Approved professional information for BECLOMIZ 100 & 250 HFA

SCHEDULING STATUS

S3

PROPRIETARY NAMES AND DOSAGE FORM

BECLOMIZ 100 HFA metered dose inhaler

BECLOMIZ 250 HFA metered dose inhaler

COMPOSITION

Active ingredient:

BECLOMIZ 100 HFA: Each actuation delivers 100 µg beclometasone dipropionate into the mouthpiece of the actuator.

BECLOMIZ 250 HFA: Each actuation delivers 250 µg beclometasone dipropionate into the mouthpiece of the actuator.

Inactive ingredients:

Ethanol (BECLOMIZ 100 HFA 7,5 % *m/v* and BECLOMIZ 250 HFA 12,7 % *m/v*) and HFA 134a propellant gas.

CATEGORY AND CLASS

A 21.5.1 Corticosteroids and analogues

PHARMACOLOGICAL ACTION

Pharmacodynamic properties:

Beclometasone dipropionate (BDP) is a synthetic glucocorticoid with weak glucocorticoid receptor binding affinity. It is hydrolysed via esterase enzymes to beclometasone-17-monopropionate (B-17-MP), the active metabolite, which has potent anti-inflammatory action within the respiratory tract when given by inhalation.

Pharmacokinetic properties:

Absorption:

Systemic absorption of unchanged beclometasone dipropionate (BDP) occurs through the lungs. BDP is extensively converted to its active metabolite B-17-MP prior to absorption. B-17-MP is systemically absorbed from lung deposition (36 %) as well as from oral absorption of the swallowed dose (26 %). Following inhalation, the absolute bioavailability is approximately 2 % and 62 % respectively for unchanged BDP and B-17-MP of the nominal dose. There is an approximately linear increase in systemic exposure with increasing inhaled dose.

Distribution:

At steady-state, the tissue distribution for BDP is moderate (20 L), but more extensive for B-17-MP (424 Lfs) and plasma protein binding is moderately high (87 %).

Biotransformation:

Esterase enzymes which are found in most tissues, are responsible for the rapid clearance of BDP from the systemic circulation by metabolising BDP to its active metabolite (B-17-MP). Minor inactive metabolites known as 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. Approximately 60 % of the dose, following oral administration, is excreted in the faeces within 96 hours and approximately 12 % is excreted in the urine; in both instances, mainly as free and conjugated metabolites. The renal clearance of BDP and its metabolites is negligible.

INDICATIONS

BECLOMIZ HFA is indicated for the prophylactic treatment of bronchospasm, in the following groups of patients with asthma:

1. Patients who are expected to be on long-term steroid maintenance therapy.
2. Asthmatic patients that are poorly controlled by bronchodilators. In these patients BECLOMIZ HFA may facilitate the control of the asthma and may reduce the need for bronchodilators.
3. Patients who are inadequately controlled by sodium cromoglicate in addition to bronchodilators.
4. Patients with severe asthma who are dependent on systemic corticosteroids, or those patients who are receiving intermittent courses of oral steroids.
5. BECLOMIZ HFA is particularly important for managing asthma in children, because effective control can be achieved without the retardation of growth commonly associated with systemic steroids.

CONTRAINDICATIONS

- Hypersensitivity to beclometasone dipropionate or any of the inactive ingredients in BECLOMIZ HFA (see **COMPOSITION**).
- Acute status asthmaticus.

WARNINGS AND SPECIAL PRECAUTIONS

Patients should be correctly instructed on the use of the inhalers to ensure that the medicine reaches the target areas within the lungs. They should also be made aware of the prophylactic nature of therapy with BECLOMIZ HFA and that it should be used regularly even when no symptoms are experienced.

BECLOMIZ HFA does not provide relief of acute asthma symptoms, which require a short- acting inhaled bronchodilator. Patients should have relief medicine 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 (e.g. higher doses of inhaled corticosteroid or a course of oral corticosteroid). Severe exacerbations of asthma must be treated in the usual way, by increasing the dose of inhaled BECLOMIZ HFA, giving a systemic steroid if necessary, and/or an appropriate antibiotic if there is an infection, together with β-agonist therapy.

In patients who have been transferred to inhalation therapy, systemic steroid therapy may need to be re-instated rapidly during periods of stress or where airway obstruction or mucus prevents absorption from the inhalation.

Adrenal suppression may occur at standard doses of BECLOMIZ HFA. In such patients, precautions should be taken to provide systemic corticosteroid cover in situations of prolonged stress. Treatment with BECLOMIZ HFA should not be stopped abruptly.

The addition of, or transfer to BECLOMIZ HFA of patients being treated with oral corticosteroids in high doses or for a prolonged time, or both, should be in a stable state and needs special care, since recovery from possible adrenocortical suppression is slow. The patient should be in a reasonably stable state before being given BECLOMIZ HFA in addition to the usual maintenance dose of systemic steroids.

Reduction of the systemic corticosteroid should be gradual and should start approximately one week after initiating treatment with BECLOMIZ HFA, by starting to reduce the systemic corticosteroid by 1 mg prednisolone (or equivalent) at intervals not less than one week.

Adrenocortical function should be monitored regularly, since the dose of the systemic corticosteroid is gradually reduced.

Patients who have been weaned off systemic corticosteroids, feel unwell during the withdrawal period, despite maintenance or improvement of respiratory function. They should be encouraged to persevere with inhaled BECLOMIZ HFA unless there are objective signs of adrenal insufficiency. These patients should carry a warning card with them indicating that systemic steroid therapy may need to be re-instated without delay during periods of stress e.g. worsening asthma attacks, chest infections, major intercurrent illness, surgery or trauma.

Discontinuation of systemic steroids, and with the replacement of BECLOMIZ HFA inhalers, may lead to the revealing of allergies such as allergic rhinitis or atopic eczema, previously treated by the systemic corticosteroids and should thus be treated symptomatically by antihistamines and/or topical preparations.

Take note that BECLOMIZ HFA is not for symptomatic relief of bronchospasm. Patients should not expect rapid relief of asthma attacks with BECLOMIZ HFA inhalers.

BECLOMIZ HFA has to be inhaled at the recommended dosage at regular intervals, and the patient should be informed that benefit may take several days to become apparent.

Special care should be taken in patients with active or dormant pulmonary tuberculosis and the therapeutic advantages should be weighed against any undesirable effects.

Chickenpox and measles can have a more serious or even fatal course in non-immune children or adults on corticosteroids. In such children or adults who have not had these diseases or been properly immunised, particular care should be taken to avoid exposure. Live vaccines should not be given to patients receiving high dose systemic corticosteroid therapy nor for at least 3 months afterwards. Killed vaccines or toxoids may be given although the response may be attenuated.

In doses greater than 400 µg per day, the incidence of candidiasis (thrush) of the mouth and throat is increased. Patients with a high blood level of Candida precipitins, indicating a previous infection, are most likely to develop this complication. Patients are advised to rinse their mouths

thoroughly with water after the use of BECLOMIZ HFA inhalers. The water should not be swallowed.

The use of an appropriate spacer may also be considered.

Systemic reactions are a possible response to BECLOMIZ HFA, especially when a high dose is prescribed for a prolonged time. These can include adrenal suppression, decrease in bone mineral density, cataract, glaucoma and growth retardation in children and adolescents and more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children). It is therefore important to titrate the dose to the lowest dose at which effective control of the patient's asthma is maintained.

For children receiving high doses for a prolonged time, it is recommended that their height is regularly monitored. If growth is slowed, treatment of BECLOMIZ HFA 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. Consideration should also be given by referring the patient to a paediatric respiratory specialist, should growth retardation be suspected.

Immediate treatment with a short-acting bronchodilator should be introduced if paradoxical bronchospasm occurs which usually presents with an increase in wheezing, shortness of breath and coughing after dosing. BECLOMIZ HFA should be discontinued immediately at this point and the patient needs to be assessed, and if necessary, introduced to an alternative therapy.

Effects on ability to drive and use machines

BECLOMIZ HFA has no influence on the ability to drive a vehicle and operate machinery.

INTERACTIONS

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 medicines.

HUMAN REPRODUCTION

Safety during pregnancy and lactation has not been established.

DOSAGE AND DIRECTIONS FOR USE

BECLOMIZ HFA is for oral inhalation use only. Do
not exceed the maximum recommended dose.
BECLOMIZ HFA may be used with an appropriate spacer device by patients who find it difficult to synchronise aerosol actuation with inspiration of breath.
The starting dose of BECLOMIZ HFA should be fitting to the severity of the disease after which the dose may be adjusted until control is achieved or reduced to the lowest dose at which effective control of asthma is maintained.

Adults (including the elderly):
The usual starting dose is 200 µg twice daily but may be started at, or increased to, 600 – 800 µg per day in severe cases and subsequently reduced when the patient's asthma has become stable.
The total daily dose should be administered as two to four divided doses. For patients presenting with severe asthma, or those showing partial response to standard inhalation doses, high dose inhalation therapy of up to 1 mg (1 000 µg) daily, in divided doses, may be used.
Maximum daily dose: 1 mg (1 000 µg) daily.

Children:

The usual starting dose is 100 µg per day given in divided doses two to four times a day.

Alternatively, 100 – 200 µg twice daily may be administered.

Maximum daily dose: 500 µg daily.

BECLOMIZ HFA should always be used with an appropriate spacer when administered to children 15 years and younger, whatever dose has been prescribed.

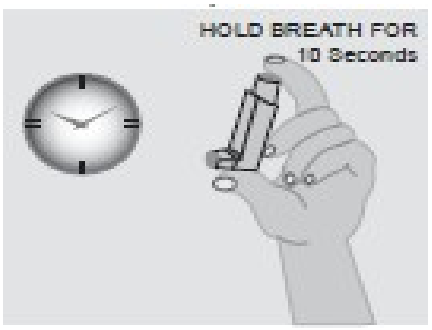
Directions for use:

1. Test the inhaler before the first time of use by releasing one puff into the air.
2. Remove mouthpiece cover and check mouthpiece to ensure it is clean before use.
3. Shake canister well before use.

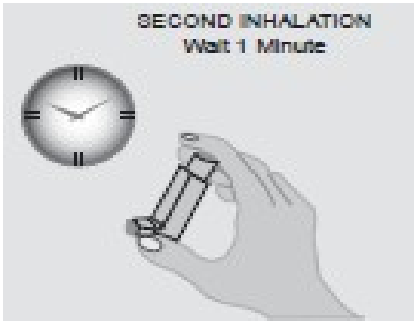
4. The patient should now exhale through mouth before placing the mouthpiece firmly between lips. Do not bite the mouthpiece.

5. Whilst breathing in slowly, the canister should be pressed down at the same time to release one dose.

6. Remove inhaler from mouth and hold breath for 5 to 10 seconds.



7. Repeat above steps if necessary (wait at least 30 seconds).



8. Rinse mouth thoroughly immediately after use with water and clean inhaler at least once a week.

For a more detailed description of the administration instructions, please refer to the patient information leaflet.

SIDE EFFECTS

Infections and infestations:

Frequent: oral candidiasis of the mouth and throat

Immune system disorders:

Frequent: hypersensitivity reactions (including rash, urticaria, erythema, pruritus, oedema of the eyes, face, lips and throat)

Endocrine disorders:

Less frequent: adrenal suppression*, growth retardation* and decreased bone density*

Metabolism and nutrition disorders:

Frequent: intolerance to adrenocorticosteroids

Less frequent: reduction of cortisol levels

Psychiatric disorders:

Frequency unknown: psychomotor hyperactivity, sleep disorders, anxiety, depression, aggression, behavioural disorders (predominantly in children)

Nervous system disorders:

Frequency unknown: headache

Eye disorders:

Less frequent: cataracts* and glaucoma*

Respiratory, thoracic and mediastinal disorders:

Frequent: hoarseness, throat irritation

Less frequent: paradoxical bronchospasm, wheezing, dyspnoea and coughing

Gastrointestinal disorders:

Frequency unknown: nausea

*These are systemic reactions which are a possible response to inhaled corticosteroids, especially when a high dose is prescribed for a prolonged time.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

Acute: No special emergency action is required when doses in excess of the recommended are inhaled, since it only leads to the temporary suppression of hypothalamic-pituitary-adrenal (HPA) function. Treatment should be continued at the recommended dose to control asthma. HPA function will recover in a day or two.

Chronic: Beclometasone dipropionate inhaled in daily doses in excess of 1 500 µg over prolonged periods, may lead to adrenal suppression in addition to suppression of HPA function. The patient should be treated as steroid-dependant and transferred to a suitable maintenance dose of systemic steroids.

IDENTIFICATION

An aluminium canister containing a white to almost white coloured solution of beclometasone dipropionate with a propellant. Each canister is clearly labelled BECLOMIZ 100 HFA or BECLOMIZ 250 HFA.

PRESENTATION

BECLOMIZ 100 HFA: A pressurised aluminium canister fitted with a metered dispensing valve contained within an actuator. The actuator has a brown body and a lilac cap embossed with a “SQUARE” logo on the cap. Each canister provides 200 metered inhalations.

BECLOMIZ 250 HFA: A pressurised aluminium canister fitted with a metered dispensing valve contained within an actuator. The actuator has a chocolate body and a brown cap embossed with a “SQUARE” logo on the cap. Each canister provides 200 metered inhalations.

STORAGE INSTRUCTIONS

Store at or below 30 °C.

Protect from frost and direct sunlight.

The canister should not be broken, punctured or burnt, even when apparently empty.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBERS

BECLOMIZ 100 HFA: 49/21.5.1/0420

BECLOMIZ 250 HFA: 49/21.5.1/0421

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

Unimed Healthcare (Pty) Ltd

Corner Birch Road and Bluegum Avenue,

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DATE OF PUBLICATION OF THE PROFESSIONAL INFORMATION

20 August 2022