

**BECLOMETASONE DIPROPIONATE 100 CYCLOCAPS
PL 00289/0570
BECLOMETASONE DIPROPIONATE 200 CYCLOCAPS
PL 00289/0571
BECLOMETASONE DIPROPIONATE 400 CYCLOCAPS
PL 00289/0572**

UKPAR

TABLE OF CONTENTS

Lay Summary	Page 2
Scientific discussion	Page 3
Steps taken for assessment	Page 10
Steps taken after authorisation – summary	Page 11
Summary of Product Characteristics	Page 12
Product Information Leaflet	Page 27
Labelling	Page 29

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**BECLOMETASONE DIPROPIONATE 200 CYCLOCAPS
PL 00289/0571**

**BECLOMETASONE DIPROPIONATE 400 CYCLOCAPS
PL 00289/0572**

LAY SUMMARY

The MHRA granted Teva UK Limited Marketing Authorisations (licences) for the medicinal product Beclometasone Dipropionate 100, 200 and 400 Cyclocaps on 5th March 2008. These products, to be available by prescription only (POM), is used to prevent the symptoms of asthma and ease breathing difficulties.

The active ingredient beclometasone dipropionate prevents inflammation of the lungs caused by conditions such as asthma.

These applications are duplicates of previously granted applications for Forabec 100, 200 and 400 Micrograms, which were originally approved on 12th August 1998 to Pharbita BV Zaandam Netherlands (PL 05322/0003-5). These products have since been renamed to Beclometasone 100, 200 and 400 Cyclocaps and the current marketing authorisation holder is Novartis Pharmaceuticals UK Limited (PL 00101/0637-9).

No new or unexpected safety concerns arose from these simple applications and it was, therefore, judged that the benefits of taking Beclometasone Dipropionate 100, 200 and 400 Cyclocaps outweigh the risks, hence Marketing Authorisations have been granted.

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PL 00289/0572**

SCIENTIFIC DISCUSSION

TABLE OF CONTENTS

Introduction	Page 4
Pharmaceutical assessment	Page 5
Preclinical assessment	Page 8
Clinical assessment	Page 9
Overall conclusions and risk benefit assessment	Page 10

INTRODUCTION

The UK granted a marketing authorisation for the medicinal product Beclometasone Dipropionate 100, 200 and 400 Cyclocaps (PL 00289/0570-2) to Teva UK Limited on 5th March 2008. The product is available as a prescription-only medicine (POM).

The application was submitted as a simple abridged, according to Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC, cross-referring to previously granted applications for Forabec 100, 200 and 400 Micrograms, which were originally approved on 12th August 1998 to Pharbata BV Zaandam Netherlands (PL 05322/0003-5). These products have since been renamed to Beclometasone 100, 200 and 400 Cyclocaps and the current marketing authorisation holder is Novartis Pharmaceuticals UK Limited (PL 00101/0637-9).

No new data were submitted nor was it necessary for these simple applications, as the data are identical to that of previously granted cross-reference products. As the cross-reference products were granted prior to the introduction of current legislation, no PAR was generated for it.

The active ingredient is beclometasone dipropionate, a glucocorticoid steroid drug that indirectly inhibits the formation of inflammatory mediators, such as prostaglandins and leukotrienes. It is indicated for the prophylactic management of asthma.

PHARMACEUTICAL ASSESSMENT

LICENCE NO: PL 00289/0570-2

PROPRIETARY NAME: Beclometasone Dipropionate 100, 200 and 400 Cyclocaps

ACTIVE(S): Beclometasone dipropionate

COMPANY NAME: Teva UK Limited

E.C. ARTICLE: Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC

LEGAL STATUS: POM

1. INTRODUCTION

These are simple, piggyback applications for Beclometasone Dipropionate 100, 200 and 400 Cyclocaps submitted under Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC. The proposed MA holder is Teva UK Limited, Brampton Road, Hampden Park, Eastbourne, East Sussex, BN22 9AG, UK.

The applications cross-refer to Forabec 100, 200 and 400 Micrograms, which were originally approved on 12th August 1998 to Pharbita BV Zaandam Netherlands (PL 05322/0003-5). These products have since been renamed to Beclometasone 100, 200 and 400 Cyclocaps and the current marketing authorisation holder is Novartis Pharmaceuticals UK Limited (PL 00101/0637-9).

The current applications are considered valid.

2. MARKETING AUTHORISATION APPLICATION FORM

2.1 Name(s)

The proposed names of the products are Beclometasone Dipropionate 100, 200 and 400 Cyclocaps. The product has been named in-line with current requirements.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes

The products contains beclometasone dipropionate, equivalent to either 100, 200 and 400micrograms per actuation. They are to be stored in a polyvinylidene chloride/polyvinylchloride/aluminium blisters in pack sizes of 10, 14, 20, 28, 30, 42, 50, 56, 60, 84, 100, 112, 120, 140, 168, 200 and 280 tablets. The proposed shelf-life (36 months) and storage conditions (store in original package and store below 25 degrees) are consistent with the details registered for the cross-reference products.

2.3 Legal status

On approval, the products will be available as prescription-only medicines (POM).

2.4 Marketing authorisation holder/Contact Persons/Company

Teva UK Limited, Brampton Road, Hampden Park, Eastbourne, BN22 9AG, UK.

The QP responsible for pharmacovigilance is stated and his CV is included.

2.5 Manufacturers

The proposed manufacturing sites are consistent with those registered for the cross-reference product and evidence of GMP compliance has been provided.

2.6 Qualitative and quantitative composition

The proposed composition is consistent with the details registered for the cross-reference product.

2.7 Manufacturing process

The proposed manufacturing process is consistent with the details registered for the cross-reference product and the maximum batch size is stated.

2.8 Finished product/shelf-life specification

The proposed finished product specification is in-line with the details registered for the cross-reference product.

2.9 Drug substance specification

The proposed drug substance specification is consistent with the details registered for the cross-reference products.

2.10 TSE Compliance

Lactose and gelatin are the only substances of animal origin in these products. Suitable TSE Certificates of Suitability have been provided for gelatin and a statement has been provided for the manufacturer of lactose. These details are consistent with those for the cross-reference products.

3. EXPERT REPORTS

The applicant has included detailed expert reports in Module 2 of the application. Signed declarations and copies of the experts' CVs are enclosed in Module 1.4 for the quality, non-clinical and clinical experts. All are considered to have sufficient experience for their responsibilities.

4. PRODUCT NAME AND APPEARANCE

See 2.1 for details of the proposed product names. The appearances of the products are identical to the cross-reference products.

5. SUMMARY OF PRODUCT CHARACTERISTICS

The proposed summaries are consistent with the details registered for the cross-reference products.

6. PATIENT INFORMATION LEAFLET/CARTON

PIL

The patient information leaflet has been prepared in-line with the details registered for the cross-reference product. The marketing authorisation holder has provided a commitment to update the marketing authorisation no later than 1st July 2008 with a package leaflet in compliance with Article 59 of Council Directive 2001/83/EC and that the leaflet shall reflect the results of consultation with target patient groups.

Carton and blister

The proposed artwork is comparable to the artwork registered for the cross-reference product and complies with statutory requirements. In-line with current legislation, the applicant has also included the name of the products in Braille on the outer packaging and has included sufficient space for a standard UK pharmacy dispensing label.

7. CONCLUSIONS

The data submitted with the applications are acceptable. Marketing Authorisations should be granted.

PRECLINICAL ASSESSMENT

No new preclinical data have been supplied with these applications and none are required for applications of this type.

CLINICAL ASSESSMENT

No new clinical data have been supplied with these applications and none are required for applications of this type.

OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY

The data for these applications are consistent with that previously assessed for the cross-reference product and as such have been judged to be satisfactory.

PRECLINICAL

No new preclinical data were submitted and none are required for applications of this type.

EFFICACY

These applications are identical to previously granted applications for Forabec 100, 200 and 400 Micrograms (PL 05322/0003-5), currently authorised as Beclametasone 100, 200 and 400 Cyclocaps to Novartis Pharmaceuticals UK Limited (PL 00101/0637-9).

No new or unexpected safety concerns arise from these applications.

The SPC, PIL and labelling are satisfactory and consistent with that for the cross-reference products.

RISK:BENEFIT ASSESSMENT

The quality of the products is acceptable and no new preclinical or clinical safety concerns have been identified. The applicant's products are identical to the cross-reference products. Extensive clinical experience with beclometasone dipropionate is considered to have demonstrated the therapeutic value of the compound. The risk:benefit is, therefore, considered to be positive.

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STEPS TAKEN FOR ASSESMENT

1	The MHRA received the marketing authorisation applications on 15/12/2003.
2	Following standard checks and communication with the applicant the MHRA considered the applications valid on 20/01/2004.
3	Following assessment of the applications, the MHRA requested further information on 17/06/2004 and 24/06/2005.
4	The applicant responded to the MHRA's requests, providing further information on 17/11/2004 and 08/11/2005.
5	The applications were determined on 04/03/2008

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STEPS TAKEN AFTER ASSESSMENT

Date submitted	Application type	Scope	Outcome

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Beclometasone dipropionate 100 Cyclocaps®

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

When used in conjunction with the Cyclohaler each capsule delivers the equivalent of 100 micrograms of beclometasone dipropionate from the mouthpiece of the device.

The 100mcg capsule has a light brown opaque cap and clear body, printed 'logo' BECLO 100, in black ink.

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Inhalation powder, hard capsule.

Inhalation powder in capsules to be used in combination with the Cyclohaler®.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Beclometasone dipropionate is a corticosteroid with a potent anti-inflammatory action in the lungs. The contents of the capsule are inhaled by means of a specially designed device called the 'Cyclohaler'.

Beclometasone dipropionate is indicated for the prophylactic management of asthma, in the following types of patients.

Adults

Mild asthma: Patients requiring symptomatic bronchodilator asthma medication on a regular basis.

Moderate asthma: Patients with unstable or worsening asthma despite prophylactic therapy or bronchodilator alone.

Severe asthma: Patients with severe chronic asthma and those who are dependent on systemic corticosteroids for adequate control of symptoms. 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.

4.2 Posology and method of administration

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

Beclometasone dipropionate 100 Cyclocaps® are for oral inhalation use only, using the Cyclohaler. They should be used regularly for optimum results. Patients should be given a starting dose of inhaled beclometasone dipropionate which is appropriate for the severity of their disease. The dose should be titrated to the lowest dose at which effective control of asthma is maintained.

Adults

400 micrograms twice daily is the minimum starting dose. The total daily dose may be administered as 2, 3 or 4 divided doses.

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

Children

The usual starting dose is 200 micrograms twice daily. Alternatively one 100 micrograms capsule two, three or four times a day may be administered, according to the response.

4.3 Contraindications

Hypersensitivity to beclometasone dipropionate or to any of the components of the preparation.

Special care is required for patients with active or inactive pulmonary tuberculosis.

4.4 Special warnings and precautions for use

It is important for the patient to understand that the gelatin capsule may very occasionally break up and small pieces of gelatin might reach the mouth or throat after inhalation. The patient may be reassured that gelatin will soften in the mouth and can be swallowed. The tendency for the capsule to break up is minimised by not piercing the capsule more than once.

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. Treatment must not be stopped abruptly.

Beclometasone dipropionate 100 Cyclocaps® are not designed to relieve acute asthmatic symptoms for which an inhaled short-acting bronchodilator is required. Patients should be advised to have such rescue medication available.

Severe asthma requires 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 β_2 -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 corticosteroids or a course of oral corticosteroids). Severe exacerbations of asthma must be treated in the usual way.

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 β -agonist therapy.

Excessive mucous secretion may stop the drug reaching the bronchioles and a course of systemic corticosteroid may be needed, together with the beclometasone dipropionate inhalations, in order to remove the mucus and reduce inflammatory changes in the bronchial tree.

Patients being treated with beclometasone dipropionate may sometimes require a short course of concomitant oral corticosteroids to control their symptoms.

Patients should be instructed in the proper use of the Cyclohaler to ensure that the drug reaches the target areas in the lungs.

Restraint is necessary in treating patients with pulmonary disorders such as bronchiectasis and pneumoconiosis in view of the possibility of fungal infections.

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 adrenal suppression, growth retardation in children and adolescents, decrease in bone mineral density, cataract and glaucoma. It is important 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 recommended doses, may result in clinically significant adrenal suppression. Additional systemic corticosteroid cover should be considered during periods of stress or elective surgery.

For the transfer of patients being treated with oral corticosteroids

Care must be taken when switching from oral corticosteroids to beclometasone dipropionate inhalations to ensure that the patient's adrenocortical reserves are adequate. In patients who have a functional disorder of the adrenal cortex due to long term use of oral corticosteroids, beclometasone dipropionate inhalation must be initially used together with the corticosteroid dose usual for the patient, the oral steroid dosage is then gradually reduced until that treatment can be safely discontinued.

After about a week, gradual withdrawal of the oral steroid is commenced. The decrements in dosage should be appropriate to the level of maintenance oral steroid, and introduced at not less than weekly intervals. For maintenance doses of prednisolone, or its 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. In any patient who has been treated with oral steroids for long periods of time, or at a high dose, it is recommended that their adrenocortical function is regularly monitored as their dose of oral steroid is reduced cautiously.

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.

Substitution of oral corticosteroids by beclometasone dipropionate may reveal allergies previously suppressed by the systemically active corticosteroid such as allergic rhinitis and eczema. These must be properly treated with antihistamines and/or topical preparations including topical corticosteroids. Any infections of air passages must be adequately treated.

4.5 Interaction with other medicinal products and other forms of interaction

None stated.

4.6 Pregnancy and lactation

There is inadequate evidence of safety in human pregnancy.

The administration of corticosteroids to pregnant animals has resulted in foetal abnormalities, i.e. cleft palate and intra-uterine growth retardation. There may therefore be a very small risk of such effects in the human foetus. However, since beclometasone dipropionate is delivered to the lungs by inhalation it significantly reduces the exposure that occurs following the systemic use of corticosteroids. The use of beclometasone dipropionate in pregnancy requires that the possible benefits of the drug be weighed against the possible hazards.

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, potential levels in milk will be low. 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

None stated.

4.8 Undesirable effects

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

Some patients feel unwell for about 2 weeks during reduction of therapy with systemic corticosteroids even though the respiratory function is maintained or even improved. These patients may therefore need encouragement to continue using beclometasone dipropionate and continue to withdraw the systemic steroid unless there are objective signs of adrenal insufficiency.

Paradoxical bronchospasm is possible. If it occurs Beclometasone 100 Cyclocaps should be discontinued immediately and immediate treatment with a fast-acting bronchodilator instituted.

Local Candida infections of the mouth, throat and larynx may occur. Special vigilance is required for patients with high titres of Candida precipitins indicating a previous infection. Local antifungal therapy appears to control these infections without necessitating interruption of the beclometasone dipropionate treatment.

Hoarseness and irritation of the throat may occur but disappear after discontinuation of therapy, reduction of dose and/or resting of the voice. To reduce the incidences of candidiasis, hoarseness or irritation, the patient may be advised to rinse out their mouth with water, after taking their dose of Beclometasone 100 Cyclocaps®.

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

4.9 Overdose

Acute toxicity of beclometasone dipropionate is low. The only harmful effect that follows inhalation of large amounts of the drug over a short time period is suppression of hypothalamic-pituitary-adrenal (HPA) function. No special emergency action need be taken. Treatment with Beclometasone 100 Cyclocaps should be continued at the recommended dose to control the asthma; HPA function recovers in a day or two.

If beclometasone dipropionate is used excessively over a long period, this may lead to adrenal suppression. In such a case, the patient should be treated as steroid dependent, transferred to a suitable maintenance dose of a systemic corticosteroid and when the condition has stabilised, be returned to the inhaled therapy at the recommended dose. To guard against adrenal suppression, regular tests of adrenal function should be considered.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: R03BA01

When used as an inhalation powder beclometasone dipropionate has a potent glucocorticoid anti-inflammatory action within the lungs but is without significant systemic activity at therapeutic doses.

5.2 Pharmacokinetic properties

Following administration by inhalation less than 25% of the steroid will enter the respiratory tract, the majority of the dose being deposited in the oropharynx and subsequently swallowed. The pharmacokinetics of intravenously administered beclometasone dipropionate are important since this represents the disposition of the portion of the inhaled dose absorbed directly from the lung. Likewise the pharmacokinetics after oral administration are relevant to the swallowed portion of the inhaled dose.

Absorption from the gastrointestinal tract is relatively slow with peak plasma levels attained at about 3-5 hours after oral administration. The absorbed compound is rapidly metabolised in the liver. Following I.V. administration, plasma elimination is biphasic with a terminal half life of 15 hours.

After both routes of administration, approximately 15% is excreted in the urine and 64% in the faeces (mostly via the biliary route) as free and conjugated metabolites.

- 5.3 Preclinical safety data**
Beclometasone dipropionate has low acute oral, subcutaneous and intraperitoneal toxicity in mice and rats, and repeat dose toxicity studies showed findings characteristic of glucocorticoids, with no evidence of irritancy to the respiratory tract. The main findings, at above therapeutic doses, were depression of corticosterone levels in rats and cortisol levels in dogs. Beclometasone dipropionate is non-genotoxic, and demonstrated no oncogenic potential following combined inhalation/oral administration to rats. Susceptibility of foetuses to cleft palate, noted in the mouse organogenesis study, is considered to have no relevance for therapeutic use.
- 6 PHARMACEUTICAL PARTICULARS**
- 6.1 List of excipients**
Lactose
- 6.2 Incompatibilities**
Not applicable
- 6.3 Shelf life**
36 months.
- 6.4 Special precautions for storage**
Store in a dry place below 25°C.
- 6.5 Nature and contents of container**
PVC/PVDC/Aluminium blister strips of 10 and 14 capsules.

100 mcg capsules are available in packs of 10, 14, 20, 28, 30, 42, 50, 56, 60, 84, 100, 112, 120, 140, 168, 200 and 280's.
- 6.6 Special precautions for disposal**
Not applicable
- 7 MARKETING AUTHORISATION HOLDER**
TEVA UK Limited
Brampton Road
Hampden Park
Eastbourne
East Sussex
BN22 9AG
United Kingdom
- 8 MARKETING AUTHORISATION NUMBER(S)**
PL 00289/0570
- 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**
05/03/2008
- 10 DATE OF REVISION OF THE TEXT**
05/03/2008

1 NAME OF THE MEDICINAL PRODUCT

Beclometasone dipropionate 200 Cyclocaps®

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

When used in conjunction with the Cyclohaler each capsule delivers the equivalent of 200 micrograms of beclometasone dipropionate from the mouthpiece of the device.

The 200mcg capsule has a medium brown opaque cap and clear body, printed 'logo' BECLO 200, in black ink.

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Inhalation powder, hard capsule.

Inhalation powder in capsules to be used in combination with the Cyclohaler®.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Beclometasone dipropionate is a corticosteroid with a potent anti-inflammatory action in the lungs. The contents of the capsule are inhaled by means of a specially designed device called the 'Cyclohaler'.

Beclometasone dipropionate is indicated for the prophylactic management of asthma, in the following types of patients.

Adults

Mild asthma: Patients requiring symptomatic bronchodilator asthma medication on a regular basis.

Moderate asthma: Patients with unstable or worsening asthma despite prophylactic therapy or bronchodilator alone.

Severe asthma: Patients with severe chronic asthma and those who are dependent on systemic corticosteroids for adequate control of symptoms. 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.

4.2 Posology and method of administration

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

Beclometasone dipropionate 200 Cyclocaps® are for oral inhalation use only, using the Cyclohaler. They should be used regularly for optimum results. Patients should be given a starting dose of inhaled beclometasone dipropionate which is appropriate for the severity of their disease. The dose should be titrated to the lowest dose at which effective control of asthma is maintained.

Adults

400 micrograms twice daily is the usual starting dose. The total daily dose may be administered as 2, 3 or 4 divided doses.

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

Children

The usual starting dose is 200 micrograms twice daily. Alternatively one 100 micrograms capsule two, three or four times a day may be administered, according to the response.

4.3 Contraindications

Hypersensitivity to beclometasone dipropionate or to any of the components of the preparation.

Special care is required for patients with active or inactive pulmonary tuberculosis.

4.4 Special warnings and precautions for use

It is important for the patient to understand that the gelatin capsule may very occasionally break up and small pieces of gelatin might reach the mouth or throat after inhalation. The patient may be reassured that gelatin will soften in the mouth and can be swallowed. The tendency for the capsule to break up is minimised by not piercing the capsule more than once.

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. Treatment must not be stopped abruptly.

Beclometasone dipropionate 200 Cyclocaps® are not designed to relieve acute asthmatic symptoms for which an inhaled short-acting bronchodilator is required. Patients should be advised to have such rescue medication available.

Severe asthma requires 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 β_2 -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 corticosteroids or a course of oral corticosteroids). Severe exacerbations of asthma must be treated in the usual way.

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 β -agonist therapy.

Excessive mucous secretion may stop the drug reaching the bronchioles and a course of systemic corticosteroid may be needed, together with the beclometasone dipropionate inhalations, in order to remove the mucus and reduce inflammatory changes in the bronchial tree.

Patients being treated with beclometasone dipropionate may sometimes require a short course of concomitant oral corticosteroids to control their symptoms.

Patients should be instructed in the proper use of the Cyclohaler to ensure that the drug reaches the target areas in the lungs.

Restraint is necessary in treating patients with pulmonary disorders such as bronchiectasis and pneumoconiosis in view of the possibility of fungal infections.

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 adrenal suppression, growth retardation in children and adolescents, decrease in bone mineral density, cataract and glaucoma. It is important 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 recommended doses, may result in clinically significant adrenal suppression. Additional systemic corticosteroid cover should be considered during periods of stress or elective surgery.

For the transfer of patients being treated with oral corticosteroids

Care must be taken when switching from oral corticosteroids to beclometasone dipropionate inhalations to ensure that the patient's adrenocortical reserves are adequate. In patients who have a functional disorder of the adrenal cortex due to long term use of oral corticosteroids, beclometasone dipropionate inhalation must be initially used together with the corticosteroid dose usual for the patient, the oral steroid dosage is then gradually reduced until that treatment can be safely discontinued.

After about a week, gradual withdrawal of the oral steroid is commenced. The decrements in dosage should be appropriate to the level of maintenance oral steroid, and introduced at not less than weekly intervals. For maintenance doses of prednisolone, or its 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. In any patient who has been treated with oral steroids for long periods of time, or at a high dose, it is recommended that their adrenocortical function is regularly monitored as their dose of oral steroid is reduced cautiously.

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.

Substitution of oral corticosteroids by beclometasone dipropionate may reveal allergies previously suppressed by the systemically active corticosteroid such as allergic rhinitis and eczema. These must be properly treated with antihistamines and/or topical preparations including topical corticosteroids. Any infections of air passages must be adequately treated.

4.5 Interaction with other medicinal products and other forms of interaction

None stated.

4.6 Pregnancy and lactation

There is inadequate evidence of safety in human pregnancy.

The administration of corticosteroids to pregnant animals has resulted in foetal abnormalities, i.e. cleft palate and intra-uterine growth retardation. There may therefore be a very small risk of such effects in the human foetus. However, since beclometasone dipropionate is delivered to the lungs by inhalation it significantly reduces the exposure that occurs following the systemic use of corticosteroids. The use of beclometasone dipropionate in pregnancy requires that the possible benefits of the drug be weighed against the possible hazards.

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, potential levels in milk will be low. 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

None stated.

4.8 Undesirable effects

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

Some patients feel unwell for about 2 weeks during reduction of therapy with systemic corticosteroids even though the respiratory function is maintained or even improved. These patients

may therefore need encouragement to continue using beclometasone dipropionate and continue to withdraw the systemic steroid unless there are objective signs of adrenal insufficiency.

Paradoxical bronchospasm is possible. If it occurs Beclometasone 200 Cyclocaps should be discontinued immediately and immediate treatment with a fast-acting bronchodilator instituted.

Local Candida infections of the mouth, throat and larynx may occur. Special vigilance is required for patients with high titres of Candida precipitins indicating a previous infection. Local antifungal therapy appears to control these infections without necessitating interruption of the beclometasone dipropionate treatment.

Hoarseness and irritation of the throat may occur but disappear after discontinuation of therapy, reduction of dose and/or resting of the voice. To reduce the incidences of candidiasis, hoarseness or irritation, the patient may be advised to rinse out their mouth with water, after taking their dose of Beclometasone 200 Cyclocaps®.

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

4.9 Overdose

Acute toxicity of beclometasone dipropionate is low. The only harmful effect that follows inhalation of large amounts of the drug over a short time period is suppression of hypothalamic-pituitary-adrenal (HPA) function. No special emergency action need be taken. Treatment with Beclometasone 200 Cyclocaps should be continued at the recommended dose to control the asthma; HPA function recovers in a day or two.

If beclometasone dipropionate is used excessively over a long period, this may lead to adrenal suppression. In such a case, the patient should be treated as steroid dependent, transferred to a suitable maintenance dose of a systemic corticosteroid and when the condition has stabilised, be returned to the inhaled therapy at the recommended dose. To guard against adrenal suppression, regular tests of adrenal function should be considered.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: R03BA01

When used as an inhalation powder beclometasone dipropionate has a potent glucocorticoid anti-inflammatory action within the lungs but is without significant systemic activity at therapeutic doses.

5.2 Pharmacokinetic properties

Following administration by inhalation less than 25% of the steroid will enter the respiratory tract, the majority of the dose being deposited in the oropharynx and subsequently swallowed. The pharmacokinetics of intravenously administered beclometasone dipropionate are important since this represents the disposition of the portion of the inhaled dose absorbed directly from the lung. Likewise the pharmacokinetics after oral administration are relevant to the swallowed portion of the inhaled dose.

Absorption from the gastrointestinal tract is relatively slow with peak plasma levels attained at about 3-5 hours after oral administration. The absorbed compound is rapidly metabolised in the liver. Following I.V. administration, plasma elimination is biphasic with a terminal half life of 15 hours.

After both routes of administration, approximately 15% is excreted in the urine and 64% in the faeces (mostly via the biliary route) as free and conjugated metabolites.

5.3 Preclinical safety data

Beclometasone dipropionate has low acute oral, subcutaneous and intraperitoneal toxicity in mice and rats, and repeat dose toxicity studies showed findings characteristic of glucocorticoids, with no evidence of irritancy to the respiratory tract. The main findings, at above therapeutic doses, were depression of corticosterone levels in rats and cortisol levels in dogs. Beclometasone dipropionate is non-genotoxic, and demonstrated no oncogenic potential following combined inhalation/oral

administration to rats. Susceptibility of foetuses to cleft palate, noted in the mouse organogenesis study, is considered to have no relevance for therapeutic use.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store in a dry place below 25°C.

6.5 Nature and contents of container

PVC/PVDC/Aluminium blister strips of 10 and 14 capsules.

200 mcg capsules are available in packs of 10, 14, 20, 28, 30, 42, 50, 56, 60, 84, 100, 112, 120, 140, 168, 200 and 280's.

6.6 Special precautions for disposal

Not applicable

7 MARKETING AUTHORISATION HOLDER

TEVA UK Limited
Brampton Road
Hampden Park
Eastbourne
East Sussex
BN22 9AG
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 00289/0571

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

05/03/2008

10 DATE OF REVISION OF THE TEXT

05/03/2008

1 NAME OF THE MEDICINAL PRODUCT

Beclometasone dipropionate 400 Cyclocaps®

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

When used in conjunction with the Cyclohaler each capsule delivers the equivalent of 400 micrograms of beclometasone dipropionate from the mouthpiece of the device.

The 400mcg capsule has a dark brown opaque cap and clear body, printed 'logo' BECLO 400, in black ink.

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Inhalation powder, hard capsule.

Inhalation powder in capsules to be used in combination with the Cyclohaler®.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Beclometasone dipropionate is a corticosteroid with a potent anti-inflammatory action in the lungs. The contents of the capsule are inhaled by means of a specially designed device called the 'Cyclohaler'.

Beclometasone dipropionate is indicated for the prophylactic management of asthma, in the following types of patients.

Adults

Mild asthma: Patients requiring symptomatic bronchodilator asthma medication on a regular basis.

Moderate asthma: Patients with unstable or worsening asthma despite prophylactic therapy or bronchodilator alone.

Severe asthma: Patients with severe chronic asthma and those who are dependent on systemic corticosteroids for adequate control of symptoms. 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.

4.2 Posology and method of administration

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

Beclometasone dipropionate 400 Cyclocaps® are for oral inhalation use only, using the Cyclohaler. They should be used regularly for optimum results. Patients should be given a starting dose of inhaled beclometasone dipropionate which is appropriate for the severity of their disease. The dose should be titrated to the lowest dose at which effective control of asthma is maintained.

Adults

400 micrograms twice daily is the minimum starting dose.

For more severe asthma, the starting dose may need to be increased up to 1600 micrograms as a total daily dose, a dose which may then need to be decreased when asthma has stabilised to the minimum effective dose. If appropriate, the total daily dose may be administered as 2, 3 or 4 divided doses.

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

Children

The usual starting dose is 200 micrograms twice daily. Alternatively one 100 micrograms capsule two, three or four times a day may be administered, according to the response.

4.3 Contraindications

Hypersensitivity to beclometasone dipropionate or to any of the components of the preparation.

Special care is required for patients with active or inactive pulmonary tuberculosis.

4.4 Special warnings and precautions for use

It is important for the patient to understand that the gelatin capsule may very occasionally break up and small pieces of gelatin might reach the mouth or throat after inhalation. The patient may be reassured that gelatin will soften in the mouth and can be swallowed. The tendency for the capsule to break up is minimised by not piercing the capsule more than once.

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. Treatment must not be stopped abruptly.

Beclometasone dipropionate 400 Cyclocaps® are not designed to relieve acute asthmatic symptoms for which an inhaled short-acting bronchodilator is required. Patients should be advised to have such rescue medication available.

Severe asthma requires 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 β_2 -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 corticosteroids or a course of oral corticosteroids). Severe exacerbations of asthma must be treated in the usual way.

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 β -agonist therapy.

Excessive mucous secretion may stop the drug reaching the bronchioles and a course of systemic corticosteroid may be needed, together with the beclometasone dipropionate inhalations, in order to remove the mucus and reduce inflammatory changes in the bronchial tree.

Patients being treated with beclometasone dipropionate may sometimes require a short course of concomitant oral corticosteroids to control their symptoms.

Patients should be instructed in the proper use of the Cyclohaler to ensure that the drug reaches the target areas in the lungs.

Restraint is necessary in treating patients with pulmonary disorders such as bronchiectasis and pneumoconiosis in view of the possibility of fungal infections.

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 adrenal suppression, growth retardation in children and adolescents, decrease in bone mineral density, cataract and glaucoma. It is important 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 recommended doses, may result in clinically significant adrenal suppression. Additional systemic corticosteroid cover should be considered during periods of stress or elective surgery.

For the transfer of patients being treated with oral corticosteroids

Care must be taken when switching from oral corticosteroids to beclometasone dipropionate inhalations to ensure that the patient's adrenocortical reserves are adequate. In patients who have a functional disorder of the adrenal cortex due to long term use of oral corticosteroids, beclometasone dipropionate inhalation must be initially used together with the corticosteroid dose usual for the patient, the oral steroid dosage is then gradually reduced until that treatment can be safely discontinued.

After about a week, gradual withdrawal of the oral steroid is commenced. The decrements in dosage should be appropriate to the level of maintenance oral steroid, and introduced at not less than weekly intervals. For maintenance doses of prednisolone, or its 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. In any patient who has been treated with oral steroids for long periods of time, or at a high dose, it is recommended that their adrenocortical function is regularly monitored as their dose of oral steroid is reduced cautiously.

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.

Substitution of oral corticosteroids by beclometasone dipropionate may reveal allergies previously suppressed by the systemically active corticosteroid such as allergic rhinitis and eczema. These must be properly treated with antihistamines and/or topical preparations including topical corticosteroids. Any infections of air passages must be adequately treated.

4.5 Interaction with other medicinal products and other forms of interaction

None stated.

4.6 Pregnancy and lactation

There is inadequate evidence of safety in human pregnancy.

The administration of corticosteroids to pregnant animals has resulted in foetal abnormalities, i.e. cleft palate and intra-uterine growth retardation. There may therefore be a very small risk of such effects in the human foetus. However, since beclometasone dipropionate is delivered to the lungs by inhalation it significantly reduces the exposure that occurs following the systemic use of corticosteroids. The use of beclometasone dipropionate in pregnancy requires that the possible benefits of the drug be weighed against the possible hazards.

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, potential levels in milk will be low. 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

None stated.

4.8 Undesirable effects

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

Some patients feel unwell for about 2 weeks during reduction of therapy with systemic corticosteroids even though the respiratory function is maintained or even improved. These patients may therefore need encouragement to continue using beclometasone dipropionate and continue to withdraw the systemic steroid unless there are objective signs of adrenal insufficiency.

Paradoxical bronchospasm is possible. If it occurs Beclometasone 400 Cyclocaps should be discontinued immediately and immediate treatment with a fast-acting bronchodilator instituted.

Local Candida infections of the mouth, throat and larynx may occur. Special vigilance is required for patients with high titres of Candida precipitins indicating a previous infection. Local antifungal therapy appears to control these infections without necessitating interruption of the beclometasone dipropionate treatment.

Hoarseness and irritation of the throat may occur but disappear after discontinuation of therapy, reduction of dose and/or resting of the voice. To reduce the incidences of candidiasis, hoarseness or irritation, the patient may be advised to rinse out their mouth with water, after taking their dose of Beclometasone 400 Cyclocaps®.

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

4.9 Overdose

Acute toxicity of beclometasone dipropionate is low. The only harmful effect that follows inhalation of large amounts of the drug over a short time period is suppression of hypothalamic-pituitary-adrenal (HPA) function. No special emergency action need be taken. Treatment with Beclometasone 100 Cyclocaps should be continued at the recommended dose to control the asthma; HPA function recovers in a day or two.

If beclometasone dipropionate is used excessively over a long period, this may lead to adrenal suppression. In such a case, the patient should be treated as steroid dependent, transferred to a suitable maintenance dose of a systemic corticosteroid and when the condition has stabilised, be returned to the inhaled therapy at the recommended dose. To guard against adrenal suppression, regular tests of adrenal function should be considered.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: R03BA01

When used as an inhalation powder beclometasone dipropionate has a potent glucocorticoid anti-inflammatory action within the lungs but is without significant systemic activity at therapeutic doses.

5.2 Pharmacokinetic properties

Following administration by inhalation less than 25% of the steroid will enter the respiratory tract, the majority of the dose being deposited in the oropharynx and subsequently swallowed. The pharmacokinetics of intravenously administered beclometasone dipropionate are important since this represents the disposition of the portion of the inhaled dose absorbed directly from the lung. Likewise the pharmacokinetics after oral administration are relevant to the swallowed portion of the inhaled dose.

Absorption from the gastrointestinal tract is relatively slow with peak plasma levels attained at about 3-5 hours after oral administration. The absorbed compound is rapidly metabolised in the liver. Following I.V. administration, plasma elimination is biphasic with a terminal half life of 15 hours.

After both routes of administration, approximately 15% is excreted in the urine and 64% in the faeces (mostly via the biliary route) as free and conjugated metabolites.

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Beclometasone dipropionate has low acute oral, subcutaneous and intraperitoneal toxicity in mice and rats, and repeat dose toxicity studies showed findings characteristic of glucocorticoids, with no evidence of irritancy to the respiratory tract. The main findings, at above therapeutic doses, were depression of corticosterone levels in rats and cortisol levels in dogs. Beclometasone dipropionate is non-genotoxic, and demonstrated no oncogenic potential following combined inhalation/oral administration to rats. Susceptibility of foetuses to cleft palate, noted in the mouse organogenesis study, is considered to have no relevance for therapeutic use.
- 6 PHARMACEUTICAL PARTICULARS**
- 6.1 List of excipients**
Lactose
- 6.2 Incompatibilities**
Not applicable
- 6.3 Shelf life**
36 months.
- 6.4 Special precautions for storage**
Store in a dry place below 25°C.
- 6.5 Nature and contents of container**
PVC/PVDC/Aluminium blister strips of 10 and 14 capsules.
- 400 mcg capsules are available in packs of 10, 14, 20, 28, 30, 42, 50, 56, 60, 84, 100, 112, 120, 140, 168, 200 and 280's.
- 6.6 Special precautions for disposal**
Not applicable
- 7 MARKETING AUTHORISATION HOLDER**
TEVA UK Limited
Brampton Road
Hampden Park
Eastbourne
East Sussex
BN22 9AG
United Kingdom
- 8 MARKETING AUTHORISATION NUMBER(S)**
PL 00289/0572
- 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**
05/03/2008
- 10 DATE OF REVISION OF THE TEXT**
05/03/2008

BECLOMETASONE DIPROPIONATE 100, 200 & 400 CYCLOCAPS[®], POWDER FOR INHALATION IN CAPSULES

PATIENT INFORMATION LEAFLET

Please read this leaflet carefully before you take Beclometasone dipropionate Cyclocaps[®]. It briefly outlines the most important things you need to know. If you want to know more about this medicine, or you are not sure about anything, ask your doctor or your pharmacist.

The name of your medicine is
Beclometasone dipropionate Cyclocaps[®].

1 WHAT ARE BECLOMETASONE DIPROPIONATE CYCLOCAPS[®] ?

When used in conjunction with the Cyclohaler[®] each capsule delivers the equivalent to 100, 200 or 400 micrograms of Beclometasone dipropionate from the mouthpiece of the device.

The other ingredient is lactose.

Beclometasone dipropionate Cyclocaps[®] 100, 200 and 400 micrograms are available in packs of 120 capsules.

See outer packaging or the pharmacy label for contents i.e. the number of capsules.

Beclometasone dipropionate belongs to a group of drugs called corticosteroids.

Beclometasone dipropionate Cyclocaps[®] are manufactured by Pharmachemie BV, Haarlem, The Netherlands on behalf of the Marketing Authorisation holder, TEVA UK Limited, Eastbourne BN22 9AG.

WHAT ARE BECLOMETASONE DIPROPIONATE CYCLOCAPS[®] USED FOR ?

Beclometasone dipropionate Cyclocaps[®] are used to reduce and prevent inflammation in the lungs. Asthma is caused by inflammation of the small airways in the lungs. Regular use of Beclometasone dipropionate Cyclocaps[®] helps to prevent symptoms of asthma and ease breathing problems. You should continue to take Beclometasone dipropionate Cyclocaps[®] regularly even if your symptoms disappear. Ask your doctor or pharmacist if you need additional information.

2 BEFORE YOU USE BECLOMETASONE DIPROPIONATE CYCLOCAPS[®]

Are you sensitive to any of the ingredients in the medicine, listed above ?

Are you pregnant, intending to become pregnant or breast-feeding ?

Do you or have you suffered from tuberculosis (TB) ?

Are you already taking another corticosteroid medicine e.g. budesonide ?

Do you suffer from any respiratory or breathing problems other than asthma ?

If the answer to any of these questions is YES, do not use Beclometasone dipropionate Cyclocaps[®] before talking to your doctor or pharmacist.

Do not use your Beclometasone dipropionate Cyclocaps[®] to treat a sudden attack of breathlessness. Your doctor will have given you a separate inhaler for this. If you have just started to use Beclometasone dipropionate Cyclocaps[®] instead of, or as well as steroid tablets you should be given a steroid warning card to carry with you until the doctor tells you that you do not need it any longer.

If you are transferring from steroid tablets to an inhaler you may find that even if you feel your chest is getting better, you might feel a bit poorly or develop a rash. Discuss this with your doctor, but **DO NOT STOP** treatment, unless your doctor tells you to. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3 USING BECLOMETASONE DIPROPIONATE CYCLOCAPS[®]

Your doctor has decided the dose which is suited to you. Always follow your doctor's instructions and those which are on the pharmacy label. If you do not understand these instructions, or you are in any doubt, ask your doctor or pharmacist. Do not stop taking this medicine except on your doctor's advice. Your doctor will want to see you regularly to check on your condition and ensure that you are taking the correct dose and on occasions will carry out some tests on your breathing to check how well your lungs are working. Some patients may also require occasional blood tests.

Beclometasone dipropionate Cyclocaps[®] contain a dry powder which is inhaled into the lungs using a specially designed device called a Cyclohaler[®]. Do not swallow the capsules or try to inhale the medicines using another inhaler. Your doctor should ensure you receive instructions on the correct use of the Cyclohaler[®]. Directions for use of the Cyclohaler[®] are enclosed with the Cyclohaler[®] device.

The usual dosage instructions are given below:

Adults

The usual starting dose is 400 micrograms twice daily which your doctor may reduce as your asthma improves. Your starting dose may differ from the dose stated above, and it may be higher depending on how severe your asthma is.

The most you would usually take is 800 micrograms twice daily.

Children

The usual starting dose is 200 micrograms twice daily which your doctor may reduce as your asthma improves. As with adults, your starting dose may differ from the dose stated above depending on how severe your asthma is.

The most you would usually take is 200 micrograms twice daily.

If you are transferring from steroid tablets to an inhaler, your doctor may reduce the tablet dose gradually after you have been using Beclometasone dipropionate Cyclocaps® for about a week.

Rinse your mouth out well after taking your medicine. Spit out the rinse water. Doing this will reduce the likelihood of developing a fungal infection (thrush) in the mouth.

Very occasionally the gelatin capsule may break up and small pieces of gelatin may reach the mouth or throat after inhalation. The gelatin is harmless and can be swallowed. To reduce the likelihood of this happening, do not pierce the capsule more than once.

If you forget to take a dose, inhale the next dose at the usual time. Never take two doses together. Take the remaining doses at the correct time.

It is important that you use your Beclometasone dipropionate Cyclocaps® regularly as instructed by your doctor. You should continue to use Beclometasone dipropionate Cyclocaps® even if you do not have any asthma symptoms, as it can help to prevent asthma attacks occurring. Do not stop treatment abruptly.

If you see another doctor or go into hospital, let him or the staff know what medicines you are taking.

If you accidentally take a larger dose than recommended or anyone else takes some of the capsules, tell your doctor.

4 AFTER USING BECLOMETASONE DIPROPIONATE CYCLOCAPS®

Beclometasone dipropionate Cyclocaps® are used by many patients without any problems. However, like many other medicines, it may occasionally cause side effects in some people. These may include:

- Infection in the mouth or throat (e.g. oral thrush)
- Hoarse voice
- Sore or irritated throat.

All of the above symptoms may be eased by rinsing out your mouth with water after taking your Beclometasone dipropionate dose.

If you notice that your wheeze, breathing or breathlessness are becoming worse than normal, or you are needing more of your Cyclohaler®, or your Cyclohaler® does not seem to be working as well as usual, tell your doctor.

Rarely, reduced growth, temper tantrums or other behavioural disturbances may occur in children and adolescents, if inhaled corticosteroids are used regularly for long periods of time.

At high doses taken for prolonged periods, a difference in the normal production of corticosteroids in the body may occur.

Bone thinning, clouding of the lens of the eye (cataract) resulting in blurred vision or loss of vision, due to abnormally high pressure in the eye may also occur.

Very rarely you may experience a sudden attack of wheezing after inhaling Beclometasone dipropionate. If this happens you should stop taking Beclometasone dipropionate and use your bronchodilator inhaler e.g. salbutamol, immediately. If you have these or any other effects whilst taking Beclometasone dipropionate, tell your doctor immediately.

In addition, an allergic type reaction characterised by swelling of the face, rashes and itching over the body, may occur. If this happens, stop taking the medicine and tell your doctor immediately.

Also, if you feel unwell in any other way, tell your doctor.

Your doctor may carry out a test on your adrenal gland function from time to time.

5 STORING BECLOMETASONE DIPROPIONATE CYCLOCAPS®

Do not use this medicine after the expiry date shown on outer carton. Store below 25°C. Store in the original blister pack to protect from moisture. **Keep out of the reach and sight of children.** This medicine is for you ONLY, do not give it to anyone else. Unless your doctor tells you to, do not keep these Cyclocaps® for longer than you need. Return all unused capsules to your pharmacist for safe disposal.

6 FURTHER INFORMATION

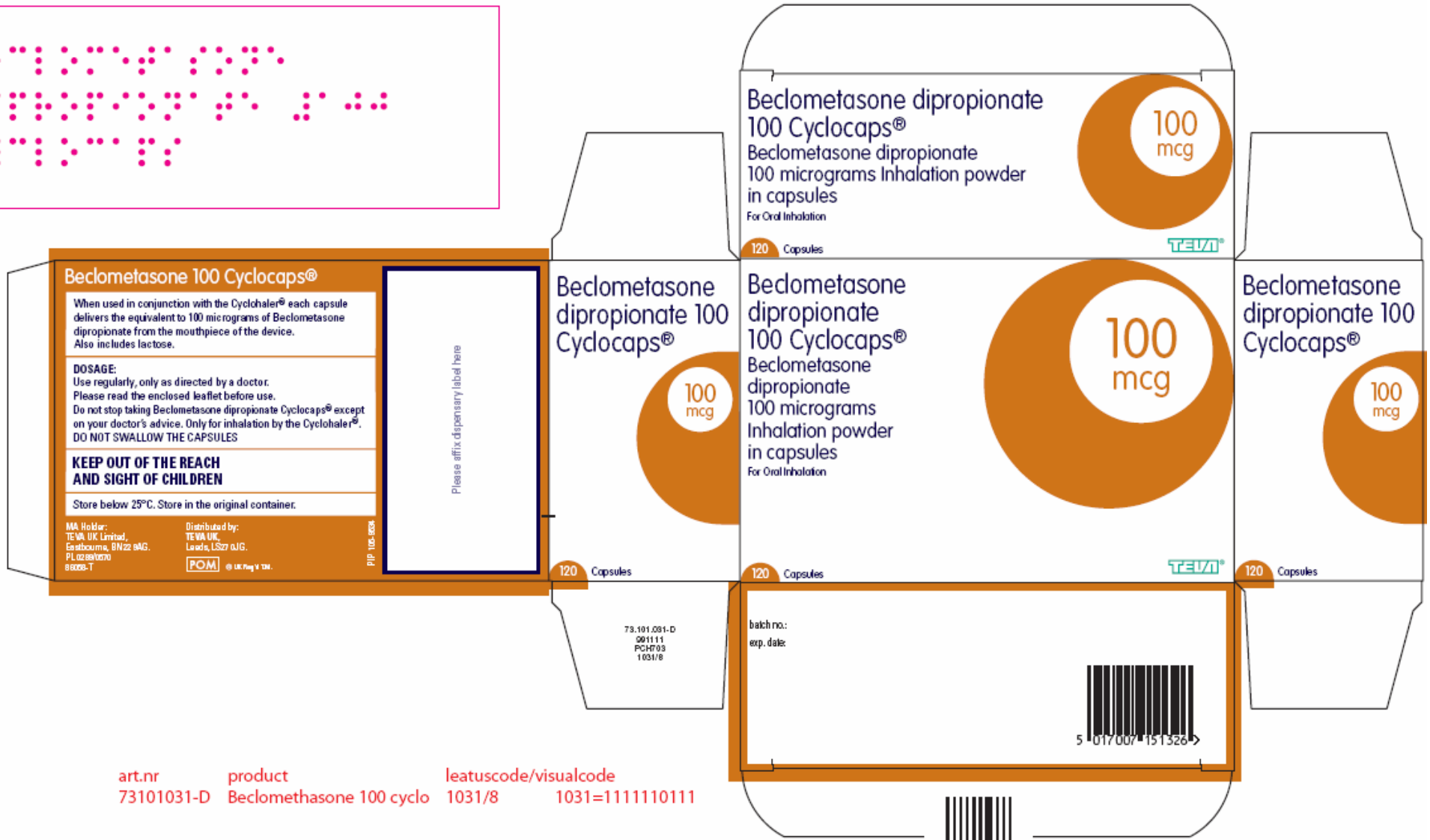
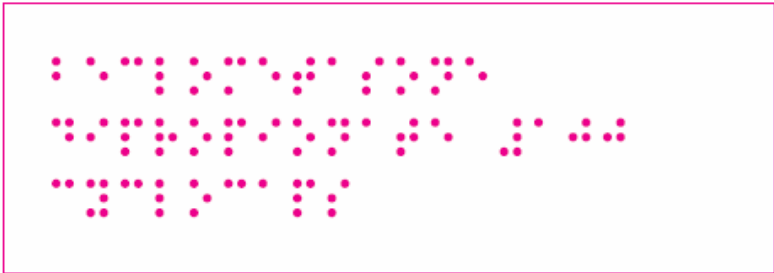
This leaflet only gives a brief outline of some of the more important points about Beclometasone dipropionate. If you want to know more about these Cyclocaps® or their effects, please ask your doctor or pharmacist.

Distributed by TEVA UK, Leeds, LS27 0JG.
Revised: July 2005



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Beclometasone 100 Cyclocaps®

When used in conjunction with the Cyclohaler® each capsule delivers the equivalent to 100 micrograms of Beclometasone dipropionate from the mouthpiece of the device. Also includes lactose.

DOSAGE:
Use regularly, only as directed by a doctor. Please read the enclosed leaflet before use. Do not stop taking Beclometasone dipropionate Cyclocaps® except on your doctor's advice. Only for inhalation by the Cyclohaler®. **DO NOT SWALLOW THE CAPSULES**

KEEP OUT OF THE REACH AND SIGHT OF CHILDREN

Store below 25°C. Store in the original container.

MA Holder: TEVA UK Limited, Ensburma, BN22 9AG, PL 02 891070 88008-T
Distributed by: TEVA UK, Leeds, LS27 7JG. **POM** © UK Reg'd TM. PIP 100-8338

Please affix dispensary label here

Beclometasone dipropionate 100 Cyclocaps®
100 mcg
120 Capsules

Beclometasone dipropionate 100 Cyclocaps®
Beclometasone dipropionate 100 micrograms Inhalation powder in capsules
For Oral Inhalation
100 mcg
120 Capsules
TEVA®

Beclometasone dipropionate 100 Cyclocaps®
Beclometasone dipropionate 100 micrograms Inhalation powder in capsules
For Oral Inhalation
100 mcg
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TEVA®

Beclometasone dipropionate 100 Cyclocaps®
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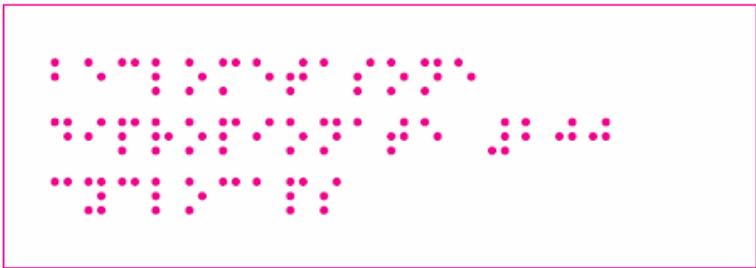
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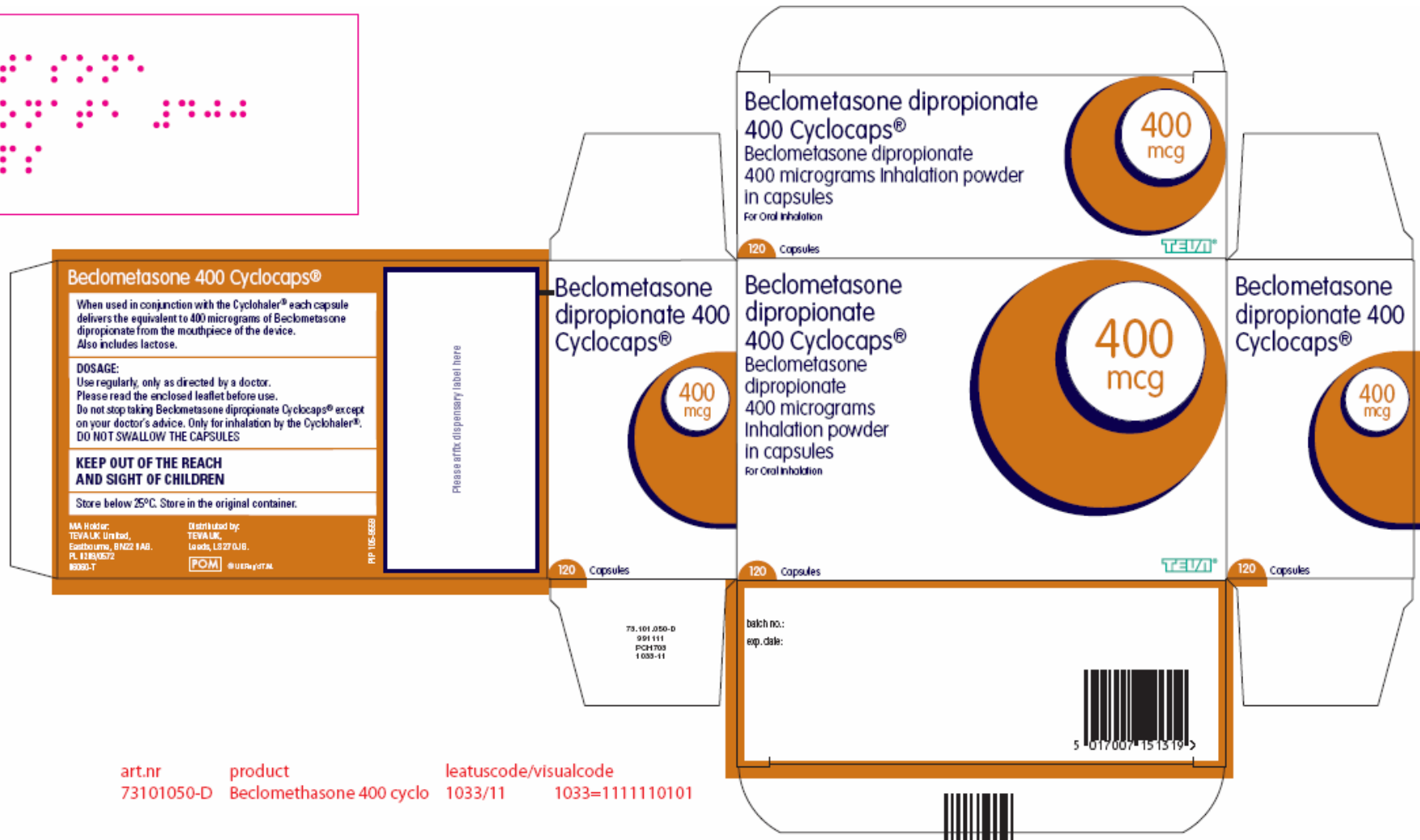
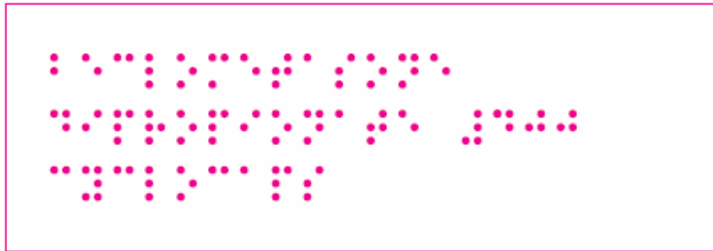
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Beclometasone dipropionate
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Beclometasone dipropionate
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MA Holder: TEVA UK Ltd
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Beclometasone dipropionate
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400 micrograms

MA Holder: TEVA UK Ltd
86063-T

Exp: