Approved Professional Information for BECEZE CFC FREE

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

BECEZE 50 CFC FREE pressurised inhaler, solution

BECEZE 100 CFC FREE pressurised inhaler, solution

BECEZE 250 CFC FREE pressurised inhaler, solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

BECEZE 50 CFC FREE: A metered-dose, pressurised, inhaler which delivers 50 micrograms beclometasone dipropionate per metered dose.

BECEZE 100 CFC FREE: A metered-dose, pressurised, inhaler which delivers 100 micrograms beclometasone dipropionate per metered dose.

BECEZE 250 CFC FREE: A metered-dose pressurised, inhaler which delivers 250 micrograms beclometasone dipropionate per metered dose.

For the full list of excipients, see section 6 .1.

3. PHARMACEUTICAL FORM

Pressurised inhaler, solution.

Aerosol for inhalation supplied in a pressurised aluminium container. Absence of external damage, corrosion or leakage.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

BECEZE CFC FREE is indicated for the prophylactic treatment of bronchospasm, in the following groups of patients with asthma:

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

4.2 Posology and method of administration

Posology:

Do not exceed the recommended dose.

The initial dose of BECEZE CFC FREE should be appropriate to the severity of the asthma. The dose is then adjusted until control is achieved or reduced to the minimum effective dose according to the individual patient's response.

Adults: The usual dose is 200 µg twice daily.

In more severe cases the dosage may be started at or increased to 600 – 800 µg per day and subsequently reduced when the patient's asthma has stabilised.

The total daily dose may be administered as two, three or four divided doses. In patients with severe asthma, or those showing only partial response to standard inhalation doses, high dose inhalation therapy may be considered, and doses of up to 1 mg daily, in divided doses, may be used.

Maximum daily dose: 1 000 µg (1 mg) daily.

Children: 50 – 100 µg should be given two, three or four times daily according to the age and response.

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

Maximum daily dose: 500 µg daily.

Method of administration:

BECEZE CFC FREE is for oral inhalation use only.

Patients should be instructed in the proper use of the inhaler and its care. Actuation of the inhaler needs to be synchronised with inspiration as the inhaler is breath operated.

An appropriate spacer device should be used in patients who struggle to coordinate aerosol actuation with inspiration of breath.

See section “How to use your inhaler” below.

4.3 Contraindications

- BECEZE CFC FREE is contraindicated in patients with a history of hypersensitivity to beclometasone dipropionate or any of its components listed in section 6.1.
- Corticosteroids have been shown to be teratogenic in animals following topical application. As beclometasone may be absorbed systemically following inhalation, teratogenicity following inhalation cannot be excluded. Therefore, BECEZE CFC FREE must not be used during pregnancy (see section 4.6).
- Acute status asthmaticus.
- Orally inhaled beclometasone dipropionate should be used with caution in patients with clinical tuberculosis or those with a history of tuberculosis. Particular care should be taken to minimise the use of topical corticosteroids in immunosuppressed patients.

4.4 Special warnings and precautions for use

BECEZE CFC FREE are not indicated for the treatment of acute attacks, but act prophylactically, the patient should thus have relief medication available. A therapeutic effect is not achieved until after a few days of use. The inhalers must be used regularly according to the instructions, the patient should thus be informed that the BECEZE CFC FREE must be used regularly, even if the patient does not experience any symptoms.

Patients who have severe asthma must be examined regularly, including lung-function testing, as these patients have a heightened risk of severe attacks, which may be fatal.

Patients must be advised to seek medical attention if therapy becomes less effective, or if more inhalations of BECEZE CFC FREE are required, as this may indicate deterioration of asthma control. If this occurs, a patient assessment should be carried out, and the need for increased anti-inflammatory medications be considered.

Severe exacerbations of asthma should be treated by increasing the dose of BECEZE CFC FREE, by giving a systemic steroid if necessary, prescribing an appropriate antibiotic if there is an infection, together with β-agonist therapy.

Prolonged and excessive administration may induce systemic corticosteroid effects with reduction in plasma cortisol levels. Systemic corticosteroid effects may include adrenal suppression, growth retardation in children and adolescents, decrease in bone mineral density, cataract, glaucoma and less frequently, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (especially in children).

It is recommended that the height of children on prolonged treatment with inhaled corticosteroids be monitored regularly. If the child’s growth is slowed, asthma therapy should be reviewed with the aim of reducing the dose of inhaled corticosteroids, to the lowest dose at which asthma control is maintained. The patient should be referred to a paediatric respiratory specialist.

Systemic steroids should be provided in appropriate cases of stress or elective surgery.

Excessive administration, (for example, greater than 1500 µg per day) of the higher dose BECEZE 250 CFC FREE may induce a degree of adrenocortical suppression. In such patients the continuing treatment with BECEZE CFC FREE should be carefully considered.

Treatment with BECEZE 250 CFC FREE should not be stopped suddenly (refer to section 4.2).

The transfer of patients from other anti-asthma therapies is preferably done when the patient is in a reasonably stable state.

Following the introduction of BECEZE CFC FREE it may be possible to reduce the other therapy. Particularly in those patients taking systemic corticosteroids, it is essential to reduce the dose slowly and with great care in view of the impairment of adrenocortical function.

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

It is important to monitor intercurrent infections and treat them appropriately.
Localised infections with Candida albicans in the mouth and throat (thrush) may occur in some patients. The occurrence is dose dependent, the incidence increasing with doses greater than 400 µg beclometasone dipropionate per day. Patients who suffered a previous infection are more likely to develop this complication.

Such patients may find it helpful to rinse their mouth with water after using the inhaler. Symptomatic oral candidiasis can be treated with a topical antifungal therapy, while continuing treatment with BECEZE CFC FREE.

Hoarseness or throat irritation may occur. Rinsing of the mouth and throat with water after each dose to remove residual medication may be helpful.

Paradoxical bronchospasm may occur, with an immediate increase in wheezing, shortness of breath and coughing after using BECEZE CFC FREE, this should be treated immediately with a fast-acting inhaled bronchodilator. Treatment with BECEZE CFC FREE should be stopped immediately, the patient should be assessed, and alternative therapy be introduced.

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.

BECEZE CFC FREE contains approximately 2 mg alcohol (ethanol) per inhalation. The small amount of ethanol in BECEZE CFC FREE will not have any noticeable effects. Also see section 4.5.

4.5 Interaction with other medicines and other forms of interaction

BECEZE CFC FREE contains ethanol as inactive ingredient. There may be an interaction in patients on disulfiram or metronidazole treatment.

Beclometasone is less dependent on CYP3A metabolism than some other corticosteroids. 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.

4.6 Fertility, pregnancy and lactation

BECEZE CFC FREE is contraindicated in pregnancy (see section 4.3).

There is no experience of the use of BECEZE CFC FREE in lactation in humans. BECEZE CFC FREE should not be used in lactation.

4.7 Effects on ability to drive and use machines

None reported.

4.8 Undesirable effects

Infections and infestations:

Frequent: Candida albicans in the mouth and throat (thrush).

Immune system disorders:

Hypersensitivity reactions with the following symptoms may occur:

Less frequent: Rash, urticaria, pruritis, erythema, oedema of the eyes, face, lips and throat.

Endocrine disorders:

Less frequent: Adrenal suppression*, slow growth rate in children* and adolescents, decreased bone density*.

Psychiatric disorders:

Frequency unknown: Psychomotor hyperactivity, sleep disorders, anxiety, depression, aggression, behavioural disorders.

Nervous system disorders:

Frequency unknown: Headache.

Eye disorders:

Less frequent: Cataract*, glaucoma*.

Frequency unknown: Blurred vision (see section 4.4).

Respiratory, thoracic and mediastinal disorders:

Frequent: Hoarseness, throat irritation.

Less frequent: Paradoxical bronchospasm, wheezing, dyspnoea, cough.

Gastrointestinal disorders:

Frequency unknown: Nausea.

*Systemic reactions are a possible response to inhaled corticosteroids, especially when a high dose is prescribed for a prolonged time (see section 4.4).

Reporting of suspected adverse reactions:

Reporting suspected adverse reactions after authorisation of BECEZE CFC FREE is important. It allows continued monitoring of the benefit/risk balance of BECEZE CFC FREE. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications:

https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

Excessive use of BECEZE CFC FREE over a long period of time could lead to adrenal suppression. It is advisable to carry out regular tests of adrenal function to guard against unexpected adrenal suppression. If excessive use has occurred, the patient should be transferred to oral corticosteroid therapy. Inhalation therapy may be resumed when the condition has stabilised and oral corticosteroids are slowly withdrawn.

Further treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 21.5.1 Corticosteroids and analogues.

Pharmacotherapeutic group: Glucocorticoids.

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:

Systemic absorption of unchanged beclometasone dipropionate occurs through the lungs. There is negligible oral absorption of the swallowed dose of unchanged beclometasone dipropionate. Prior to absorption there is extensive conversion of beclometasone dipropionate 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 beclometasone dipropionate and B-17-MP, respectively. Beclometasone dipropionate 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 beclometasone dipropionate 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 beclometasone dipropionate is moderate (20 L) but more extensive for B-17-MP (424 L). Plasma protein binding is moderately high (87 %).

Biotransformation:

Beclometasone dipropionate 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 beclometasone dipropionate 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 beclometasone dipropionate, 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 beclometasone dipropionate and its metabolites is negligible.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Anhydrous ethanol

Hydrofluoroalkane.

6.3 Shelf life

BECEZE 50 and 100 CFC FREE: 36 months.

BECEZE 250 CFC FREE: 24 months.

6.4 Special precautions for storage

Store at or below 25 °C.

Avoid storage in direct sunlight or heat.

Do not refrigerate.

Protect from freezing.

The canister should not be punctured, broken or burnt even if it is apparently empty.

6.5 Nature and contents of container

The container is a seamless aluminium canister with metered dispensing valve crimped in place.

Each canister of BECEZE CFC FREE provides 200 metered inhalations.

6.6 Special precautions for disposal and other handling

Not applicable.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Biotech Laboratories (Pty) Ltd

Ground Floor, Block K West, Central Park,

400 16th Road, Randjespark, Midrand 1685

South Africa

8. REGISTRATION NUMBERS

BECEZE 50 CFC FREE: 36/21.5.1/0192

BECEZE 100 CFC FREE: 36/21.5.1/0193

BECEZE 250 CFC FREE: 36/21.5.1/0194

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

08 April 2005

10. DATE OF REVISION OF THE TEXT

4 April 2022

HOW TO USE YOUR INHALER:

1. Remove the cap from the inhaler. Make sure the mouthpiece is clean and free from fluff and dirt.

2. Holding the inhaler upright, with your thumb on the base and your first finger on the top of the can. Now shake the inhaler vigorously up and down

3. Breathe out fully to empty the lungs, then place the mouthpiece firmly between the lips.

4. Now breathe in slowly and deeply. At the same time, press the aerosol with your first finger to fire the aerosol and release beclometasone dipropionate.

5. Remove the inhaler from your mouth and hold your breath for 10 seconds, or as long as possible.

6. If more than one puff is required, wait at least one minute and repeat the procedure from step 2. Replace the cap.

7. To clean, remove the aerosol can and rinse the plastic container in warm water. Dry thoroughly, then replace the aerosol can.

IMPORTANT:

It is essential that the beclometasone dipropionate inhaler is fired at the same time as you breathe in. If you have not used as inhaler before, it may be useful to practice steps 3 and 4 of the diagram without actually triggering the inhaler, so that breathing in and firing the inhaler can be done at the same time.

Namibia:

Beceze 50 CFC Free, Reg. No.: 11/21.5.1/0185 NS2

Beceze 100 CFC Free, Reg. No.: 16/21.5.1/0072 NS2

Beceze 250 CFC Free, Reg. No.: 16/21.5.1/0073 NS2