

1.3.2 Summary of Product Characteristics (SmPC)

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Summary of Product Characteristics (SPC)

1. Name of the medicinal product

Decomit 100 HFA Inhalation Aerosol

2. Qualitative and quantitative composition

Beclometasone Dipropionate 100 micrograms per actuation.

3. Pharmaceutical form

Pressurized metered-dose aerosol.

A colourless solution in a pressurised aluminium canister fitted with a metering valve and an actuator.

Decomit contains a propellant, which does not contain any chlorofluorocarbons (CFCs).

4. Clinical particulars

4.1 Therapeutic indications

Prophylactic management of mild, moderate or severe asthma.

4.2 Posology and method of administration

Posology

Decomit is for inhalation use only.

Patients should be instructed in the proper use of their inhaler, including rinsing out their mouth with water after use.

NOTE: The recommended total daily dose of Decomit is lower than that for current beclometasone dipropionate containing products and should be adjusted to the needs of the individual patient.

ADULT STARTING AND MAINTENANCE DOSE:

It is important to gain control of asthma symptoms and optimize pulmonary function as soon as possible. When patients' symptoms remain under satisfactory control, the dose should be titrated to the lowest dose at which effective control of asthma is maintained.

To be effective, inhaled Decomit must be used on a regular basis even when patients are asymptomatic.

THERAPY IN NEW PATIENTS SHOULD BE INITIATED AT THE FOLLOWING

Mild asthma: 100 to 200 micrograms per day in two divided doses.

Moderate asthma: 200 to 400 micrograms per day in two divided doses.

Severe asthma: 400 to 800 micrograms per day in two divided doses.

Patients on budesonide inhalers may be transferred to Decomit as described below

The general approach to switching patients to Decomit involves two steps as detailed below. Specific guidance on switching well-controlled and poorly-controlled (symptomatic) patients is given below the table.

Step 1: Consider the dose of budesonide-containing inhalers appropriate to the patient's current condition.

Step 2: Convert the budesonide inhaler dose to the Decomit HFA dose according to the table below.

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Total Daily Dose (mcg/day)								
Budesonide inhaler	200-250	300	400-500	600-750	800-1000	1100	1200-1500	1600-2000
Decomit HFA	100	150	200	300	400	500	600	800

Patients with well-controlled asthma using budesonide inhaler products should be switched to Decomit at a dose in accordance with the table above.

For example:

Patients on 2 puffs twice daily of budesonide 100 micrograms would change to 2 puffs twice daily of Decomit 50 micrograms.

Patients with poorly-controlled asthma may be switched from budesonide inhaler products to Decomit at the same microgram for microgram dose up to 800 micrograms daily.

Alternatively the patient's current budesonide inhaler dose can be doubled and this dose can be converted to the Decomit dose according to the table above.

Patients on fluticasone inhalers may be transferred to the same total daily dose of Decomit up to 800 micrograms daily.

Once transferred to Decomit HFA the dose should be adjusted to meet the needs of the individual patient. The maximum recommended dose is 800 micrograms per day in divided doses.

The same total daily dose in micrograms from either Decomit 50 or Decomit 100 (a higher strength) aerosol provides the same clinical effect.

Paediatric population

There are no data to date on Decomit HFA in children under 12 years of age, hence no definitive dosage recommendation can be made.

Special patient groups

No special dosage recommendations are made for elderly or patients with hepatic or renal impairment.

Method of administration

Decomit HFA is a breath-actuated inhaler which automatically releases the metered dose of medication during a patient's inhalation through the mouthpiece and overcomes the need for patients to have good manual co-ordination.

The patient should read the instruction leaflet before use.

Before first use of the inhaler, or if the inhaler has not been used for two weeks or more, prime the inhaler by releasing two puffs into the air.

Decomit HFA delivers a consistent dose

- whether or not the canister is shaken by the patient
- without the need for the patient to wait between individual actuations
- regardless of storage orientation or periods without use of up to 14 days
- at temperatures as low as -10°C.

4.3 Contraindications

Hypersensitivity to beclometasone dipropionate or to any of the excipients listed in section 6.1.

4.4 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. To be effective, Decomit HFA must be used by patients on a regular

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basis, even when patients do not have asthma symptoms. When symptoms are controlled, maintenance Decomit HFA therapy should be reduced in a stepwise manner to the minimum effective dose. Inhaled steroid treatment should not be stopped abruptly.

Patients with asthma are at risk of acute attacks and should have regular assessments of their asthma control including pulmonary function tests.

Decomit HFA is not indicated for the immediate relief of asthma attacks. Patients therefore need to have relief medication (inhaled short-acting bronchodilator) available for such circumstances.

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 asthma exacerbations should be managed in the usual way i.e. 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 Decomit HFA should not be stopped abruptly

However, systemic effects of inhaled corticosteroids may occur, particularly at high doses prescribed for prolonged periods. These effects are much less likely to occur than with oral corticosteroids. Possible systemic effects include Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, decrease in bone mineral density, cataract, 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, therefore, 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 corticosteroid, if possible, to the lowest dose at which effective control of asthma is maintained. In addition, consideration should be given to referring the patient to a paediatric respiratory specialist.

Prolonged treatment with high doses of inhaled corticosteroids, particularly higher than the recommended doses, may result in clinically significant adrenal suppression.

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

Patients who have received systemic steroids for long periods of time or at high doses, or both, need special care and subsequent management when being transferred to inhaled steroid therapy.

Patients should have stable asthma before being given inhaled steroids in addition to the usual maintenance dose of systemic steroid. Withdrawal of systemic steroids should be gradual, starting about seven days after the introduction of Decomit HFA therapy. For daily oral doses of prednisolone of 10mg or less, dose reduction in 1mg steps, at intervals of not less than one week is recommended. For patients on daily maintenance doses of oral prednisolone greater than 10mg, larger weekly reductions in the dose might be acceptable. The dose reduction scheme should be chosen to correlate with the magnitude of the maintenance systemic steroid dose.

As recovery from impaired adrenocortical function, caused by prolonged systemic steroid therapy is slow, adrenocortical function should be monitored regularly.

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Patients should be advised that they may feel unwell in a non-specific way during systemic steroid withdrawal despite maintenance of, or even improved respiratory function. Patients should be advised to persevere with their inhaled product and to continue withdrawal of systemic steroids, even if feeling unwell, unless there is evidence of HPA axis suppression.

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, e.g. worsening asthma attacks, chest infections, major intercurrent illness, surgery, trauma, etc.

Discontinuation of systemic steroids may also cause exacerbation of allergic diseases such as atopic eczema and rhinitis. These should be treated as required with topical therapy, including corticosteroids and/or antihistamines.

Like other corticosteroids, caution is necessary in patients with active or latent pulmonary tuberculosis.

Patients should be advised to seek medical attention for review of maintenance Decomit HFA therapy if peak flow falls, symptoms worsen or if the short-acting bronchodilator becomes less effective and increased inhalations are required. This may indicate worsening asthma.

Most patients can be successfully transferred to inhaled steroids with maintenance of good respiratory function, but special care is necessary for the first few months after the transfer, until the hypothalamic-pituitary-adrenal (HPA) system has sufficiently recovered to enable the patient to cope with stressful emergencies such as trauma, surgery or serious infections. Patients should, therefore, carry a steroid warning card to indicate the possible need to re-instate systemic steroid therapy rapidly during periods of stress or where airways obstruction or mucus significantly compromises the inhaled route of administration. In addition, it may be advisable to provide such patients with a supply of corticosteroid tablets to use in these circumstances. The dose of inhaled steroids should be increased at this time and then gradually reduced to the maintenance level after the systemic steroid has been discontinued.

Beclometasone dipropionate, like other inhaled steroids, is absorbed into the systemic circulation from the lungs. Beclometasone dipropionate and its metabolites may exert detectable suppression of adrenal function. Within the dose range 100-800 micrograms daily, clinical studies with Decomit HFA have demonstrated mean values for adrenal function and responsiveness within the normal range.

Patients should be advised that this product contains small amounts of ethanol. At the normal doses, the amounts of ethanol are negligible and do not pose a risk to patients.

4.5 Interaction with other medicinal products and other forms of interaction

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

4.6 Fertility, pregnancy and lactation

The potential risk of this product for humans is unknown.

Decomit HFA There is no experience of this product in pregnancy and lactation in humans, therefore the product should only be used if the expected benefits to the mother are thought to outweigh any potential risk to the foetus or neonate

Beclometasone dipropionate

There is inadequate evidence of safety in human pregnancy. Administration of corticosteroids to pregnant animals can cause abnormalities of foetal development including cleft palate and intra-

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uterine growth retardation. There may therefore, be a risk of such effects in the human foetus. It should be noted, however, that the foetal 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.

No specific studies examining the transfer of beclometasone dipropionate into the milk of lactating animals have been performed. It is probable that beclometasone dipropionate is excreted in milk. However, given the relatively low doses used by the inhalation route, the levels are likely to be low. In mothers breast feeding their baby the therapeutic benefits of the drug should be weighed against the potential hazards to mother and baby.

The use of beclometasone dipropionate in pregnancy requires that the possible benefits of the drug be weighed against the possible hazards. The drug has been in widespread use for many years without apparent ill consequence.

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

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

A serious hypersensitivity reaction including oedema of the eye, face, lips and throat (angioedema) has been reported rarely.

As with other inhaled therapy, paradoxical bronchospasm may occur after dosing. Immediate treatment with a short-acting bronchodilator should be initiated, Decomit HFA should be discontinued immediately and an alternate prophylactic treatment introduced.

Systemic effects of inhaled corticosteroids may occur, particularly with high doses prescribed for prolonged periods. These include adrenal suppression, growth retardation in children, decrease in bone mineral density and the occurrence of cataract and glaucoma.

Commonly, when taking Decomit HFA, hoarseness and candidiasis of the throat and mouth may occur. To reduce the risk of hoarseness and candida infection, patients are advised to rinse their mouth after using their inhaler.

Based on the MedDra system organ class and frequencies, adverse events are listed in the table below according to the following frequency estimate: very common ($\geq 1/10$); common ($\geq 1/100$ to $< 1/10$); Uncommon ($\geq 1/1,000$ to $< 1/100$); rare ($\geq 1/10,000$ to $< 1/1,000$); very rare ($< 1/10,000$), not known (cannot be estimated from the available data).

MedDra – system organ class	Frequency and Symptom
Infections and infestations	<i>Common:</i> Candidiasis in mouth and throat
Immune system disorders	<i>Rare:</i> Allergic reactions, angioedema in eyes, throat, lips and face
Endocrine disorders	<i>Very rare:</i> Adrenal suppression*, growth retardation* (in children and adolescents), bone density decreased*
Nervous system disorders	<i>Uncommon:</i> Headache, vertigo, tremor
Eye disorders	<i>Very rare:</i> Cataract*, glaucoma*

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Respiratory, thoracic and mediastinal disorders	<i>Common:</i> Hoarseness, pharyngitis <i>Uncommon:</i> Cough, increased asthma symptoms <i>Rare:</i> Paradoxical bronchospasm
Gastrointestinal disorders	<i>Common:</i> Taste disturbances <i>Uncommon:</i> Nausea
Skin and subcutaneous tissue disorders	<i>Uncommon:</i> Urticaria, rash, pruritus, erythema, purpura
Musculoskeletal and connective tissue disorders	<i>Very rare:</i> Decrease bone mineral density
Psychiatric Disorders	<i>Unknown:</i> Psychomotor hyperactivity, sleep disorders, anxiety, depression, aggression, behavioural changes (predominantly in children)

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

4.9 Overdose

Acute overdosage is unlikely to cause problems. The only harmful effect that follows inhalation of large amounts of the drug over a short time period is suppression of HPA function. Specific emergency action need not be taken. Treatment with Decomit HFA should be continued at the recommended dose to control the asthma; HPA function recovers in a day or two.

If excessive doses of beclometasone dipropionate were taken over a prolonged period a degree of atrophy of the adrenal cortex could occur in addition to HPA suppression. In this event the patient should be treated as steroid dependent and transferred to a suitable maintenance dose of a systemic steroid such as prednisolone. Once the condition is stabilized, the patient should be returned to Decomit HFA by the method described above in section 4.4.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Glucocorticoids, ATC Code: R03B A01

Decomit HFA contains beclometasone dipropionate in solution in propellant HFA-134a resulting in an extrafine aerosol. The aerosol droplets are on average much smaller than the beclometasone dipropionate particles delivered by CFC-suspension formulations or dry powder formulations of beclometasone dipropionate. The extrafine particle fraction will be $60\% \pm 20\%$ of the drug particles ≤ 3.3 microns per shot, ex-actuator.

Radio-labelled deposition studies in adults with mild asthma have demonstrated that the majority of drug ($>55\%$ ex-actuator) is deposited in the lung and a small amount ($< 35\%$ ex-actuator) is deposited in the oropharynx. These studies were performed with Decomit HFA Aerosol. Decomit HFA Aerosol is a 'press and breathe' inhaler, whereas Decomit HFA Inhaler is a breath-activated inhaler.

Inhaled beclometasone dipropionate is now well established in the management of asthma. It is a synthetic glucocorticoid and exerts a topical, anti-inflammatory effect on the lungs, with fewer systemic effects than oral corticosteroids.

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Comparative clinical studies have demonstrated that asthma patients achieve equivalent pulmonary function and control of symptoms with Decomit HFA at lower total daily doses than CFC containing beclometasone dipropionate aerosol inhalers.

Pharmacodynamic studies in patients with mild asthma given Decomit HFA for 14 days, have shown that there is a linear correlation among urinary free cortisol suppression, dose administered, and serum total-beclometasone levels obtained. At a daily dose of 800 micrograms Decomit HFA, suppression of urinary free cortisol was comparable with that observed with the same daily dose of CFC containing beclometasone dipropionate, indicating a wider safety margin, as Decomit HFA is administered at lower doses than the CFC product.

5.2 Pharmacokinetic properties

The pharmacokinetic profile of Decomit HFA shows that the peak serum concentration for total-beclometasone (BOH) (total of any beclometasone OH and beclometasone dipropionate or monopropionate hydrolysed to beclometasone OH) after single and multiple doses is achieved after 30 minutes.

The value at the peak is approximately 2 nanograms/ml after a total daily dose of 800 micrograms and the serum levels after 100, 200 and 400 micrograms are proportional. The principal route of elimination of beclometasone dipropionate and its several metabolites is in the faeces. Between 10% and 15% of an orally administered dose is excreted in the urine, as both conjugated and free metabolites of the drug.

In both single dose and multiple dose pharmacokinetic studies, a dose of 200 micrograms of Decomit HFA achieved comparable total-BOH levels, as a dose of 400 micrograms of CFC containing beclometasone dipropionate aerosol. This provided the scientific rationale for investigating lower total daily doses of Decomit HFA to achieve the same clinical effect.

Pharmacokinetic studies with Decomit HFA have not been carried out in any special populations.

5.3 Preclinical safety data

In animal studies, propellant HFA-134a has been shown to have no significant pharmacological effects other than at very high exposure concentrations, and then narcosis and a relatively weak cardiac sensitising effect were found. The potency of the cardiac sensitisation was less than that of CFC-11 (trichlorofluoromethane).

In studies to detect toxicity, repeated high dose levels of propellant HFA-134a indicated that safety margins based on systemic exposure would be of the order 2200, 1314 and 381 for mouse, rat and dog with respect to humans.

There are no reasons to consider propellant HFA-134a as a potential mutagen, clastogen or carcinogen judged from *in vitro* and *in vivo* studies including long-term administration by inhalation in rodents.

Studies of propellant HFA-134a administered to pregnant and lactating rats and rabbits have not revealed any special hazard.

In animals, systemic administration of relatively high doses can cause abnormalities of foetal development including growth retardation and cleft palate. There may therefore be a very small risk of such effects in the human foetus. However, inhalation of beclometasone dipropionate into the lungs avoids the high level of exposure that occurs with administration by systemic routes.

Safety studies with this product in rat and dog showed few, if any, adverse effects other than those normally associated with general steroid exposure including lymphoid tissue alterations

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such as reduction in thymus, adrenal and spleen weights. An inhalation reproductive study with Decomit HFA Aerosol (an equivalent inhaler) in rats did not exhibit any teratogenic effects.

6. Pharmaceutical particulars

6.1 List of excipients

Propellant HFA-134a (Norflurane)
Dehydrated Alcohol

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Do not store above 25°C. Protect from frost and direct sunlight.

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

6.5 Nature and contents of container

Each canister contains 200 metered doses, each containing 100 mcg of beclometasone dipropionate BP. It does not contain CFC as propellant

6.6 Special precautions for disposal and other handling

Not applicable.

7. Marketing authorization holder

BEXIMCO PHARMACEUTICALS LTD.
17, Dhanmondi R/A, Road No. 2,
Dhaka-1205, Bangladesh.

8. Marketing authorization number(s)

186-556-044

9. Date of first authorization/renewal of the authorization

06-09-2006

10. Date of revision of the text

05-09-2021