

## NEW ZEALAND DATA SHEET

### **Beclazone™ 50 CFC-Free Inhaler** **Beclazone™ 100 CFC-Free Inhaler** **Beclazone™ 250 CFC-Free Inhaler** **Beclometasone dipropionate**

#### **Qualitative and Quantitative Composition**

BECLAZONE 50 CFC-Free Inhaler is a metered dose aerosol inhaler which delivers 50 micrograms of beclometasone dipropionate per metered dose (or "puff").

BECLAZONE 100 CFC-Free Inhaler is a metered dose aerosol inhaler which delivers 100 micrograms of beclometasone dipropionate per metered dose (or "puff").

BECLAZONE 250 CFC-Free Inhaler is a metered dose aerosol inhaler which delivers 250 micrograms of beclometasone dipropionate metered dose (or "puff").

#### **Pharmaceutical Form**

Pressurised inhalation, suspension.

BECLAZONE CFC-Free Inhaler is a metered dose aerosol inhaler consisting of a pressurised aluminium canister fitted with a metered dispensing valve, and fitted into a plastic actuator/mouthpiece with a cap, as follows:

BECLAZONE 50 CFC-Free Inhaler, cream colour actuator/mouthpiece and brown colour cap

BECLAZONE 100 CFC-Free Inhaler, brown colour actuator/mouthpiece and white colour cap

BECLAZONE 250 CFC-Free Inhaler, wine colour actuator/mouthpiece and pink colour cap.

Each canister contains 200 metered doses. The Inhaler contains the CFC-free propellant HFA 134a.

#### **Clinical Particulars**

##### **Therapeutic Indications**

Beclometasone dipropionate provides effective anti-inflammatory action in the lungs and offers preventive background treatment of asthma.

Severe asthma requires regular medical assessment as death may occur. Patients with severe asthma have constant symptoms and frequent exacerbations, with limited physical capacity, and PEF values below 60% predicted at baseline with greater than 30% variability, usually not returning entirely to normal after a bronchodilator. These patients will require high dose inhaled (see dosage instructions) or oral corticosteroid therapy. Sudden worsening of symptoms may require increased corticosteroid dosage which should be administered under urgent medical supervision.

##### **Adults:-**

Prophylactic management in:-

Mild asthma (PEF values greater than 80% predicted at baseline with less than 20% variability): Patients requiring intermittent symptomatic bronchodilator asthma medication on more than an occasional basis.

Moderate asthma (PEF values 60 - 80% predicted at baseline with 20 - 30% variability): Patients requiring regular asthma medication and patients with unstable or worsening asthma on other prophylactic therapy or bronchodilator alone.

Severe asthma (PEF values less than 60% predicted at baseline with greater than 30% variability): Patients with severe chronic asthma. On transfer to high dose inhaled beclometasone dipropionate, 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.

##### **Children:-**

Any child who requires prophylactic asthma medication (see Posology and Method of Administration).

## **Posology and Method of Administration**

BECLAZONE CFC-Free Inhaler is administered by the inhaled route only.

Patients should be made aware of the prophylactic nature of therapy with inhaled beclometasone dipropionate and that it should be taken regularly even when they are asymptomatic. The dosage of beclometasone dipropionate should be adjusted according to the individual response. If patients find that short-acting relief bronchodilator treatment becomes less effective or they need more inhalations than usual, medical attention must be sought. In patients who find co-ordination of a pressurised metered dose inhaler difficult a spacer device may be used with BECLAZONE CFC-Free Inhaler.

### **Adults and children over 12 years of age:-**

Patients should be given a starting dose of inhaled beclometasone dipropionate (BECLAZONE 50 CFC-Free Inhaler or BECLAZONE 100 CFC-Free Inhaler or BECLAZONE 250 CFC-Free Inhaler) which is appropriate for the severity of their disease based on the following guidance:

Mild asthma: 200 to 600mcg per day in divided doses.

Moderate asthma: 600 to 1000mcg per day in divided doses.

Severe asthma: Up to 1000mcg per day in divided doses.

The dose may then be adjusted until control is achieved or reduced to the minimum effective dose according to the individual response.

### **Children over 7 years of age:-**

Up to 200mcg per day in divided doses.

Children should be given a starting dose of inhaled beclometasone dipropionate 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 the individual response. There are no data on the use of Beclazone CFC-Free in children aged under seven years.

### **Special patient groups:-**

There is no need to adjust the dose in elderly patients or in those with hepatic or renal impairment.

When transferring a patient to Beclazone CFC-Free Inhaler from CFC-containing Beclazone Inhaler, switch at same strength and dose and adjust if necessary according to the individual response.

### **Contra-indications**

BECLAZONE CFC-Free Inhaler is contra-indicated in patients with a history of hypersensitivity to any of its components.

### **Special Warnings and Special Precautions for Use**

The management of asthma should follow a stepwise programme, and patient response should be monitored clinically and by lung function tests. Increasing use of short-acting inhaled  $\beta_2$  agonists to control symptoms indicates deterioration of asthma control. Under these conditions, the patient's therapy plan should be reassessed. Sudden and progressive deterioration in asthma control is potentially life-threatening and consideration should be given to increasing corticosteroid dosage. In patients considered at risk, daily flow monitoring may be instituted.

BECLAZONE CFC-Free Inhaler is not for use in acute attacks but for routine long-term management. Patients will require a fast- and short-acting inhaled bronchodilator to relieve acute asthmatic symptoms.

Patients' inhaler technique should be checked to make sure that aerosol actuation is synchronised with inspiration of breath for optimum delivery of the medicine to the lungs.

Lack of response or severe exacerbations of asthma should be treated by increasing the dose of inhaled beclometasone dipropionate and, if necessary, by giving a systemic steroid and/or an antibiotic if there is an infection.

Systemic effects may occur with any inhaled corticosteroid, particularly at high doses prescribed for long periods; these effects are much less likely to occur than with oral corticosteroids. Possible systemic effects include adrenal suppression, decrease in bone mineral density, cataract and glaucoma. It is important, therefore, that the dose of inhaled corticosteroid is titrated to the lowest dose at which effective control is maintained (see Undesirable Effects).

Possible systemic effects also include growth retardation in children and adolescents. It is recommended that the height of children receiving prolonged treatment with inhaled corticosteroid is regularly monitored.

Certain individuals can show greater susceptibility to the effects of inhaled corticosteroid than do most patients.

Because of the possibility of impaired adrenal response, patients transferring from oral steroid therapy to inhaled beclometasone dipropionate therapy should be treated with special care, and adrenocortical function regularly monitored.

Following introduction of inhaled beclometasone dipropionate, withdrawal of systemic therapy should be gradual and patients encouraged to carry a steroid warning card indicating the possible need for additional therapy in times of stress.

In rare cases inhaled therapy may unmask underlying eosinophilic conditions (e.g. Churg Strauss syndrome). These cases have usually been associated with reduction or withdrawal of oral corticosteroid therapy. A direct causal relationship has not been established.

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

Treatment with BECLAZONE CFC-Free Inhaler should not be stopped abruptly.

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

### **Use During Pregnancy and Lactation**

There is inadequate evidence of safety of beclometasone dipropionate in human pregnancy. In animal reproduction studies adverse effects typical of potent corticosteroids are only seen at high systemic exposure levels; direct inhaled application ensures minimal systemic exposure. Administration of medicines during pregnancy should only be considered if the expected benefit to the mother is greater than any possible risk to the foetus.

No specific studies examining the transference 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. The use of beclometasone dipropionate in mothers breast feeding their babies requires that the therapeutic benefits of the medicine be weighed against the potential hazards to the mother and baby.

### **Effects on Ability to Drive and Use Machines**

Beclometasone dipropionate is unlikely to produce an effect.

### **Interaction with Other Medicinal Products and Other Forms of Interaction**

There are no proven drug interactions.

### **Undesirable Effects**

Candidiasis of the mouth and throat (thrush) occurs in some patients, the incidence of which is increased with doses greater than 400mcg beclometasone dipropionate per day. Patients with high blood levels of Candida precipitins, indicating a previous infection, are most likely to develop this complication. Patients may find it helpful to rinse out their mouth with water after using the inhaler. Symptomatic candidiasis can be treated with topical anti-fungal therapy whilst still continuing with the BECLAZONE CFC-Free Inhaler.

In some patients inhaled beclometasone dipropionate may cause hoarseness or throat irritation. It may be helpful to rinse out the mouth with water immediately after inhalation. The use of a large volume 'spacer' device may be considered.

As with other inhalation therapy, paradoxical bronchospasm may occur with an immediate increase in wheezing after dosing. This should be treated immediately with a fast-acting inhaled bronchodilator. BECLAZONE CFC-Free Inhaler should be discontinued immediately, the patient assessed, and if necessary alternative therapy instituted.

Hypersensitivity reactions including rashes, urticaria, pruritus, erythema and oedema of the eyes, face, lips and throat have been reported.

Possible systemic effects include adrenal suppression, growth retardation in children and adolescents, decrease in bone mineral density, cataract and glaucoma (see Special Warnings and Special Precautions for Use).

### **Overdose**

Acute inhalation of beclometasone dipropionate doses in excess of those recommended may lead to temporary suppression of adrenal function. This does not need emergency action as adrenal function is recovered in a few days, as verified by plasma cortisol measurements. However if higher than recommended dosage is continued over prolonged periods, some degree of adrenal suppression may result. Monitoring of adrenal reserve may be necessary. In cases of beclometasone dipropionate overdose, therapy may still be continued at a suitable dosage for symptom control.

## **Pharmacological Properties**

### **Pharmacodynamic Properties**

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

### **Pharmacokinetic Properties**

#### **Absorption**

When administered via inhalation (via metered dose inhaler), systemic absorption of unchanged BDP occurs through the lungs with negligible oral absorption of the swallowed dose. There is extensive conversion of BDP to its active metabolite B-17-MP within the lung prior to absorption. 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 first being 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.

#### **Metabolism**

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.

#### **Distribution**

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

#### **Elimination**

The elimination of BDP and B-17-MP are characterised by high plasma clearance (150 and 120L/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.

### **Preclinical Safety Data**

Preclinical safety studies indicate that beclometasone dipropionate shows negligible systemic toxicity when administered by the inhaled route. Inhaled beclometasone dipropionate has been used clinically, as a formulation containing chlorofluorocarbon (CFC) propellants, for over twenty years. Preclinical studies in rats and dogs with beclometasone dipropionate in the hydrofluoroalkane propellant, norflurane (1,1,1,2-tetrafluoroethane) or HFA-134a, have shown a comparative safety profile to the current CFC-containing products.

## **Pharmaceutical Particulars**

### **List of Excipients**

Ethanol (Anhydrous) 99.5%

Hydrofluoroalkane 134a (HFA-134a).

### **Incompatibilities**

None reported.

### **Shelf Life**

BECLAZONE 50 CFC-Free Inhaler, BECLAZONE 100 CFC-Free Inhaler, BECLAZONE 250 CFC-Free Inhaler: 36 months.

### **Special Precautions for Storage**

Do not store above 25°C. Do not refrigerate or freeze. The canister is pressurised: it must not be burnt, punctured or broken even when apparently empty. Do not expose to temperatures higher than 50°C. As with most inhaled medicines in aerosol canisters, the therapeutic effect of this medicine may decrease when the canister is cold.

### **Instructions for Use/Handling**

#### **Using the inhaler:-**

Test spray the inhaler before you use it for the first time and also if you have not used it for a while.

1. Take the cap of the inhaler. Make sure the mouthpiece clean and free of fluff and dirt.
2. Hold the inhaler upright with your thumb on the base and your first finger on top of the can. Shake the inhaler vigorously up and down.
3. Breathe out normally as far as is comfortably can. Then hold the mouthpiece between your lips. Breathe in slowly and deeply. As you start to breathe in, press the aerosol can with your first finger to spray the aerosol and release the medicine. Continue to breathe in slowly and deeply.
4. Take the inhaler out of your mouth and hold your breath for 10 seconds, or as long as you comfortably can.
5. If you need more than one puff, wait for about one minute and then start again from step 2. Put the cap back on the inhaler.

*Note:-*Do not rush step 3. It is important that you start to breathe in as slowly as possible just before using your inhaler. Practice in front of a mirror for the first few times. If you see 'mist' coming from the top of the inhaler or from the sides of your mouth you should start again from step 2.

#### **Cleaning your inhaler:-**

You must keep your inhaler clean, especially the mouthpiece. This will prevent deposits from the aerosol building up. Clean your inhaler at least once a week.

Take the metal can from the plastic body and rinse the plastic body and cap in warm water. Do not use very hot water to clean your inhaler. Dry thoroughly (leave to dry overnight if possible) but do not use direct heat. Put the metal can back in the plastic mouthpiece and replace the cap. Do not put the metal can into water. Failure to allow the mouthpiece to dry will result in an increase in blockage problems.

## **Medicines Classification**

Prescription Medicine

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**Further Information**

BECLAZONE is a trade-mark.

*Asthma and Respiratory Foundation of New Zealand (Inc.):* AirFlow Products Ltd is a wholly owned subsidiary of the Asthma and Respiratory Foundation of New Zealand (Inc.). Funds raised will support the work of the Asthma and Respiratory Foundation of New Zealand (Inc.).

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