For the use of a Registered Medical Practitioner or a Hospital or a Laboratory Only.

Beclate-100 Inhaler (CFC FREE)

Composition
Each actuation delivers:
Beclometasone dipropionate BP…….. 100µg
Excipients
Ethanol BP…….5%w/w
Propellant HFA-134a

Description
A piece filled metal container fitted with a valve with plastic stem and printed with product name, batch number and container number. On visual examination there should be no sign of physical damage such as dents, budged containers bent valve stem and uneven crimping. A colourless solution is obtained after opening the container.

PHARMACODYNAMICS

Effect on Bronchial and Nasal Mucosa
Since the local application of powerful corticosteroids can cause dermal atrophy, the possibility that long term inhalation of beclomethasone dipropionate may cause atrophic changes of the bronchial mucosa has been raised.

Histological and electron microscope studies of the bronchial mucosa of the patients treated with usual therapeutic doses of inhaled beclomethasone for upto 3 years have revealed no important treatment related changes.

Effect on Adrenal Function
Studies have compared the adrenal function in asthmatic patients receiving inhaled beclomethasone with that in asthmatics receiving no corticosteroids or alternate-day oral corticosteroid therapy. Some of these studies confirm that suppression of endogenous cortisol secretion can occur when the dosage of inhaled beclomethasone is increased above usual dosages and indicate that usual therapeutic doses may cause some suppression of adrenal function compared with that in untreated control patients.

However, other studies have found some improvement in adrenal function following substitution with alternate-day oral corticosteroids.

In the study of Wyatt et al., the degree of adrenal suppression with inhaled beclomethasone dipropionate (mean dose 550 – 576 mcg daily) was similar to alternate day prednisolone 20 – 40 mgs.
When beclomethasone dipropionate was substituted for alternate day oral steroids, a return to normal of diurnal plasma cortisol in 16 of the 28 children were observed and of the response to

tetracosactrin in 9 of the 12 patients in whom it was abnormal before starting beclomethasone dipropionate.

The intravenous metyrapone test remained abnormal in 22 of the 34 children after 12 weeks treatment with beclomethasone dipropionate. Importantly, the addition or substitution of beclomethasone dipropionate for alternate day prednisolone resulted in improved control of asthma without materially affecting adrenal function and has not been associated with iatrogenic Cushing's syndrome in children maintained on beclomethasone dipropionate inhalation.

Effect on Antigen-Induced Asthmatic Reactions

As a result of early studies which found that single 200 mcg doses of beclomethasone dipropionate did not inhibit type I immediate asthmatic reactions, it was concluded that pre-challenge inhalation of beclomethasone inhibited late type III but not early reactions to inhaled antigens.

Effect on Hematological Immune function

The effect of inhaled beclomethasone dipropionate on circulating leucocytes and eosinophils has varied in asthmatic and healthy individuals according to dosage. In patients with asthma there have been reports of a decrease in eosinophils, but no significant suppression of mitogen- stimulated lymphocyte proliferation, E-rose He formation, or immunoglobulin concentration other than IgG following usual therapeutic doses of inhaled beclomethasone dipropionate (400 – 1600 µ) caused an increase in the mean white blood cells and neutrophils and a decrease in the eosinophil and lymphocyte count.

PHARMACOKINETICS

Absorption

Systemic absorption occurs after all routes of absorption. When inhaled Beclomethasone dipropionate (BDP) is deposited in the mouth and nasal passages, trachea, bronchi and lungs, part of the drug is swallowed but any drug absorbed from the gut undergoes first pass metabolism. Consequently the bioavailability of BDP is poor after oral intake. Absorption from lungs after inhalation is good, and may be responsible for the systemic effects since the oral dose of BDP required to suppress plasma cortisol is higher than inhalation dose. The pharmacokinetics of BDP are not well characterized.

Distribution

Few details are available about the distribution of BDP and its binding to plasma proteins in the humans. But distribution does occur and BDP given by any route in sufficiently high doses can cause HPA axis suppression. Animal studies show that BDP crosses the placenta and is excreted into the breast milk. Human data are not available but any excretion into the breast milk is likely to be negligible.

BDP is shown to be teratogenic in mice but not in rats. Human data are not available.

Metabolism
Lung tissue can metabolize BDP into BMP and free base. The latter has very weak activity. The absorbed BDP is rapidly metabolized by esterases in tissues and liver into monopropionate and free base, which are mostly conjugated.

Excretion
After metabolism most of the absorbed BDP is excreted in the faeces mainly via the bile. About 15 % of the absorbed BDP is excreted in the urine as conjugates and free base.

INDICATIONS

Beclate CFC free inhaler is indicated in the maintenance treatment of asthma as prophylactic therapy. It is also indicated for asthma patients who require systemic corticosteroid administration, where adding Beclate CFC free inhaler may reduce or eliminate the need for the systemic corticosteroids.

Beclate is NOT indicated for the relief of acute bronchospasm.

DOSAGE AND ADMINISTRATION

Adults: and Children (above 12 years)
The usual doses 200 mcg twice daily. In most severe case, 600-800 mcg per day may be given and subsequently reduced according to the response. The maximum daily dose recommended is 840 mcg per day.

Children (6-12 years)
50-100 mcg should be given two, three or four times daily according to the response. Alternately 100 mcg or 200 mcg twice daily may be administered.

Patients inadequately controlled by bronchodilator therapy
Patients should be given a starting dose of inhaled beclomethasone which is appropriate for the severity of their disease. The dose may then be adjusted until control is achieved, or reduced to the minimum effective dose according to individual response.

Patients being treated with oral corticosteroids
The patient should be in a reasonably stable before being given inhaled BDP in addition to the usual maintenance dose of systemic steroid. After about a week, gradual withdrawal of the systemic steroid is started by reducing the daily dose by one milligram prednisolone or its equivalent, at not less than weekly intervals.

Method of Administration
Oral Inhalation

CONTRAINDICATIONS

BECLATE is contraindicated in the primary treatment of status asthmaticus or other acute episodes of asthma where intensive measures are required.

Hypersensitivity to any of the ingredients of this preparation contraindicates its use. Though highly effective for the treatment of asthma, corticosteroids do not affect asthma symptoms immediately. However, improvement following inhaled administration of beclomethasone can occur within 24 hours of beginning treatment, although maximum benefit may not be achieved for 1 to 2 weeks or corticosteroids are discontinued, asthma longer after starting treatment.

WARNINGS AND PRECAUTIONS

Particular care is needed in patients who are transferred from systemically active corticosteroids to BECLATE because deaths due to adrenal insufficiency have occurred in asthmatic patients during and after transfer from systemic corticosteroids to beclomethasone dipropionate HFA inhaler. After withdrawal from systemic corticosteroids, a number of months are required for recovery of hypothalamic- pituitary-adrenal (HPA) function. During this period of HPA suppression, patients may exhibit signs and symptoms of adrenal insufficiency when exposed to trauma, surgery, or infections, particularly gastroenteritis. Although BECLATE may provide control of asthmatic symptoms during these episodes, it does NOT provide the systemic steroid that is necessary for coping with these emergencies.

During periods of stress or a severe asthmatic attack, patients who have been withdrawn from systemic corticosteroids should be instructed to resume systemic steroids (in large doses) immediately and to contact their physician for further instruction. These patients should also be instructed to carry a warning card indicating that they may need supplementary systemic steroids during periods of stress or a severe asthma attack. To assess the risk of adrenal insufficiency in emergency situations, routine tests of adrenal cortical function, including measurement of early morning resting cortisol levels, should be performed periodically in all patients. An early morning resting cortisol level may be accepted as normal only if it falls at or near the normal mean level.

Localized infections with Candida albicans or Aspergillus niger have occurred in the mouth and pharynx and occasionally in the larynx. Positive cultures for oral Candida may be present in up to 75% of patients. Although the frequency of clinically apparent infection is considerably lower, these infections can develop with any inhaled corticosteroid and may require treatment with appropriate antifungal therapy or discontinuation of treatment with BECLATE.

DRUG INTERACTIONS

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 agent.

PREGNANCY AND LACTATION

Pregnancy

There is inadequate evidence of safety in human pregnancy. The use of beclomethasone dipropionate during pregnancy requires that the possible benefits of the drug be weighed against the possible hazards.

Nursing Mothers

Corticosteroids are secreted in human milk. Because of the potential for serious adverse reactions in nursing infants for BECLATE, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

SIDE EFFECTS

Candidiasis of the mouth and throat (Thrush) occurs in some patients, the incidence of which is increased with doses greater than 400 mcg of beclomethasone dipropionate per day. Patients with high blood levels of Candida preciptinis, indicating a previous infection, are most likely to develop this complication. Some patients may find it helpful to rinse their mouth after mouth thoroughly with water after inhalation.

In some patients, inhaled beclomethasone dipropionate may cause hoarsness or throat irritation. It may be helpful to rinse out the mouth with water immediately after inhalation.

As with other inhalation therapy, paradoxical bronchospasm may occur with an immediate increases in wheezing after dosing. This responds to fast-acting inhaled bronchodilator. The preparation should be discontinued immediately, the patient assessed and if necessary alternative therapy (e.g. Beclate Rotacaps) instituted.

OVERDOSE, TREATMENT AND ANTIDOTES

In the event of excessive and prolonged use of any beclomethasone dipropionate preparations singly or collectively that could possibly lead to adrenal suppression, treatment should be

discontinued.

Chronic overdosage may result in signs and symptoms of hypercorticism. No deaths occurred when beclomethasone dipropionate was given as single oral doses of 3000mg/kg to mice and 2000 mg/kg to rats (appr. 12 000 and 16 000 times respectively, the maximum recommended human daily inhalation dose on mg/m2 basis).

STORAGE CONDITION

Store below 30°C. Do not freeze.

CAUTION

The metal canister of Beclate Inhaler is pressurised. It should not be broken, punctured or burnt, even when apparently empty.

SHELF LIFE

24 months

PACK SIZE

Each pack containing one spray container with product label, pack insert and an actuator.

PRESENTATION

200 metered doses

REGISTRATION HOLDER IN MALAYSIA

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DATE OF REVISION

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