressurised inhalation solution (beclometasone dipropionate and formoterol fumarate dihydrate)

This is a summary of the Public Assessment Report (PAR) for Luforbec 100/6 micrograms per actuation pressurised inhalation solution. It explains how this product was assessed and its authorisation recommended, as well as its conditions of use. It is not intended to provide practical advice on how to use this product.

This product will be referred to as Luforbec in this lay summary for ease of reading.

For practical information about using Luforbec, patients should read the Patient Information Leaflet (PIL) or contact their doctor or pharmacist.

### What is Luforbec and what is it used for?

This application is for a hybrid medicine. This means that the medicine is similar to a reference medicine already authorised in the United Kingdom (UK) called Fostair 100/6 micrograms per actuation pressurised inhalation solution.

Luforbec is indicated in the regular treatment of asthma in adult patients in whom:

- asthma is not adequately controlled by using inhaled corticosteroids and "as needed" short-acting bronchodilators

or

- asthma is responding well to treatment with both corticosteroids and long-acting bronchodilators.

Luforbec can also be used to treat the symptoms of severe COPD in adult patients. COPD is a long term disease of the airways in the lungs which is primarily caused by cigarette smoking.

### How does Luforbec work?

Luforbec is a pressurised inhalation solution containing two active substances which are inhaled through the mouth and delivered directly into the lungs.
The two active substances are beclometasone dipropionate and formoterol fumarate dihydrate. Beclometasone dipropionate belongs to a group of medicines called corticosteroids which have an anti-inflammatory action reducing the swelling and irritation in the lungs.
Formoterol fumarate dihydrate belongs to a group of medicines called long-acting bronchodilators which relax the muscles in the airways and helps the patient to breathe more easily.
Together these two active substances make breathing easier, by providing relief from symptoms such as shortness of breath, wheezing and cough in patients with asthma or chronic obstructive pulmonary disease (COPD) and also help to prevent the symptoms of asthma.

### How is Luforbec used?

The pharmaceutical form of this medicine is pressurised inhalation solution and the route of administration is via inhalation through the mouth.

Luforbec contains two active substances beclometasone dipropionate and formoterol fumarate dihydrate. Beclometasone dipropionate belongs to a group of medicines called corticosteroids which have an anti-inflammatory action reducing the swelling and irritation in

the lungs. Formoterol fumarate dihydrate belongs to a group of medicines called long-acting bronchodilators which relax the muscles in the airways and helps the patient to breathe more easily. Together these two active substances make breathing easier, by providing relief from symptoms such as shortness of breath, wheezing and cough in patients with asthma or chronic obstructive pulmonary disease (COPD) and also help to prevent the symptoms of asthma.

For further information on how Luforbec is used, refer to the PIL and Summary of Product Characteristics (SmPC) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

This medicine can only be obtained with a prescription.

The patient should always take this medicine exactly as their doctor/pharmacist has told them. The patient should check with their doctor or pharmacist if they are not sure.

**What benefits of Luforbec have been shown in studies?**
Because Luforbec is a hybrid medicine, studies in healthy volunteers consist of tests to determine that it is therapeutically equivalent to the reference medicine.

**What are the possible side effects of Luforbec?**
For the full list of all side effects reported with this medicine, see Section 4 of the PIL or the SmPC available on the MHRA website.

If a patient gets any side effects, they should talk to their doctor, pharmacist or nurse. This includes any possible side effects not listed in the product information or the PIL that comes with the medicine. Patients can also report suspected side effects themselves, or a report can be made on behalf of someone else they care for, directly via the Yellow Card scheme at www.mhra.gov.uk/yellowcard or search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of this medicine.

Because Luforbec is a hybrid medicine and is therapeutically equivalent to the reference medicine, its benefits and possible side effects are taken as being the same as the reference medicine.

**Why was Luforbec approved?**
It was concluded that Luforbec has been shown to be therapeutically equivalent to the reference medicine. Therefore, the MHRA decided that, as for the reference medicine, the benefits are greater than the risks and recommended that it can be approved for use.

**What measures are being taken to ensure the safe and effective use of Luforbec?**
A Risk Management Plan (RMP) has been developed to ensure that Luforbec is used as safely as possible. Based on this plan, safety information has been included in the SmPC and the PIL, including the appropriate precautions to be followed by healthcare professionals and patients.

Known side effects are continuously monitored. Furthermore, new safety signals reported by patients/healthcare professionals will be monitored and reviewed continuously.

**Other information about Luforbec**
A Marketing Authorisation for Luforbec was granted in the United Kingdom (UK) on 11 June 2021.

The full PAR for Luforbec follows this summary.

This summary was last updated in August 2021.

# TABLE OF CONTENTS

# I INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the application for Luforbec 100/6 micrograms per actuation pressurised inhalation solution (PL 35507/0204) could be approved.

The product is approved for the following indications:

***Asthma***

Luforbec 100/6 micrograms per actuation pressurised inhalation solution is indicated in the regular treatment of asthma where use of a combination product (inhaled corticosteroid and long-acting beta$_2$-agonist) is appropriate:

- patients not adequately controlled with inhaled corticosteroids and 'as needed' inhaled rapid-acting beta$_2$-agonist or
- patients already adequately controlled on both inhaled corticosteroids and long-acting beta$_2$-agonists.

***COPD***

Symptomatic treatment of patients with severe COPD (FEV1 < 50% predicted normal) and a history of repeated exacerbations, who have significant symptoms despite regular therapy with long-acting bronchodilators.

Luforbec 100/6 micrograms per actuation pressurised inhalation solution contains beclometasone dipropionate and formoterol. These two actives have different modes of action. In common with other inhaled corticosteroids and beta$_2$-agonist combinations, additive effects are seen in respect of reduction in asthma exacerbations.

Beclometasone dipropionate given by inhalation at recommended doses has a glucocorticoid anti-inflammatory action within the lungs, resulting in reduced symptoms and exacerbations of asthma with less adverse effects than when corticosteroids are administered systemically.

Formoterol is a selective beta$_2$-adrenergic agonist that produces relaxation of bronchial smooth muscle in patients with reversible airways obstruction. The bronchodilating effect sets in rapidly, within 1-3 minutes after inhalation, and has a duration of 12 hours after a single dose.

This application was approved under Regulation 52B of The Human Medicines Regulation 2012, as amended (previously Article 10(3) of Directive 2001/83/EC, as amended), claiming to be a hybrid medicinal product of a suitable originator product, Fostair 100/6 micrograms per actuation pressurised inhalation solution that has been licensed within the UK for a suitable time, in line with the legal requirements.

No new non-clinical studies were conducted, which is acceptable given that the application is for a hybrid medicinal product of a suitable reference product.

Data from one pharmacokinetic study was submitted with this application. This study was conducted in-line with current Good Clinical Practice (GCP).

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for this product at all sites responsible for the manufacture, assembly and batch release of this product.

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

Advice was sought from the Commission of Human Medicines (CHM) on 23 January 2020 and as a result of its consideration was of the opinion that on the grounds relating to quality, safety and efficacy it may be unable to advise the licensing authority to grant the authorisation. In response, the Applicant submitted further quality, safety and efficacy data for the medicinal product addressing these concerns which were deemed acceptable and a Marketing Authorisation was granted on 11 June 2021**.**

# II QUALITY ASPECTS

## II.1 Introduction

Each metered dose (ex-valve) contains 100 micrograms of beclometasone dipropionate and 6 micrograms of formoterol fumarate dihydrate. This is equivalent to a delivered dose (ex-actuator) of 84.6 micrograms of beclometasone dipropionate and 5.0 micrograms of formoterol fumarate dihydrate.

In addition to beclometasone dipropionate and formoterol fumarate dihydrate, this product also contains ethanol anhydrous, water for injections, maleic acid and norflurane (HFA 134a).

The inhalation solution is contained in a pressurised aluminium container sealed with a metering valve and fitted into a white polypropylene plastic actuator which incorporates a mouthpiece and is provided with a pink plastic protective cap. The actuator has an integrated dose indicator which indicates the number of actuations (puffs) remaining. Each pack contains 1 pressurised container which provides 120 actuations.

Satisfactory specifications and Certificates of Analysis have been provided for all packaging components. All primary packaging complies with the current regulations concerning materials in contact with food.

## II.2 ACTIVE SUBSTANCES

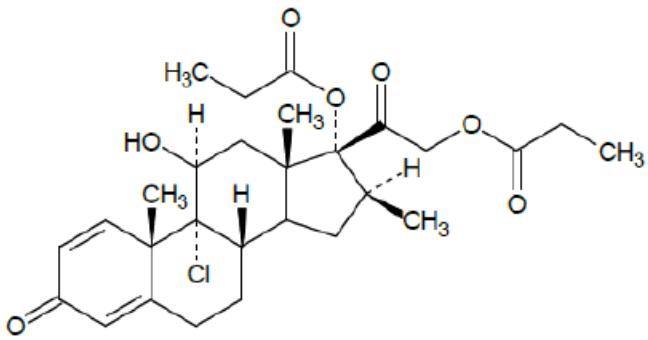
### 1. Beclometasone dipropionate

**rINN: Beclometasone dipropionate**

Chemical Name: [2-[(6S,9R,16R)-9-chloro-6-fluoro-11-hydroxy-10,13,16-trimethyl-3-oxo-7,8,11,12,14,15,16,17-octahydro-6H-cyclopenta[a]phenanthren-17-yl]-2-oxoethyl] 2,2- dimethylpropanoate (IUPAC)

Molecular Formula: $C_{28}H_{37}Cl\ O_7$

Chemical Structure:




Molecular Weight: 521.1 g/mol

Appearance: White or almost white, crystalline powder.

Solubility: It is practically insoluble in water, freely soluble in acetone and sparingly soluble in alcohol. It is slightly hygroscopic (increase in mass lower than 0.2%).

Beclometasone dipropionate is the subject of a European Pharmacopoeia monograph.

All aspects of the manufacture and control of the active substance are covered by a European Directorate for the Quality of Medicines and Healthcare (EDQM) Certificate of Suitability.

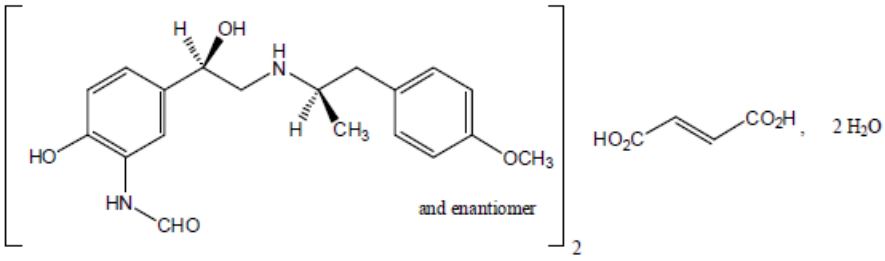
## 2. Formoterol fumarate

**rINN: Formoterol fumarate**

Chemical Name: (±)-2'-Hydroxy-5'-[(*R**)-1-hydroxy-2-[[(*R**)-*p*-methoxy- *α*-ethylphenethyl]amino]ethyl] formanilide fumarate (2:1) (salt), dihydrate

Molecular Formula: $(C_{19}H_{24}N_2O_4)_2 \cdot C_4H_4O_4 \cdot 2H_2O$
$C_{42}H_{52}N_4O_{12} \cdot 2H_2O$

Chemical Structure:




Molecular Weight: 521.1 g/mol

Appearance: White or almost white or slightly yellow powder.

Solubility: It is slightly soluble in water, freely soluble dimethyl sulfoxide and in acetic acid, soluble in methanol, slightly soluble in 2-propranol and in ethanol; practically insoluble in acetonitrile, acetone, ethyl acetate and in diethyl ether.

Formoterol fumarate is the subject of a European Pharmacopoeia monograph.

All aspects of the manufacture and control of the active substance are covered by a European Directorate for the Quality of Medicines and Healthcare (EDQM) Certificate of Suitability.

# II.3 DRUG PRODUCT

## Pharmaceutical development

A satisfactory account of the pharmaceutical development has been provided.

All excipients comply with either their respective European/national monographs, or a suitable in-house specification. Satisfactory Certificates of Analysis have been provided for all excipients.

No excipients of animal or human origin are used in the finished product.

This product does not contain or consist of genetically modified organisms (GMO).

## Manufacture of the product

A description and flow-chart of the manufacturing method has been provided.

Satisfactory batch formulation data have been provided for the manufacture of the product, along with an appropriate account of the manufacturing process. The manufacturing process has been validated and has shown satisfactory results.

**Finished Product Specifications**
The finished product specifications at release and shelf-life are satisfactory. The test methods have been described and adequately validated. Batch data have been provided that comply with the release specifications. Certificates of Analysis have been provided for any working standards used.

**Stability**
Finished product stability studies have been conducted in accordance with current guidelines, using batches of the finished product stored in the packaging proposed for marketing. Based on the results, a shelf-life of 21 months, with the storage conditions:
Prior to dispensing to the patient:
Must be stored in upright position in a refrigerator (2-8°C) for a maximum of 18 months.

After dispensing:
Do not store above 25°C for a maximum of 3 months.

The canister contains a pressurised liquid. Do not expose to temperatures higher than 50°C. Do not pierce the canister,
is acceptable.

Suitable post approval stability commitments have been provided to continue stability testing on batches of finished product.

### II.4 Discussion on chemical, pharmaceutical and biological aspects
The grant of a marketing authorisation is recommended.

## III NON-CLINICAL ASPECTS

### III.1 Introduction
As the pharmacodynamic, pharmacokinetic and toxicological properties of beclometasone dipropionate and formoterol fumarate dihydrate are well-known, no new non-clinical studies are required, and none have been provided. An overview based on the literature review is, thus, appropriate.

### III.2 Pharmacology
No new pharmacology data were provided and none were required for this application.

### III.3 Pharmacokinetics
No new pharmacokinetic data were provided and none were required for this application.

### III.4 Toxicology
No new toxicology data were provided and none were required for this application.

### III.5 Ecotoxicity/Environmental Risk Assessment
Suitable justification has been provided for non-submission of an Environmental Risk Assessment. As this is a hybrid application of an already authorised product, it is not expected that environmental exposure will increase following approval of the Marketing Authorisation for the proposed product.

### III.6 Discussion on the non-clinical aspects
The grant of a marketing authorisation is recommended.

# IV CLINICAL ASPECTS

## IV.1 Introduction

In accordance with the regulatory requirements, data from one pharmacokinetic (PK) study has been submitted with this application. This study was conducted in-line with current Good Clinical Practice (GCP).

## IV. 2 Pharmacokinetics

In support of the application, the applicant submitted the following PK study using their higher strength medicinal product, Luforbec 200/6 micrograms per actuation pressurised inhalation solution:

STUDY

The study was an open-label, randomised, 4-period, 4-treatment, 4-sequence, crossover, single-dose bioequivalence study to compare the pharmacokinetic and safety profiles following 2 inhalations each of Luforbec 200/6 micrograms per actuation pressurised inhalation solution and Fostair 200/6 micrograms per actuation pressurised inhalation solution with and without charcoal block, administered in healthy volunteers under fasting conditions.

The primary objectives of the study were to:
• assess and compare the PK profiles of beclometasone-17-monopropionate (17-BMP) and formoterol following 2 inhalations from
(i) Lupin beclometasone dipropionate/formoterol fumarate dihydrate 200/6 mcg per actuation pressurised inhalation solution (BDP/FF 200/6 mcg) and
(ii) FOSTAIR 200/6 mcg per actuation pressurised inhalation solution (FOSTAIR 200/6 mcg) without charcoal block,
• assess and compare the PK profiles of formoterol following administration of BDP/FF 200/6 mcg and FOSTAIR 200/6 mcg with charcoal block.

Treatments:

- Treatment A: Test (Lupin BDP/FF 200/6 mcg) − 2 inhalations
- Treatment B: Reference (Fostair 200/6 mcg) − 2 inhalations
- Treatment C: Test (Lupin BDP/FF 200/6 mcg) with oral charcoal − 2 inhalations
- Treatment D: Reference (Fostair 200/6 mcg) with oral charcoal − 2 inhalations

Subjects were dosed in 4 cohorts for each period.

For periods which employed concurrent administration of oral charcoal, a suspension of 5 g activated charcoal in 25 mL of water was administered 2 minutes before and 0.5, 60, 120, and 240 minutes after dose inhalation.

Blood samples were taken pre-dose and up to 36 hours post dose, with a washout period of 20 days between the treatment periods.

A summary of the pharmacokinetic results are presented below:
Results from statistical analysis for BDP, 17-BMP and formoterol are provided in the tables below:

BDP:

**Table 22: Summary of Statistical Comparisons of Plasma BDP Pharmacokinetic Parameters $C_{max}$, $AUC_{0-t}$, and $AUC_{0-\infty}$ (PK Analysis Set)**

| Parameter (unit) | Lupin BDP/FF 200/6 mcg (2 inhalations) Total Dose = 400/12 mcg (Treatment A) GLSM | FOSTAIR 200/6 mcg (2 inhalations) Total Dose = 400/12 mcg (Treatment B) GLSM | GMR (90% CI) A vs B | Intrasubject CV% A vs B |
|---|---|---|---|---|
| $C_{max}$ (pg/mL) | 2363.9272 | 2421.7765 | 97.61 (89.81, 106.09) | 35.68 |
| $AUC_{0-t}$ (pg×hr/mL) | 235.4247 | 242.1470 | 97.22 (90.97, 103.91) | 28.19 |
| $AUC_{0-\infty}$ (pg×hr/mL) | 245.7612 | 255.6832 | 96.12 (89.58, 103.14) | 25.88 |

The following subjects were excluded from the PK Analysis Set for both Treatments A and B (see Section 11.1 for details):
Subjects 007, 008, 011, 031, 033, 035, 047, 053, 054, 067, 069, 074, 098, 102, and 103.
Source: Table 14.2.1.17.

17-BMP:

**Table 14: Summary of Statistical Comparisons of Plasma 17-BMP Pharmacokinetic Parameters $C_{max}$, $AUC_{0-t}$, and $AUC_{0-\infty}$ (PK Analysis Set)**

| Parameter (unit) | Lupin BDP/FF 200/6 mcg (2 inhalations) Total Dose = 400/12 mcg (Treatment A) GLSM | FOSTAIR 200/6 mcg (2 inhalations) Total Dose = 400/12 mcg (Treatment B) GLSM | GMR (90% CI) A vs B | Intrasubject CV% A vs B |
|---|---|---|---|---|
| $C_{max}$ (pg/mL) | 534.3078 | 521.5587 | 102.44 (96.47, 108.79) | 25.38 |
| $AUC_{0-t}$ (pg×hr/mL) | 2304.7341 | 2301.7928 | 100.13 (95.10, 105.42) | 21.66 |
| $AUC_{0-\infty}$ (pg×hr/mL) | 2623.5814 | 2603.3801 | 100.78 (96.18, 105.60) | 18.99 |

The following subjects were excluded from the PK Analysis Set for both Treatments A and B (see Section 11.1 for details):
Subjects 007, 008, 011, 031, 033, 035, 047, 053, 054, 067, 069, 074, 098, 102, and 103.
Source: Table 14.2.1.13.

Formoterol:

**Table 18: Summary of Statistical Comparisons of Plasma Formoterol Pharmacokinetic Parameters $C_{max}$, $AUC_{0-t}$, and $AUC_{0-\infty}$, Without and With Oral Charcoal (PK Analysis Set)**

| Parameter (unit) | Treatments: Lupin BDP/FF 200/6 mcg (2 inhalations) Total Dose = 400/12 mcg (Treatment A) GLSM | FOSTAIR 200/6 mcg (2 inhalations) Total Dose = 400/12 mcg (Treatment B) GLSM | Lupin BDP/FF 200/6 mcg (2 inhalations) Total Dose = 400/12 mcg with Oral Charcoal (Treatment C) GLSM | FOSTAIR 200/6 mcg (2 inhalations) Total Dose = 400/12 mcg with Oral Charcoal (Treatment D) GLSM |
|---|---|---|---|---|
| $C_{max}$ (pg/mL) | 16.0682 | 15.2830 | 14.6351 | 13.2526 |
| $AUC_{0-t}$ (pg×hr/mL) | 44.1205 | 42.9461 | 23.5434 | 21.0990 |
| $AUC_{0-\infty}$ (pg×hr/mL) | 52.4552 | 51.6675 | 43.5534 | 41.5183 |

| Parameter (unit) | GMR (90% CI) Treatment A vs Treatment B (without Oral Charcoal) | GMR (90% CI) Treatment C vs Treatment D (with Oral Charcoal) | Intrasubject CV% |
|---|---|---|---|
| $C_{max}$ (pg/mL) | 105.14 (98.67, 112.03) | 110.43 (103.48, 117.85) | 26.75 |
| $AUC_{0-t}$ (pg×hr/mL) | 102.73 (94.21, 112.03) | 111.59 (102.12, 121.93) | 37.03 |
| $AUC_{0-\infty}$ (pg×hr/mL) | 101.52 (95.30, 108.15) | 104.90 (98.32, 111.92) | 22.00 |

The following subjects were excluded from the PK Analysis Set for both Treatments A and B (see Section 11.1 for details):
Subjects 007, 008, 011, 031, 033, 035, 047, 053, 054, 067, 069, 074, 098, 102, and 103.
The following subjects were excluded from the PK Analysis Set for both Treatments C and D (see Section 11.1 for details):
Subjects 003, 008, 015, 025, 026, 030, 031, 033, 035, 042, 054, 055, 057, 058, 060, 067, 068, 075, 084, 098, 103, 106, and 107. Additionally, Subject 038 was excluded from the PK Analysis Set for both Treatments C and D due to the inability to quantify all formoterol samples.
Source: Table 14.2.1.15.

Formoterol:

**Table 10: Summary of Statistical Comparisons of Plasma Formoterol Pharmacokineti Parameters $C_{max}$ and $AUC_{0-t}$, Without and With Oral Charcoal (PK Analys Set) Including Data of Subject 38 in Treatment C and D (PK Analysis Set)**

| Parameter (unit) | Treatment A | Treatment B | Treatment C | Treatment D |
|---|---|---|---|---|
| | Geometric LSM | Geometric LSM | Geometric LSM | Geometric LSM |
| $C_{max}$ (pg/mL) | 16.0550 | 15.3691 | 13.8623 | 12.9004 |
| $AUC_{0-t}$ (pg×hr/mL) | 44.0182 | 43.1192 | 22.8771 | 20.2643 |

| Parameter (unit) | Geometric Mean Ratio (90% Confidence Interval) Treatment A vs Treatment B (without Oral Charcoal) | Geometric Mean Ratio (90% Confidence Interval) Treatment C vs Treatment D (with Oral Charcoal) | Intrasubject CV% |
|---|---|---|---|
| $C_{max}$ (pg/mL) | 104.46 [96.31,113.30] | 107.46 [98.66,117.03] | 35.20 |
| $AUC_{0-t}$ (pg×hr/mL) | 102.08 [93.62,111.32] | 112.89 [103.07,123.65] | 37.68 |

According to the regulatory requirements, the Test/Reference ratios and their 90% confidence intervals were within the specified limits to show bioequivalence between the test product and the reference products.

As the additional strength of the product meet the biowaiver criteria specified in the current bioequivalence guideline the results and conclusions from the bioequivalence study on the 200/6 mcg product strength can be extrapolated to the other strength.

## IV.3 Pharmacodynamics

No new pharmacodynamic data have been submitted for this application and none were required.

## IV.4 Clinical efficacy

No new efficacy data have been submitted for this application and none were required.

## IV.5 Clinical safety

With the exception of the safety data from the clinical study submitted with this application, no new safety data were submitted. The safety data submitted showed that the product was well-tolerated. No new or unexpected safety issues were raised from these data.

## IV.6 Risk Management Plan (RMP)

The applicant has submitted an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulation 2012, as amended. The applicant proposes only routine pharmacovigilance and routine risk minimisation measures for all safety concerns. This is acceptable.

### IV.7 Discussion on the clinical aspects

The grant of a marketing authorisation is recommended for this application.

## V USER CONSULTATION

A full colour mock-up of the Patient Information Leaflet (PIL) has been provided with the application, in accordance with legal requirements.

The PIL has been evaluated via a user consultation study in accordance with legal requirements. The results show that the PIL meets the criteria for readability as set out in the guideline on the readability of the label and package leaflet of medicinal products for human use.

## VI OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified.

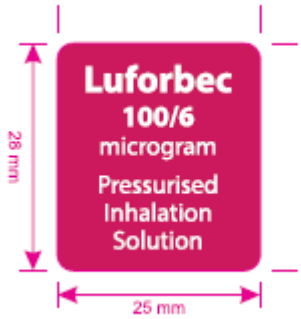
Extensive clinical experience with beclometasone dipropionate and formoterol fumarate dihydrate is considered to have demonstrated the therapeutic value of the product.

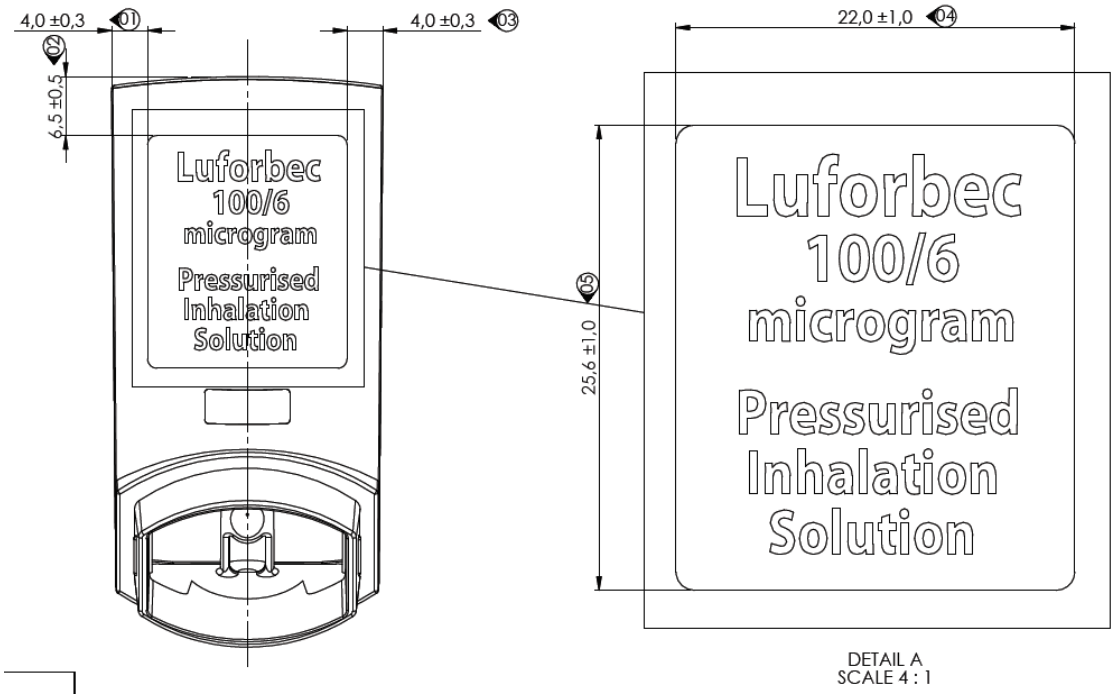
The benefit/risk is, therefore, considered to be positive.

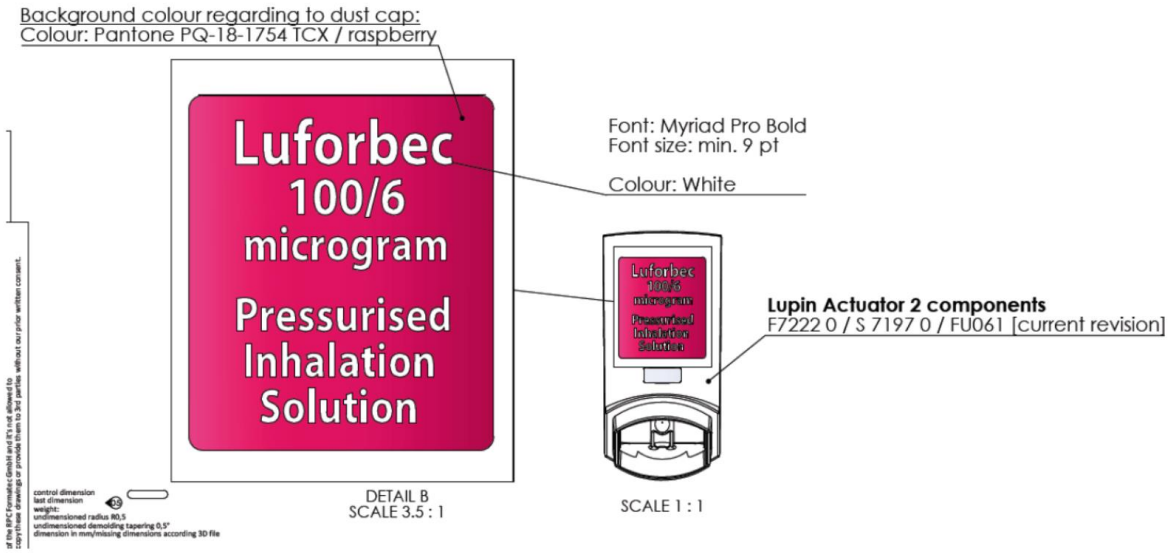
The Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and labelling are satisfactory and in line with current guidelines.

In accordance with legal requirements, the current approved versions of the SmPC and PIL for this product are available on the MHRA website.

Representative copies of the labels at the time of licensing are provided below.




4,0 ±0,3
01
4,0 ±0,3
03
22,0 ±1,0
04
02
6,5 ±0,5
05
25,6 ±1.0
Luforbec
100/6
microgram
Pressurised
Inhalation
Solution
DETAIL A
SCALE 4 : 1


Background colour regarding to dust cap:
Colour: Pantone PQ-18-1754 TCX / raspberry
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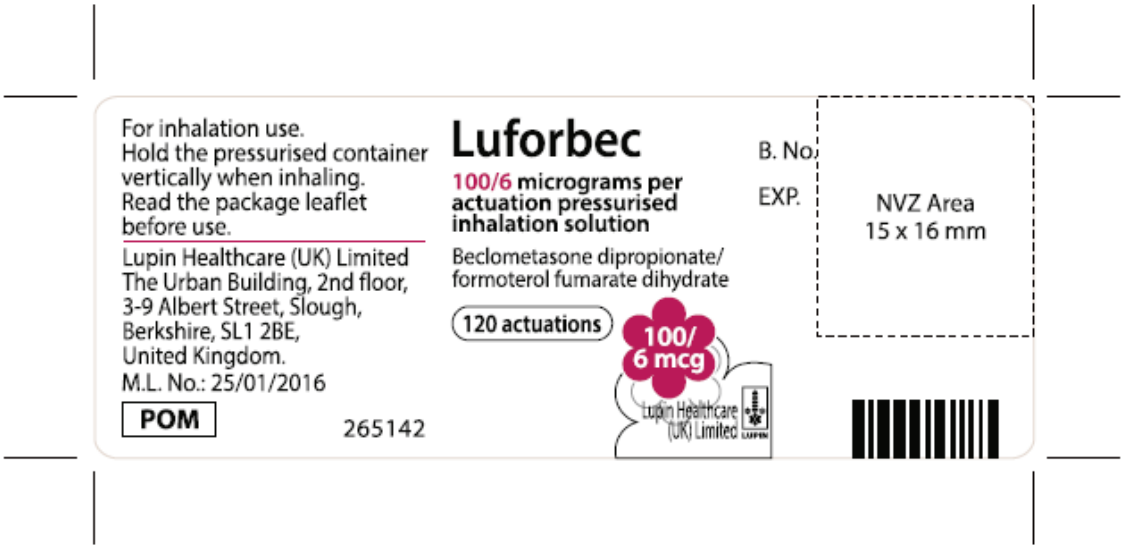
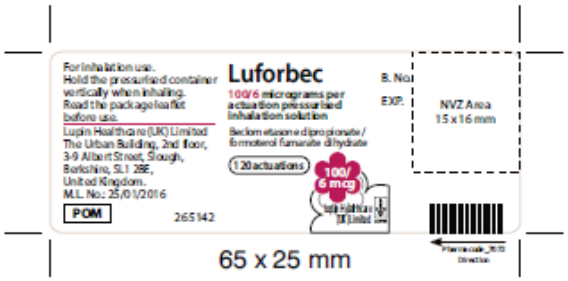
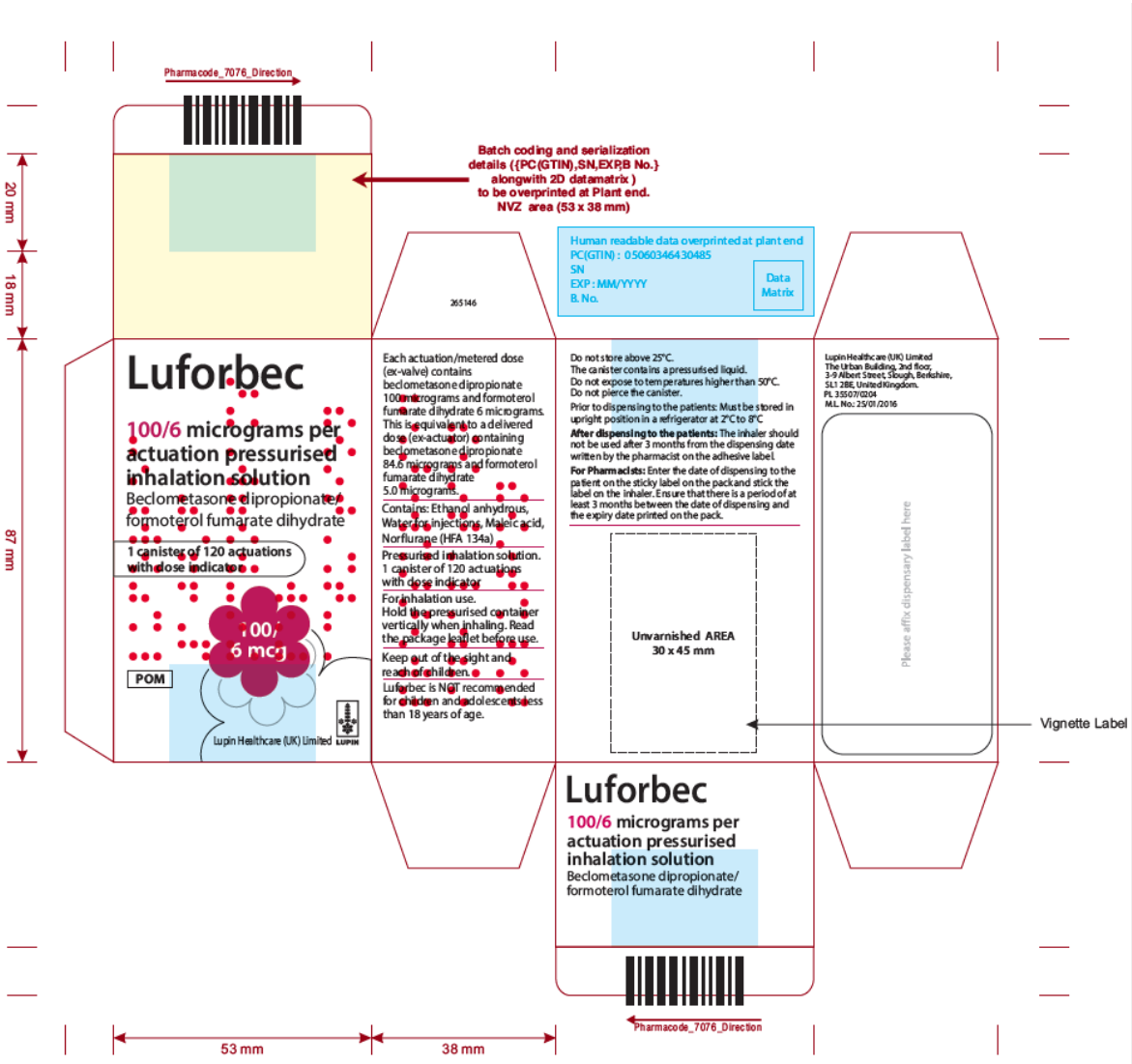
Font size: min. 9 pt
Colour: White
Luforbec
100/6
microgram
Pressurised
Inhalation
Solution
Lupin Actuator 2 components
F7222 0 / S 7197 0 / FU061 [current revision]
DETAIL B
SCALE 3.5 : 1
SCALE 1 : 1




200% enlarged




Pharmacode_7076_Direction
Batch coding and serialization details ({PC(GTIN),SN,EXP,B No.} alongwith 2D datamatrix ) to be overprinted at Plant end. NVZ area (53 x 38 mm)
Human readable data overprinted at plant end
PC(GTIN) : 05060346430485
SN
EXP : MM/YYYY
B. No.
Data Matrix
20 mm
18 mm
87 mm
Luforbec
100/6 micrograms per actuation pressurised inhalation solution
Beclometasone dipropionate/ formoterol fumarate dihydrate
1 canister of 120 actuations with dose indicator
POM
Lupin Healthcare (UK) Limited
265146
Each actuation/metered dose (ex-valve) contains beclometasone dipropionate 100micrograms and formoterol fumarate dihydrate 6 micrograms. This is equivalent to a delivered dose (ex-actuator) containing beclometasone dipropionate 84.6 micrograms and formoterol fumarate dihydrate 5.0 micrograms.
Contains: Ethanol anhydrous, Water for injections, Maleic acid, Norflurane (HFA 134a)
Pressurised inhalation solution. 1 canister of 120 actuations with dose indicator
For inhalation use. Hold the pressurised container vertically when inhaling. Read the package leaflet before use.
Keep out of the sight and reach of children.
Luforbec is NOT recommended for children and adolescents less than 18 years of age.
Do not store above 25°C.
The canister contains a pressurised liquid.
Do not expose to temperatures higher than 50°C.
Do not pierce the canister.
Prior to dispensing to the patients: Must be stored in upright position in a refrigerator at 2°C to 8°C
After dispensing to the patients: The inhaler should not be used after 3 months from the dispensing date written by the pharmacist on the adhesive label
For Pharmacists: Enter the date of dispensing to the patient on the sticky label on the pack and stick the label on the inhaler. Ensure that there is a period of at least 3 months between the date of dispensing and the expiry date printed on the pack.
Unvarnished AREA 30 x 45 mm
Lupin Healthcare (UK) Limited
The Urban Building, 2nd floor,
3-9 Albert Street, Slough, Berkshire,
SL1 2BE, United Kingdom.
PL 35507/0204
M.L. No.: 25/01/2016
Please affix dispensary label here
Vignette Label
Luforbec
100/6 micrograms per actuation pressurised inhalation solution
Beclometasone dipropionate/ formoterol fumarate dihydrate
Pharmacode_7076_Direction
53 mm
38 mm

**100/6**

**Dispensing Date**

_____ /_____ /_____

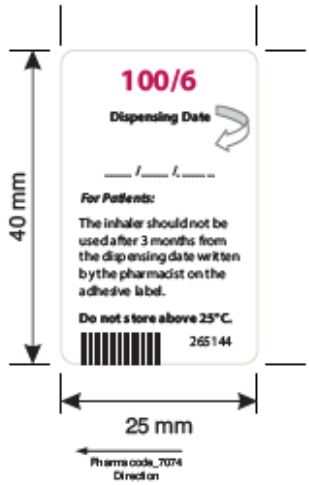
***For Patients:***

The inhaler should not be used after 3 months from the dispensing date written by the pharmacist on the adhesive label.

**Do not store above 25°C.**

265144

300% enlarged



# TABLE OF CONTENT OF THE PAR UPDATE

Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations where significant changes are made are recorded on the MHRA website or European Medicines Agency (EMA) website. Minor changes to the marketing authorisation are recorded in the current SmPC and/or PIL available on the MHRA website.

| **Application type** | **Scope** | **Product information affected** | **Date of grant** | **Outcome** | **Assessment report attached Y/N** |
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