SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Easyhaler® Beclometasone 200 micrograms/dose inhalation powder

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Name of active ingredient	Amount in metered dose	Amount in delivered dose
Beclometasone dipropionate	200 micrograms	180 micrograms

Excipient with known effect: Lactose monohydrate

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Inhalation powder administered from multidose powder inhaler.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Beclometasone dipropionate given by inhalation offers preventative treatment for asthma. It provides effective anti-inflammatory action in the lungs with a lower incidence and severity of adverse effects than those observed when corticosteroids are administered systemically. It also offers preventive treatment of asthma.

Easyhaler® Beclometasone 200 micrograms/dose is indicated in the following:

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 a regular 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 despite 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.

4.2 Posology and method of administration

Easyhaler® Beclometasone 200 micrograms/dose is for oral inhalation use only.

Patients should be made aware of the prophylactic nature of therapy with inhaled beclometasone dipropionate and that it should be taken regularly everyday even when they are asymptomatic.

Patients should be given a starting dose of inhaled beclometasone dipropionate appropriate to the severity of their disease. The dose may then be adjusted until control is achieved and should be titrated to the lowest dose at which effective control of asthma is maintained.

Adults

The usual starting dose is 200 micrograms twice a day. In more severe cases the starting dose may need to increase to 600 to 800 micrograms per day which may then be reduced when the patient's asthma has stabilised. The total daily dose may be administered as two, three, or four divided doses.

Paediatric population

Easyhaler® Beclometasone 200 micrograms/dose is not recommended for children.

Special Patient Groups

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

4.3 Contraindications

Hypersensitivity to Beclometasone dipropionate or to the excipients listed in section 6.1 (lactose monohydrate, which contains small amounts of milk proteins).

Special care is necessary in patients with active or quiescent pulmonary tuberculosis.

4.4 Special warnings and precautions for use

Patients should be instructed in the proper use of the inhaler, and their technique checked, to ensure that the drug reaches the target areas within the lungs. They should also be made aware that Easyhaler® Beclometasone 200 micrograms/dose has to be used regularly every day for optimum benefit. Patients should be made aware of the prophylactic nature of therapy with Easyhaler® Beclometasone 200 micrograms/dose and that they should be used regularly, even when they are asymptomatic.

Easyhaler® Beclometasone 200 micrograms/dose is not designed to relieve acute asthma symptoms for which an inhaled short-acting bronchodilator is required. Patients should be advised to have such rescue medication available.

Severe asthma requires regular medical assessment, including lung-function testing, as patients are at risk of severe attacks and even death.

Increasing use of bronchodilators, in particular short-acting inhaled beta2 agonists to relieve symptoms indicates deterioration of asthma control. 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 this situation, patients should be reassessed and consideration given to the need for increased anti-inflammatory therapy (e.g. higher doses of inhaled corticosteroid or a course of oral corticosteroid) considered. Severe exacerbations of asthma must be treated in the normal way.

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 and 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.

Visual disturbance

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.

Prolonged treatment with high doses of inhaled corticosteroids, particularly higher than recommended doses, may result in clinically significant adrenal suppression. Additional systemic corticosteroid cover should be considered during periods of stress or elective surgery.

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 antibiotic if there is an infection, and by use of beta-agonist therapy.

<u>For the transfer of patients being treated with oral corticosteroids:</u>

The transfer of oral steroid-dependent patients to Easyhaler® Beclometasone 200 micrograms/dose and their subsequent management needs special care as recovery from impaired adrenocortical function, caused by prolonged systemic steroid therapy, may take a considerable time.

Patients who have been treated with systemic steroids for long periods of time or at a high dose may have adrenocortical suppression. With these patients adrenocortical function should be monitored regularly and their dose of systemic steroid reduced cautiously.

After approximately a week, gradual withdrawal of the systemic steroid is commenced. Decrements in dosages should be appropriate to the level of maintenance systemic steroid, and introduced at not less than weekly intervals. For maintenance doses of prednisolone (or equivalent) of 10mg daily or less, the decrements in dose should not be greater than 1mg per day, at not less than weekly intervals. For maintenance doses of prednisolone in excess of 10mg daily, it may be appropriate to employ cautiously, larger decrements in dose at weekly intervals.

Some patients feel unwell in a non-specific way during the withdrawal phase despite maintenance or even improvement of the respiratory function. They should be encouraged to persevere with Easyhaler® Beclometasone 200 micrograms/dose and withdrawal of systemic steroid continued, unless there are objective signs of adrenal insufficiency.

Patients weaned off oral steroids whose adrenocortical function is impaired should carry a steroid warning card indicating that they may need supplementary systemic steroid during periods of stress, e.g. worsening asthma attacks, chest infections, major intercurrent illness, surgery, trauma, etc.

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

Treatment with Easyhaler® Beclometasone 200 micrograms/dose should not be stopped abruptly.

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

Easyhaler® Beclometasone contains approximately 7mg of lactose per dose. This amount does not normally cause problems in lactose intolerant people. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

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 agents.

4.6 Fertility, pregnancy and lactation

Pregnancy

There is inadequate evidence of safety in human pregnancy. Administration of corticosteroids to pregnant animals can cause abnormalities of fetal development including cleft palate and intra-uterine growth retardation. There may therefore be a very small risk of such effects in the human fetus. It should be noted, however, that the fetal changes in animals occur after relatively high systemic exposure. Easyhaler® Beclometasone 200 micrograms/dose delivers the drug 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.

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

Breast-feeding

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 drug be weighed against the potential hazards to the mother and baby.

4.7 Effects on ability to drive and use machines

Easyhaler® Beclometasone 200 micrograms/dose has no influence on the ability to drive and use machine.

4.8 Undesirable effects

Adverse events are listed below by system organ class and frequency. Frequencies are defined as: very common (1/10), common (1/100 and <1/10), uncommon (1/1000 and <1/100), rare (1/10,000 and <1/1000), very rare (<1/10,000) including isolated reports and not known (cannot be estimated from the available data). Very common, common and uncommon events were generally determined from clinical trial data. The incidence in placebo and comparator group has not been taken into account in estimation of these frequencies. Rare and very rare events were generally determined from spontaneous data.

System Organ Class	Adverse Event	Frequency
Infections & Infestations	Candidiasis of the mouth and throat.	Very Common
Immune System Disorders	Hypersensitivity reactions with the following manifestations:	
	Rashes, urticaria, pruritis, erythema.	Uncommon
	Oedema of the eyes, face, lips and throat	Very Rare
	Respiratory symptoms (dyspnoea and/or bronchospasm)	Very Rare
	Anaphylactoid/anaphylactic reactions	Very Rare
Endocrine Disorders	Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, decrease in bone	Very Rare

	mineral density, cataract, glaucoma	
Psychiatric Disorders	Psychomotor hyperactivity, sleep disorders, anxiety, depression, aggression, behavioural changes (predominantly in children)	Not known
Eye disorders	Vision blurred (see also section 4.4)	Not known
Respiratory, Thoracic & Mediastinal Disorders	Hoarseness/throat irritation, cough	Common
	Paradoxical bronchospasm	Very Rare
	Eosinophilic pneumonia	Not Known
Skin and subcutaneous tissue disorders	Easy bruising, skin thinning	Not known

Candidiasis of the mouth and throat (thrush) occurs in some patients, the incidence increasing with doses greater than 400 micrograms of 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 their mouth thoroughly with water after using the inhaler. Symptomatic candidiasis can be treated with topical anti-fungal therapy whilst still continuing with Easyhaler® Beclometasone 200 micrograms/dose treatment.

Systemic effects of inhaled corticosteroids may occur, particularly at high doses prescribed for prolonged periods. Possible systemic effects include Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, decrease in bone mineral density, cataract, glaucoma (see 4.4 Special Warnings and Precautions for Use).

In some patients inhaled beclometasone dipropionate may cause hoarseness, cough, throat irritation and sore throat. It may be helpful to rinse the mouth out with water immediately after inhalation.

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. The beclometasone dipropionate preparation should be discontinued immediately, the patient assessed, and if necessary alternative therapy instituted.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal

product. Healthcare professionals are asked to report any suspected adverse reactions via Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

4.9 Overdose

Acute: Inhalation of the drug in doses in excess of those recommended may lead to temporary suppression of adrenal function. This does not require emergency action. In these patients treatment with beclometasone diproprionate by inhalation should be continued at a dose sufficient to control asthma; adrenal function recovers in a few days and can be verified by measuring plasma cortisol.
Chronic: Use of inhaled beclometasone dipropionate in daily doses in excess of 1,500 micrograms over prolonged periods may lead to some degree of adrenal suppression. Monitoring of adrenal reserve may be indicated. Treatment should be continued at a dose sufficient to control asthma.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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

5.2 Pharmacokinetic properties

Absorption

When administered via inhalation (via metered dose inhaler) there is extensive conversion of BDP to the active metabolite B-17-MP within the lungs prior to systemic absorption. The systemic absorption of B-17-MP arises from both lung deposition and oral absorption of the swallowed dose. When administered orally, in healthy male volunteers, the bioavailability of BDP is negligible but pre-systemic conversion to B-17-MP results in 41% (95% CI 27- 62 %) of the dose being available as B-17-MP.

Metabolism

BDP is cleared very rapidly from the systemic circulation, owing to extensive first pass metabolism. 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 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/h) with corresponding terminal elimination half lives of 0.5h and 2.7h. 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.

5.3 Preclinical safety data

No clinically relevant findings were observed in preclinical studies.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate (which contains small amounts of milk proteins)

6.2 Incompatibilities

None

6.3 Shelf life

3 years in aluminium foil and 6 months after opening of the foil

6.4 Special precautions for storage

Do not store above 25°C

6.5 Nature and contents of container

The Easyhaler inhaler, which consists of seven plastic parts and a stainless steel spring, is wrapped in aluminium foil. The inhaler with aluminium foil and the protective cover are packed in a cardboard box.

Packages:
Easyhaler® Beclometasone 200 micrograms/dose inhalation powder:

- 200 doses protective cover
- 200 doses
- 2 x 200 doses

6.6 Special precautions for disposal

Patients have to be instructed to perform a rapid and forced inhalation through the Easyhaler device. Patients have to be instructed not to exhale into the device. Illustrated user's instructions for use accompany each package.

7 MARKETING AUTHORISATION HOLDER

Orion Corporation
Orionintie 1
Fin-02200 Espoo
Finland

8 MARKETING AUTHORISATION NUMBER(S)

PL 27925/0001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

21/12/1999 / 11/08/2009

10 DATE OF REVISION OF THE TEXT

02/06/2017