Beclometasone Dipropionate 0.05% Aqueous Nasal Spray, 50 micrograms/spray

PL 16431/0176

UKPAR

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BECLOMETASONE DIPROPIONATE 0.05% AQUEOUS NASAL SPRAY, 50 MICROGRAMS/SPRAY

PL 16431/0176

LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted a Marketing Authorisation (licence) for the medicinal product Beclometasone Dipropionate 0.05% Aqueous Nasal Spray, 50 micrograms/spray (product licence number: 16431/0176). This medicine is only available on prescription.

Beclometasone Dipropionate 0.05% Aqueous Nasal Spray, 50 micrograms/spray is a steroid. It is used for the treatment and prevention of seasonal and perennial allergic rhinitis, hayfever and vasomotor rhinitis. It acts by reducing the inflammation of the nose, which may be the cause of an itchy, blocked or runny nose or sneezing.

Beclometasone Dipropionate 0.05% Aqueous Nasal Spray, 50 micrograms/spray raised no clinically significant safety concerns and it was, therefore, judged that the benefits of using this product outweigh the risks; hence a Marketing Authorisation has been granted.
SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the UK granted a marketing authorisation for the medicinal product Beclometasone Dipropionate 0.05% Aqueous Nasal Spray, 50 micrograms/spray to Ayrton Saunders Ltd on 23 March 2009.

This is an abridged application for Beclometasone Dipropionate 0.05% Aqueous Nasal Spray, 50 micrograms/spray submitted under Article 10(c) of EC Directive 2001/83, last paragraph. The applicant claims that this product is identical to Beclometasone Dipropionate Aqueous Nasal Spray 50 micrograms per spray (PL 16431/0121). Beclometasone Dipropionate Aqueous Nasal Spray 50 micrograms per spray is currently licensed to Ayrton Saunders Ltd, following a change of ownership from INYX Pharma Ltd (PL 20165/0001) on 28 February 2008. INYX Pharma Ltd obtained the marketing authorisation for this product on 1 July 2003, following a change of ownership from Miza Pharmaceuticals UK Ltd (PL 18856/0014). Miza Pharmaceuticals UK Ltd obtained the marketing authorisation for this product on 11 June 2001 following a change of ownership from Parkfields Pharmaceuticals Ltd (PL 14229/0030). Parkfields Pharmaceuticals Ltd obtained the marketing authorisation for this product on 27 August 1997.

No new data were submitted, nor was it necessary for this simple application, as the data are identical to those of the previously granted cross-reference product.

Beclometasone Dipropionate Aqueous Nasal Spray is indicated for the treatment and prevention of seasonal and perennial allergic rhinitis, hayfever and vasomotor rhinitis. The drug has a potent anti-inflammatory effect within the respiratory tract.
PHARMACEUTICAL ASSESSMENT

BECLOMETASONE DIPROPIONATE
The beclometasone dipropionate used in this product complies with the Ph.Eur. monograph and is identical to the beclometasone dipropionate used in the already approved product. This is satisfactory.

DESCRIPTION AND COMPOSITION OF THE DRUG PRODUCT
The product is a suspension containing 50 mcg beclometasone dipropionate in each 100 mg actuation. The container is a white plastic bottle with a spray pump. There appear to be no differences between the composition of the proposed product and that of the already licensed cross reference product.

ADDITIONAL DATA REQUIREMENTS
The manufacturing processes, finished product specifications and active ingredient specifications are in line with the reference product and are satisfactory.

EXPERT REPORTS
Satisfactory expert reports in the form of quality, non-clinical and clinical overall summaries are provided, with signed declarations from each expert confirming that the applicant’s product is identical to the reference product in all particulars. Expert CVs are also submitted and are acceptable.

PRODUCT LITERATURE
The proposed SPC, PIL and labels are identical to the reference product and are satisfactory. The package leaflet has been submitted to the MHRA along with results of consultations with target patient groups ("user testing"), in accordance with Article 59 of Council Directive 2001/83/EC. The results indicate that the package leaflet is well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that it contains.

ASSESSOR’S OVERALL CONCLUSIONS
A product licence may be granted for this product.
PRECLINICAL ASSESSMENT

No new preclinical data have been supplied with this application and none is required for an application of this type.
CLINICAL ASSESSMENT

OVERVIEW
A statement has been provided confirming that the clinical particulars for Beclometasone Dipropionate 0.05% Aqueous Nasal Spray, 50 micrograms/spray are identical to those for the already licensed product; Beclometasone Dipropionate Aqueous Nasal Spray 50 micrograms per spray (PL 16431/0121). This is satisfactory.

BIOAVAILABILITY AND BIOEQUIVALENCE
No bioequivalence study has been performed to support this application and none is needed.

PRODUCT LITERATURE
All product literature is medically satisfactory.

ASSESSOR’S OVERALL CONCLUSIONS
It is recommended that a marketing authorisation can be granted.
OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY
Beclometasone Dipropionate 0.05% Aqueous Nasal Spray, 50 micrograms/spray is identical to the already licensed reference product. This product is, therefore, pharmaceutically satisfactory.

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

EFFICACY
The efficacy of beclometasone dipropionate is well established. The SPC, PIL and labelling are satisfactory and consistent with those for the cross-reference product.

RISK BENEFIT ASSESSMENT
The quality of the product is acceptable, no significant preclinical or clinical safety concerns were identified, and benefit has been shown to be associated with beclometasone dipropionate. The risk benefit ratio is therefore considered to be acceptable.
### STEPS TAKEN FOR ASSESSMENT

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SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Beclometasone Dipropionate 0.05% Aqueous Nasal Spray, 50 micrograms/spray

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each spray contains: Beclometasone Dipropionate 50 micrograms

3 PHARMACEUTICAL FORM
Nasal spray suspension

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
Beclometasone Dipropionate Aqueous Nasal Spray is indicated for the treatment and prevention of seasonal and perennial allergic rhinitis, hayfever and vasomotor rhinitis. The drug has a potent anti-inflammatory effect within the respiratory tract.

4.2 Posology and method of administration
Beclometasone Dipropionate Aqueous Nasal Spray for intranasal administration only.
The minimum effective dose according to individual response should be used at which the control of symptoms is maintained (200 to 400 micrograms/day)
Adults and children:
There is insufficient clinical data at present to support the recommended use of this product in children under the age of six.
The recommended dosage for adults and children is two sprays into each nostril twice daily. In some cases a single spray into each nostril three or four times a day may be the preferred dosage regimen. When good effect has been achieved the dosage may be reduced to one spray into each nostril twice a day. The total daily dose should not normally exceed eight sprays (400 micrograms/day).
For full therapeutic benefit, regular use is essential. Furthermore, it should be explained to the patient that maximum relief may not be obtained with the first few doses and the patient’s co-operation to comply with the regular dosage schedule should be sought.

4.3 Contraindications
Beclometasone Dipropionate Aqueous Nasal Spray is contra-indicated in patients with a history of hyper-sensitivity to any of the components.
4.4 Special warnings and precautions for use
Nasal passage infections and paranasal sinuses should be appropriately treated. Beclometasone Dipropionate Aqueous Nasal Spray may be used in conjunction with other medicaments if required.
Caution should be exercised whilst transferring patients from systemic steroid treatment to Beclometasone Dipropionate Aqueous Nasal Spray if there is doubt that their adrenal function is impaired.
Beclometasone Dipropionate Aqueous Nasal Spray will control seasonal allergic rhinitis in most cases. However, an abnormally heavy challenge of summer allergies, may in certain situations, necessitate appropriate additional therapy, especially to control eye symptoms.
Systemic effects of nasal corticosteroids may occur particularly at high doses prescribed for prolonged periods. Growth retardation has been reported in children receiving nasal corticosteroids at licensed doses.
It is recommended that the height of children receiving prolonged treatment with nasal corticosteroids is regularly monitored. If growth is slowed, therapy should be reviewed with the aim of reducing the dose of nasal corticosteroid, if possible, to the lowest dose at which effective control of symptoms is maintained. In addition, consideration should be given to referring the patient to a paediatric specialist.
Treatment with higher than recommended doses may result in clinically significant adrenal suppression. If there is evidence for higher than recommended doses being used then additional systemic corticosteroid cover should be considered during periods of stress or elective surgery.

4.5 Interaction with other medicinal products and other forms of interaction
None known.

4.6 Pregnancy and lactation
The use of Beclometasone Dipropionate in pregnancy requires that the 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.
Safety in pregnancy has not been established. Corticosteroid administration to pregnant animals can cause abnormalities of foetal development including cleft palate and intra uterine growth retardation. Therefore there may be a very small risk of such effects in the human foetus.
Lactation:
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.
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 intranasal administration there is low potential for significant levels in breast milk.

4.7 Effects on ability to drive and use machines
None known.
4.8 Undesirable effects
Systemic effects of nasal corticosteroids may occur, particularly when prescribed at high doses for prolonged periods. Such effects may include hypothalmic-pituitary-adrenal (HPA) suppression and growth retardation in children.
Rare cases of nasal septal perforation have been reported following the use of intranasal corticosteroids.
Rare cases of raised intra-ocular pressure or glaucoma have been reported.
As with other nasal sprays, dryness and irritation of the nose and throat, unpleasant taste and smell and epistaxis have been reported rarely.

4.9 Overdose
The only harmful effect that follows inhalation of large amounts of the drug over a short time period is suppression of the hypothalmic-pituitary-adrenal (HPA) function. No special emergency action need be taken. Treatment with a Beclometasone Dipropionate Aqueous Nasal Spray should be continued at the recommended dose. HPA function reverses in one or two days.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Beclometasone Dipropionate is a glucocorticoid. It is a synthetic corticosteroid esterified at the 17 position and is more potent topically than systemically. This drug is currently only used topically for its anti-inflammatory activity. In addition to the local anti-inflammatory action it exerts it also has immunosuppressive activity. There are a number of factors contributing to the mechanisms behind these actions. Firstly and foremost the drug inhibits the adherence of neutrophils and monocyte-macrophages to the capillary endothelial cells of the inflamed area. Secondly it obstructs the effect of macrophage migration inhibitory factor. Finally, Beclometasone Dipropionate also decreases the activation of plasminogen to plasmin and by inhibition of phospholipase A2 activity, it reduces the formation of prostaglandins and leukotrienes in the local tissue. (SPC pharmacokinetics).

5.2 Pharmacokinetic properties
The greater part of any drug administered by inhalation is ultimately swallowed after being deposited in the mouth and oro-pharynx. It has been shown that when 4mg Beclometasone Dipropionate was administered to man as a microfine suspension over 90% of the drug was absorbed. The rate of absorption is slow, peak serum levels being attained at about 3 to 5 hours after administration.
Beclometasone Dipropionate is widely distributed in the body tissues. It is found in the liver, in the kidney and in white blood cells. It is 87 per cent bound to human plasma protein (cortisol binds 90%).
Beclometasone Dipropionate is hydrolysed after oral administration by tissue and faecal esterases in vitro. It is therefore probable that the Beclometasone Monopropionate and Beclometasone present in faeces after oral administration result from hydrolysis of unabsorbed drug by gut esterases, and that the polar
metabolites found in human faeces probably arise from the biliary excretion of metabolites of absorbed drug.
It is thought likely that any absorbed steroid is converted to pharmacologically inactive metabolites Beclometasone-17-propionate, Beclometasone and unidentified polar metabolites during its passage through the liver (first pass effect).
Studies using tritiated Beclometasone Dipropionate show that after oral administration 10-15% of the dose was recovered in the urine as metabolites over a period of 72 to 96 hours. Faecal excretion accounted for 37% to 47% of a 4 mg dose.

5.3 Preclinical safety data
No data is available on the toxic effects of Beclometasone Dipropionate but these are likely to be similar to toxic effects reported for other halogenated topical corticosteroids. Toxic effects of corticosteroids in acute toxicity studies in mouse and rat include reduction in adrenal weight, liver changes, lung consolidation and gastrointestinal effects. These are dose related, the more potent the topical steroid the greater the effect; there is no evidence to suggest that these findings have any clinical relevance in man.
Potential carcinogenic effects have been found in mice following prolonged topical application of potent corticosteroids, but there is no evidence for carcinogenicity occurring in man. No data for Beclometasone is available. Halogenated topical corticosteroids have been found to be teratogenic in mice but the relevance of this in man is unknown.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Dextrose Anhydrous
Polysorbate 80
Dispersible Cellulose
Benzalkonium Chloride 95%
Phenylethanol
Purified Water

6.2 Incompatibilities
None known

6.3 Shelf life
3 years – unopened
3 months opened

6.4 Special precautions for storage
Store below 30°C. Do not refrigerate. Protect from light.

6.5 Nature and contents of container
Beclometasone Dipropionate Aqueous Nasal Spray is supplied in a white plastic (high density polyethylene) bottle fitted with a screw on pump covered by a dustcap. The bottle provides 200 sprays.
6.6 Special precautions for disposal
Not applicable

7 MARKETING AUTHORISATION HOLDER
Ayrton Saunders Ltd
Ayrton House
Commerce Way
Parliament Business Park
Liverpool
L8 7BA
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)
PL 16431/0176

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORIZATION
23/03/2009

10 DATE OF REVISION OF THE TEXT
23/03/2009
PATIENT INFORMATION LEAFLET

PATIENT LEAFLET: INFORMATION FOR THE USER

BECLOMETASONE DIPROPIONATE AQUEOUS NASAL SPRAY 50MCG/SPRAY

Contains 50 micrograms of Beclometasone Dipropionate per spray
The name of your medicine is Beclometasone Dipropionate Aqueous Nasal Spray 50mcg/spray, which will be referred to as Beclometasone Spray throughout the rest of this document.

Read all of this leaflet carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious or if you notice any side effects not listed in the leaflet, please tell your doctor or pharmacist.

In this leaflet:
1. What Beclometasone Spray is and what it is used for
2. Before you use Beclometasone Spray
3. How to use Beclometasone Spray
4. Possible side effects
5. How to store Beclometasone Spray
6. Further information

1. WHAT BECLOMETASONE SPRAY IS AND WHAT IT IS USED FOR
Beclometasone Dipropionate is a steroid. It is used for the treatment and prevention of seasonal and perennial allergic rhinitis, hayfever and vasomotor rhinitis. It acts by reducing the inflammation of your nose which may be the cause of your sneezing, or an itchy, blocked or runny nose.

2. BEFORE YOU USE BECLOMETASONE SPRAY
Do not take Beclometasone Spray if you:
- are allergic (hypersensitive) to Beclometasone Dipropionate or any of the other ingredients of Beclometasone Spray (see Section 6 for all the ingredients of this medicine).
- Not recommended for children under six years old.

Take special care and tell your doctor if you:
- have kidney problems
- have ever suffered from glaucoma (increased pressure in the eye, eye pain or blurred vision)
- are suffering from either a nose infection or sinus trouble

If you develop a rash or swelling, stop taking this medicine and tell your doctor immediately.

Pregnancy and breast-feeding
If you are pregnant, think you might be pregnant, intend to become pregnant, or are breast-feeding, speak with your doctor before using this medicine. Ask your doctor or pharmacist for advice before taking any medicine.

3. HOW TO USE BECLOMETASONE SPRAY
Always use Beclometasone Spray exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

Using this medicine (Adults and children over six years):
The recommended dose is two sprays into each nostril twice a day. However in some cases, a single spray into each nostril three or four times a day may be preferred. The maximum daily dose is a total of eight sprays.

Use your nasal spray regularly for maximum relief. It may take a few days for your medicine to work.

Do not exceed the dose that your doctor advises.

Once your symptoms have improved your doctor may wish to reduce your daily dose to one spray into each nostril twice a day. However, if you notice that your symptoms become worse you should increase the daily dose to two sprays into each nostril twice a day and talk to your doctor as soon as possible.

If you are suffering from an allergy which also causes watery or irritated eyes, then your doctor may decide to give you some extra medication.

Method of administration
If you have any problems about using your nasal spray, ask your pharmacist.

1. Remove the dust-cap and lock-ring. Shake the bottle gently.
2. On first using the nasal spray prepare for use by pressing down on the white collar using both your index and middle fingers. Keep the base supported with your thumb (figure 2). Continue to press down until the collar stops and then allow it to return to its original position. Repeat this action until a fine spray appears.
The first five attempts to produce a spray should be allowed to go to waste. Now the spray is ready to use.
3. To use the spray, first blow your nose gently. Closing one nostril off as shown, bend your head forward slightly. Hold the bottle upright and carefully insert the applicator into the other nostril (figure 3).
4. Slowly begin to breathe in through your nose and whilst doing so press down firmly on the white collar to produce a fine spray inside your nose. Breathe out through your mouth (figure 4).
5. Repeat step 3 and 4 to squirt a second spray in the same nostril.
   Wash the nozzle frequently with warm water. This will prevent it from getting blocked. If the pump has not been used for a short period of time, re-priming may be necessary (see Step 2 above).

If you use more Beclometasone Spray than you should contact your doctor immediately.

If you forget to take Beclometasone Spray take a dose as soon as you remember. If it is almost time for your next dose though, do not double the dose, just carry on as before.

If you stop using Beclometasone Spray
Do not stop taking the medicine even if you feel better without your doctor’s advice.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS
Like all medicines, Beclometasone Spray can cause side effects, although not everybody gets them.

The most common side effects are dryness, irritation of the nose and throat, and unpleasant taste and smell.

Other side effects include:
• nose bleeds
• glaucoma (raised pressure in the eye, eye pain or blurred vision)
• sores inside the nose

• slow growth in children (only in rare cases where the child received treatment with this drug for a very long time. In this case, your doctor may wish to monitor the height of your child at regular intervals).

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE BECLOMETASONE SPRAY
Keep out of the reach and sight of children
Do not use Beclometasone Spray after the expiry date which is stated on the label and carton. The expiry refers to the last day of that month.
Discard the contents 3 months after first opening.

• Store below 30°C
• Do not refrigerate
• Protect from light

Medicines should not be disposed of via wastewater or household waste. Ask your Pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION
What Beclometasone Spray contains
The active substance is Beclometasone Dipropionate and each spray contains 50 mcg.

The other ingredients are dextrose anhydrous, polysorbate 80, dispersible cellulose, benzalkonium chloride 95%, phenylethanol and purified water.

Beclometasone Spray is supplied in a white plastic (high density polyethylene) bottle fitted with a screw on pump covered by a dustcap. The bottle provides 200 sprays.

Marketing Authorisation Holder and Manufacturer
The marketing authorisation is held by Ayton Saunders Ltd of Ayton House, Commerce Way, Parliament Business Park, Liverpool, L8 7BA.

The medicine is made by Pharmaserve (North West) Ltd, 9 Arkwright Road, Astmoor Industrial Estate, Runcorn, Cheshire. WA7 1NU.

This leaflet was revised March 2008.
LABELLING

Label:

Spray into the nose as prescribed by your doctor. The active substance is beclometasone dipropionate 0.05%w/w. Also contains benzalkonium chloride, phenylethanol, dextrose, polysorbate 80, dispersible cellulose and purified water.

Contains 200 metered sprays.

Keep out of the reach and sight of children.

Store below 30°C.

Do not refrigerate.

Protect from light.

Discard three months after first use.

For further information refer to the enclosed leaflet.

The active substance is beclometasone dipropionate 0.05% w/w.

The other ingredients are:
- dextrose anhydrous,
- polysorbate 80,
- dispersible cellulose,
- benzalkonium chloride,
- 95% phenylethanol and purified water.

**Directions for use:**

Adults and children over six years:
- Two sprays into each nostril twice daily.
- In some cases a single spray into each nostril three or four times a day may be preferred.

The product is not recommended for children under six years.

Do not exceed 8 sprays in 24 hours.

Store below 30°C.
- Do not refrigerate.
- Protect from light.
- Discard three months after first use.
- Keep out of the reach and sight of children.

**For the treatment and prevention of seasonal and perennial allergic rhinitis, hayfever and vasomotor rhinitis.**

Lot:

Exp: