1. Name of the medicinal product

Beclomin 250 HFA Inhaler (Beclometasone Dipropionate 250 HFA Inhaler).

1.1 Strength : 250 µg/ Puff
1.2 Pharmaceutical Form: Pressurised inhalation solution

2. Qualitative and quantitative composition

Each single actuation provides 250 micrograms of Beclometasone dipropionate from the actuator.

For the full list of excipients, see section 6.1

3. Pharmaceutical form

Pharmaceutical Form: Pressurised inhalation solution.

An easily actuated aerosol having plastic actuator of chocolate color body and brown color cap embossed "SQUARE" logo on cap. The canister contains a solution of Beclometasone Dipropionate along with a propellant filled in a metallic can which is fitted with a metering valve; imprinted with batch number & code number.

4. Clinical particulars

4.1 Therapeutic indications

Beclomin 250 HFA Inhaler is indicated in the prophylactic management of mild, moderate or severe asthma in adults or children. Beclometasone dipropionate given by inhalation oers preventative treatment for asthma. It provides eective anti-in-ammatory action in the lungs with a lower incidence and severity of adverse eects than those observed when corticosteroids are administered systemically. Mild asthma: Patients requiring symptomatic bronchodilator asthma medication on a regular basis. Moderate asthma: Patients with unstable or worsening asthma despite prophylactic therapy or bronchodilator alone. Severe asthma: Patients with severe chronic asthma and those who are dependent on systemic corticosteroids for adequate control of symptoms. Many patients who are dependent on systemic corticosteroids for adequate control of symptoms may be able to reduce significantly or eliminate, their requirement for oral corticosteroids when they are transferred to high dose inhaled beclometasone dipropionate.

4.2 Posology and method of administration

Posology

Beclometasone dipropionate is for inhalation use only. The Volumatic™ spacer device may be used by patients who have difficulty synchronising aerosol actuation with inspiration of breath.

The starting dose of inhaled beclometasone dipropionate should be adjusted to the severity of the disease. The dose may then be adjusted until control is achieved and then should be titrated to the lowest dose at which effective control of asthma is maintained.

Adults (including the elderly): Usually 1000 micrograms daily, which may be increased to 2000 micrograms daily. This may then be reduced when the patient's asthma has stabilised. The total daily dosage should be administered as two to four divided doses.

The Volumatic™ spacer device must always be used when Beclometasone dipropionate is administered to adults and adolescents 16 years of age and older taking total daily doses of 1000 micrograms or greater.

Children: Beclometasone dipropionate is not recommended for children.

Patients with hepatic or renal impairment: No dosage adjustment is needed in patients with hepatic or renal impairment.

4.3 Method of Administration

The aerosol spray is inhaled through the mouth into the lungs. The correct administration is essential for successful therapy. The patient must be instructed on how to use Beclometasone dipropionate correctly and advised to read and follow the instructions printed on the Patient Information Leaflet carefully.

Instructions for Use

Patients should be instructed in the proper use of their inhaler (see patient information leaflet)

During inhalation, the patient should preferably sit or stand. The inhaler has been designed for use in a vertical position.

Testing the inhaler:

If the inhaler is new or has not been used for three days or more, one puff should be released into the air. It is not necessary to shake the inhaler before use because this is a solution aerosol.

Instruct the patient to remove the mouthpiece cover and check that it is clean and free from foreign objects. The patient should then be instructed to breathe out before placing the inhaler into their mouth. They should then close their lips around the mouthpiece and breathe in steadily and deeply. They must not bite the mouthpiece. After starting to breathe in through the mouth, the top of the inhaler should be pressed down. Whilst the patient is still breathing in, the patient should then remove the inhaler from their mouth and hold their breath for about 5 to 10 seconds, or as long as is comfortable, and then breathe out slowly. The patient must not breathe out into the inhaler. If another dose is required, the patient should be advised to wait 30 seconds before repeating the procedure just described. Finally, patients should breathe out slowly and replace the mouthpiece cover.

The patient should be told not to rush the procedure described. It is important that the patient breathes in as slowly as possible prior to actuation. Inform the patient that if a mist appears on inhalation, the procedure should be repeated.

There is a dose indicator on the back of the inhaler which tells you how many puffs are left, the dose indicator rotates by a small amount when a puff is delivered. The number of puffs remaining is displayed in intervals of 20.

Patients should consider getting a replacement when the indicator shows the number 20. The indicator will stop at 0 when all the recommended puffs have been used. Replace the inhaler when the indicator reads 0.

It may be helpful to advise children and patients with weak hands to hold the inhaler with two hands, by placing both forefingers on top of the inhaler and both thumbs at the bottom of the device.

Patients who find it difficult to co-ordinate actuation with inspiration of breath should be told to use a Volumatic™ spacer device to ensure proper administration of the product.

Young children may find it difficult to use the inhaler properly and will require help. Using the inhaler with the Volumatic™ spacer device with a face mask may help in children under 5 years.

Advise the patient to thoroughly rinse the mouth or gargle with water or brush the teeth immediately after using the inhaler.

The patient should be told of the importance of cleaning the inhaler at least weekly to prevent any blockage and to carefully follow the instructions on cleaning the inhaler printed on the Patient Information Leaflet. The inhaler must not be washed or put in water.

The patient should be told also to refer to the Patient Information Leaflet accompanying the Volumatic™ spacer device for the correct instructions on its use and cleaning.

4.4 Contraindications
Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.5 Special warnings and precautions for use
Patients should be properly instructed on the use of the inhaler to ensure that the drug reaches the target areas within the lungs. Patients should also be informed that Beclometasone dipropionate should be used on a regular basis, even when they are asymptomatic.

Beclometasone dipropionate does not provide relief of acute asthma symptoms, which require a short-acting inhaled bronchodilator. Patients should have relief medication available.

Severe asthma requires regular medical assessment, including lung-function testing, as there is a risk of severe attacks and even death. Patients should be instructed to seek medical attention if short-acting relief bronchodilator treatment becomes less effective, or more inhalations than usual are required as this may indicate deterioration of asthma control. If this occurs, patients should be assessed and the need for increased anti-inflammatory therapy considered (eg. higher doses of inhaled corticosteroid or a course of oral corticosteroid).

Severe exacerbations of asthma must be treated in the usual way, ie. by increasing the dose of inhaled beclometasone dipropionate, giving a systemic steroid if necessary, and/or an appropriate antibiotic if there is an infection, together with β-agonist therapy.

Treatment with Beclometasone dipropionate should not be stopped abruptly.

Systemic effects of inhaled corticosteroids may occur, particularly when prescribed at high doses for prolonged periods. These effects are much less likely to occur than with oral corticosteroids. Possible systemic effects include adrenal suppression, growth retardation in children and adolescents, decrease in bone mineral density, cataract and glaucoma and more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children). It is important that the dose of inhaled corticosteroid is titrated to the lowest dose at which effective control of asthma is maintained.

It is recommended that the height of children receiving prolonged treatment with inhaled corticosteroids is regularly monitored. If growth is slowed, therapy should be reviewed with the aim of reducing the dose of inhaled corticosteroids, if possible, to the lowest dose at which effective control of asthma is maintained. In addition, consideration should also be given to referring the patient to a paediatric respiratory specialist.

Prolonged treatment with high doses of inhaled corticosteroids may result in clinically significant adrenal suppression.

Additional systemic corticosteroid cover should be considered during periods of stress or elective surgery.

The transfer to Beclometasone dipropionate of patients who have been treated with systemic steroids for long periods of time or at high doses needs special care, since recovery from possible adrenocortical suppression may take considerable time. Reduction of the dose of systemic steroid can be commenced approximately one week after initiating treatment with Clenil Modulite. The size of the reduction should correspond to the maintenance dose of systemic steroid. For patients receiving maintenance doses of 10 mg daily or less of prednisolone (or equivalent) reductions in dose of not more than 1 mg are suitable. For higher maintenance doses, larger reductions in dose may be appropriate. These oral dosage reductions should be introduced at not less than weekly intervals.

Adrenocortical function should be monitored regularly as the dose of systemic steroid is gradually reduced.

Some patients feel unwell during withdrawal of systemic steroids despite maintenance or even improvement of respiratory function. They should be encouraged to persevere with inhaled beclometasone dipropionate and to continue withdrawal of systemic steroid, unless there are objective signs of adrenal insufficiency.

Patients weaned off oral steroids whose adrenocortical function is impaired should carry a steroid warning card indicating that they may need supplementary systemic steroids during periods of stress, eg. worsening asthma attacks, chest infections, major intercurrent illness, surgery, trauma, etc.

Replacement of systemic steroid treatment with inhaled therapy sometimes unmasks allergies such as allergic rhinitis or eczema previously controlled by the systemic drug. These allergies should be symptomatically treated with antihistamine and / or topical preparations, including topical steroids.

As with all inhaled corticosteroids, special care is necessary in patients with active or quiescent pulmonary tuberculosis.

Visual disturbance

Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

Patients should be advised that this product contains small amounts of ethanol (approximately 9 mg per actuation) and glycerol. At the normal doses, the amounts of ethanol and glycerol are negligible and do not pose a risk to patients (see section 4.5, Interaction with other medicinal products and other forms of interaction).

System organ Class	Adverse Reaction	Frequency
Infections and Infestations	Oral candidiasis (of the mouth and throat)	Very Common
Immune System Disorders	Hypersensitivity reaction with the following manifestations:	
	Rash, urticaria, pruritus, erythema	Uncommon
	Oedema of the eyes, face, lips and throat	Very Rare
Endocrine Disorders	Adrenal suppression*, growth retardation* (in children and adolescents), bone density decreased*	Very Rare
Psychiatric Disorders (see section 4.4 Special warnings and precautions for use)	Psychomotor hyperactivity, sleep disorders, anxiety, depression, aggression, behavioural disorders (predominantly in children)	Unknown
Nervous System Disorders	Headache	Unknown
Eye Disorders	Cataract*, glaucoma*	Very Rare
	Vision, blurred (see also section 4.4)	Unknown
Respiratory, Thoracic and Mediastinal Disorders	Hoarseness, throat irritation	Common
	Paradoxial bronchospasm, wheezing, dyspnoea, cough	Very Rare
Gastrointestinal Disorders	Nausea	Unknown

4.6 Paediatric population

Paediatric population Growth retardation and behavioral disorders may be more prevalent in children than in adults, particularly at high doses administered for prolonged periods of time.

4.7 Interaction with other medicinal products and other forms of interaction

Beclometasone dipropionate contains a small amount of ethanol. There is a theoretical potential for interaction in particularly sensitive patients taking disulfiram or metronidazole.

Beclometasone is less dependent on CYP3A metabolism than some other corticosteroids, and in general interactions are unlikely; however the possibility of systemic effects with concomitant use of strong CYP3A inhibitors (e.g. ritonavir, cobicistat) cannot be excluded, and therefore caution and appropriate monitoring is advised with the use of such agents.

4.8 Additional information on special populations

Not Available

4.9 Paediatric population

Paediatric population Growth retardation and behavioral disorders may be more prevalent in children than in adults, particularly at high doses administered for prolonged periods of time

4.10 Fertility, pregnancy and lactation

4.10.1 General principles

There is no experience of the use of this product in pregnancy and lactation in humans. It should not be used in pregnancy or lactation unless the expected benefits to the mother are thought to outweigh any potential risks to the fetus or neonate.

4.10.2 Women of childbearing potential / Contraception in males and females

Not Available

4.10.3 Pregnancy

There is no experience of the use of this product in pregnancy and lactation in humans. It should not be used in pregnancy or lactation unless the expected benefits to the mother are thought to outweigh any potential risks to the fetus or neonate

There is inadequate evidence of safety of beclometasone dipropionate in human pregnancy. Administration of corticosteroids to pregnant animals can cause abnormalities of fetal development including cleft palate and intra-uterine growth retardation. There may therefore, be a risk of such effects in the human fetus. It should be noted, however, that the fetal changes in animals occur after relatively high systemic exposure. Beclometasone dipropionate is delivered directly to the lungs by the inhaled route and so avoids the high level of exposure that occurs when corticosteroids are given by systemic routes.

4.10.4 Breastfeeding

No specific studies examining the transfer of beclometasone dipropionate into the milk of lactating animals have been performed. It is reasonable to assume that beclometasone dipropionate is secreted in milk, but at the dosages used for direct inhalation there is low potential for significant levels in breast milk.

There is no experience with or evidence of safety of propellant HFA-134a in human pregnancy or lactation. However, studies of the effect of HFA-134a on reproductive function and embryofetal development in animals have revealed no clinically relevant adverse effects.

4.10.5 Fertility

No specific studies have been performed with beclometasone dipropionate with regard to the safety in human fertility. Although results of animal studies have shown some impaired fertility, this occurs at high doses levels.

4.11 Effects on ability to drive and use machines
None reported

4.12 Undesirable effects
a) Summary of the safety profile: The most common adverse reactions observed during clinical trials using inhaled beclometasone in the treatment of asthma and wheezing were laryngitis, pharyngitis and oral candidiasis. A serious hypersensitivity reaction including oedema of the eye, face, lips and throat (angioedema) has been reported rarely. Paradoxical bronchospasm may occur after dosing.

b) Tabulated list of adverse reactions: Adverse reactions observed in clinical trials with inhaled beclometasone in the treatment of asthma and wheezing are listed in the table below according the MedDRA system organ class and frequencies.

System Organ Class	Adverse Reaction	Frequency
Infections and infestations	Laryngitis, pharyngitis	Very common
	Oral candidiasis	Common
	Herpes simplex	*Rare
Endocrine disorders	Adrenal suppression**	Very Rare
Immune system disorders	Hypersensitivity reactions with the following manifestations: angioedema, rash, urticaria, pruritus,	*Rare
Psychiatric disorders	Psychomotor hyperactivity, sleep disorders anxiety, depression, aggressiveness, behavioural changes (predominantly in children)	Not known
Nervous system disorders	Headache	Uncommon
	Tremor	*Rare
Eye disorders	Cataract**, glaucoma**	Very Rare
	Vision, blurred (see also section 4.4)	Uncommon
Respiratory, thoracic and mediastinal disorders	Cough	Common
	Throat irritation, hoarseness, dysphonia, paradoxical bronchospasm, wheezing	Uncommon
	Dyspnoea	*Rare
Gastrointestinal disorders	Nausea, dyspepsia	Common
Musculoskeletal and connective tissue disorders	Growth retardation* (in children and adolescents), bone density decreased*	Very rare
General disorders and administration site conditions	Asthenia	*Rare

* From spontaneous reporting
**systemic effects of inhaled corticosteroids

C) Description of selected adverse reactions: Systemic effect of inhaled corticosteroids (including beclometasone dipropionate) may occur particularly when administered at high doses for prolonged periods of time: these may include adrenal suppression, decrease in bone mineral density, growth retardation in children and adolescents, cataract and glaucoma (see section 4.4). Measures to minimize the occurrence of candidiasis, hoarseness and paradoxical bronchospasm are described in section 4.4.

d) Paediatric population: Growth retardation and behavioural disorders may be more prevalent in children than in adults, particularly at high doses administered for prolonged periods of time.

4.13 Overdose

Acute: Inhalation of doses in excess of those recommended may lead to temporary suppression of adrenal function. This does not require emergency action. In these patients treatment should be continued at a dose sufficient to control asthma; adrenal function recovers in a few days and can be verified by measuring plasma cortisol.

Chronic: Use of inhaled beclometasone dipropionate in daily doses in excess of 1,500 micrograms over prolonged periods may lead to adrenal suppression. Monitoring of adrenal reserve may be indicated. Treatment should be continued at a dose sufficient to control asthma.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Glucocorticoid

ATC Code: R03B A01

Beclometasone dipropionate is a pro-drug with weak glucocorticoid receptor binding affinity. It is extensively hydrolysed via esterase enzymes to the active metabolite beclometasone-17-monopropionate (B-17-MP), which has potent topical anti-inflammatory activity.

5.2 Pharmacokinetic properties

Absorption when administered via inhalation by a MDI

Systemic absorption of unchanged beclometasone dipropionate (BDP) occurs through the lungs. There is negligible oral absorption of the swallowed dose of unchanged BDP. Prior to absorption there is extensive conversion of BDP to its active metabolite B-17-MP. The systemic absorption of B-17-MP arises from both lung deposition (36%) and oral absorption of the swallowed dose (26%). The absolute bioavailability following inhalation is approximately 2% and 62% of the nominal dose for unchanged BDP and B-17-MP, respectively. BDP is absorbed rapidly with peak plasma concentrations observed (t_{max}) at 0.3 hours. B-17-MP appears more slowly with a t_{max} of 1 hour. There is an approximately linear increase in systemic exposure with increasing inhaled dose. When administered orally the bioavailability of BDP is negligible but pre-systemic conversion to B-17-MP results in 41 % of the dose being absorbed as B-17-MP.

Distribution

The tissue distribution at steady-state for BDP is moderate (20 L) but more extensive for B-17-MP (424 L). Plasma protein binding is moderately high (87%).

Biotransformation

BDP is cleared very rapidly from the systemic circulation, by metabolism mediated via esterase enzymes that are found in most tissues. The main product of metabolism is the active metabolite (B-17-MP). Minor inactive metabolites, beclometasone-21-monopropionate (B-21-MP) and beclometasone (BOH), are also formed but these contribute little to the systemic exposure.

Elimination

The elimination of BDP and B-17-MP are characterised by high plasma clearance (150 L/hour and 120 L/hour) with corresponding terminal elimination half-lives of 0.5 hours and 2.7 hours. Following oral administration of tritiated BDP, approximately 60% of the dose was excreted in the faeces within 96 hours mainly as free and conjugated polar metabolites. Approximately 12% of the dose was excreted as free and conjugated polar metabolites in the urine. The renal clearance of BDP and its metabolites is negligible.

5.3 Preclinical safety data

Preclinical safety studies indicate that beclometasone dipropionate shows negligible systemic toxicity when administered by inhalation.

The non-CFC propellant HFA-134a has been shown to have no toxic effect at very high vapour concentrations, far in excess of those likely to be experienced by patients, in a wide range of animal species exposed daily for periods of up to two years.

6. Pharmaceutical particulars

6.1 List of excipients

- ✓ Absolute Ethanol
- ✓ Norflurane {1,1,1,2-Tetrafluoroethane (HFA 134a)}

6.2 Incompatibilities

Not Applicable

6.3 Shelf life

2 years

6.4 Special precautions for storage

The Inhaler should be stored below 30°C, protected from direct sunlight and heat. The canister should not be broken, punctured or burnt, even when apparently empty. Keep away from eyes. Keep out of reach of children.

6.5 Nature and contents of container

Beclomin 250 HFA Inhaler : Each Inhaler delivers 200 puff..

6.6 Special precautions for disposal and other handling

None

7. Marketing authorisation holder

Square Pharmaceuticals Ltd.
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48, Mohakhali C.A, Dhaka – 1212,
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Tel : +880 2 8833047-56, +880 2 8859007 (10 lines)

Fax : +880 2 8828768, +880 2 8834941
E-mail : info@squaregroup.com

8. Marketing authorization number(s)

N/A

9. Date of first registration/renewal of the registration

Not Applicable

10. Date of revision of the text

22 November 2021

Reference:

- ✓ https://www.medicines.org.uk/emc/product/6977/smpc#gref
- ✓ https://www.hpra.ie/img/uploaded/swedocuments/LicenseSPC_PA0584-004-001_24052018165049.pdf
- ✓ https://www.squarepharma.com.bd/downloads/1610952476_pdoc_Beclomin%20DS.pdf