SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Nasobec Aqueous 50 microgram Nasal Spray
Beclometasone Dipropionate Aqueous Nasal Spray

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 100 milligrams spray contains 50 micrograms beclometasone dipropionate.

Excipient(s) with known effect
Each 100 milligrams contains 0.040 mg benzalkonium chloride.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Nasal Spray, Suspension.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Beclometasone Dipropionate Aqueous Nasal Spray is indicated for the prophylaxis and treatment of seasonal and perennial allergic rhinitis and vasomotor rhinitis. Beclometasone Dipropionate has anti-inflammatory glucocorticoid properties.

4.2 Posology and method of administration

Beclometasone Dipropionate Aqueous Nasal Spray is for administration by the intranasal route only.

Adults and children over six years old: Two sprays twice daily into each nostril (400 micrograms beclometasone dipropionate per day) is the recommended initial dosage. It may be preferable for some patients to administer a single spray into each nostril three or four times daily.

Once control of symptoms has been achieved move the dosage down to one spray twice daily into each nostril (200 micrograms beclometasone dipropionate per day). A dosage regimen of one spray into each nostril morning and evening has been shown to be efficacious in some patients. If symptoms reoccur, patients should revert to the recommended dosage of two sprays into each nostril morning and evening.

The minimum dose should be used at which effective control of symptoms is maintained. Total daily administration should not normally exceed eight sprays.

For full therapeutic benefit regular usage is essential. The co-operation of the patient should be sought to comply with the regular dosage schedule and it should be explained that maximum relief may not be obtained within the first few applications. It should be made clear to patients that full therapeutic benefit will only be achieved after a few days treatment.

Elderly: Dosage as for adults.

Children less than six years old: Beclometasone Dipropionate Aqueous Nasal Spray is not indicated for children under six years old, due to insufficient clinical data.

4.3 Contraindications

Hypersensitivity to the active substance or any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Systemic effects of nasal corticosteroids may occur, particularly at high doses prescribed for prolonged periods. These effects are much less likely to occur than with oral corticosteroids and may vary in individual patients and between different corticosteroid preparations. Potential systemic effects may include Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, cataract, glaucoma, blurred vision and more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children).

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.

Care must be taken while transferring patients from systemic steroid treatment to Beclometasone Dipropionate Aqueous Nasal Spray if there is any reason to suppose that their adrenal function is impaired.

Infections of the nasal passages and paranasal sinuses should be appropriately treated but do not constitute a specific contra-indication to treatment with Beclometasone Dipropionate Aqueous Nasal Spray.

Although Beclometasone Dipropionate Aqueous Nasal Spray will control seasonal allergic rhinitis in most cases, an abnormally heavy challenge of summer allergens may in certain instances necessitate appropriate additional therapy particularly to control eye symptoms.

Benzalkonium chloride may cause irritation or swelling inside the nose, especially if used for a long time.
Medical advice should be sought before using Beclometasone Dipropionate Aqueous Nasal Spray in the case of recent injury or surgery to the nose, or problems with ulceration in the nose.

Benzalkonium chloride may cause wheezing and breathing difficulties (bronchospasm), especially if the patient has asthma.

Visual disturbance

Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

Excipient(s):

Benzalkonium chloride
Long-term use may cause oedema of the nasal mucosa.

4.5 Interaction with other medicinal products and other forms of interaction

Beclometasone is less dependent on CYP3A metabolism than some other corticosteroids, and in general interactions are unlikely; however the possibility of systemic effects with concomitant use of strong CYP3A inhibitors (e.g. ritonavir, cobicistat) cannot be excluded, and therefore caution and appropriate monitoring is advised with the use of such agents.

4.6 Fertility, pregnancy and lactation

Pregnancy
There is inadequate evidence of safety in human pregnancy. Administration of corticosteroids to pregnant animals can cause abnormalities of foetal development including cleft palate and intra-uterine growth retardation. There may therefore be a very small risk of such effects in the human foetus. It should be noted, however, that the foetal changes in animals occur after relatively high systemic exposure. Nasobec Aqueous Nasal Spray delivers beclometasone dipropionate directly to the nasal mucosa and so minimises systemic exposure.

The use of beclometasone dipropionate should be avoided during pregnancy unless thought essential by the doctor.

Breast-feeding
No specific studies examining the transference of beclometasone dipropionate into the milk of lactating animals have been performed. It is reasonable to assume that beclometasone dipropionate is secreted in milk but at the dosages used for direct intranasal administration there is low potential for significant levels in breast milk. The use of beclometasone dipropionate in mothers breast feeding their babies requires that the therapeutic benefits of the drug be weighed against the potential hazards to the mother and baby.

4.7 Effects on ability to drive and use machines

Beclometasone Dipropionate Aqueous Nasal Spray does not affect the ability to operate and drive machines.

4.8 Undesirable effects

Adverse reactions are listed below by system organ class and frequency. Frequencies are defined as: very common (≥1/10), common (≥1/100 and <1/10), uncommon (≥ 1/1000 and <1/100), rare (≥1/10,000 and <1/1000), very rare (<1/10,000) including isolated reports and not known (cannot be estimated from the available data). Very common, common and uncommon reactions were generally determined from clinical trial data. Rare and very rare reactions were generally determined from spontaneous data. In assigning adverse reaction frequencies, the background rates in placebo groups were not taken into account, since these rates were generally comparable to those in the active treatment group.

System Organ Class	Adverse Reaction	Frequency
Immune system disorders	Hypersensitivity reactions including:	
	Rashes, urticaria, pruritis, erythema.	Common
	Oedema of the eyes, face, lips and throat	Very rare
	Dyspnoea and/or bronchospasm	Very rare
	Anaphylactoid/anaphylactic reactions	Very rare
Nervous system disorders	Unpleasant taste, unpleasant smell.	Common
Eye disorders	Blurred vision (see also section 4.4)	Rare
	Glaucoma, raised intraocular pressure, cataract.	Very rare
	Central serous retinopathy	Not known
Respiratory, Thoracic & Mediastinal disorders	Epistaxis, nasal dryness, nasal irritation, throat dryness, throat irritation	Common
	Nasal septum perforation.	Very rare

Systemic effects of nasal corticosteroids may occur, particularly when prescribed at high doses for prolonged periods.

Blood stained crusts in the nose can occur when taking nasal sprays but these conditions are not progressive and are seldom troublesome.

Widespread use of beclometasone dipropionate for a decade has shown no serious local damage to mucous membranes.

Paediatric population

Growth retardation has been reported in children receiving nasal corticosteroids (see section 4.4).

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Suppression of the HPA function is the only harmful effect that would arise from taking large amounts of beclometasone dipropionate over a short period of time. No emergency procedure need be undertaken and treatment with Beclometasone Dipropionate Aqueous Spray should continue at the recommended dose. The HPA function reverts back to normal within a day or two.

Further management should be as clinically indicated or as recommended by the national poisons centre, where available.

There is no specific treatment for an overdose of beclometasone dipropionate. If overdose occurs, the patient should be treated supportively with appropriate monitoring as necessary.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Beclometasone dipropionate is the diester of beclometasone, a synthetic glucocorticoid which demonstrates anti-inflammatory and immunosuppressant properties. This drug is stated to exert a topical effect on the lungs without significant systemic activity at recommended doses, although the mechanisms of action are as yet unknown.

Following topical administration, beclometasone 17,21-dipropionate (BDP) produces potent anti-inflammatory and vasoconstrictor effects.

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

Beclometasone dipropionate offers a preventative background treatment for hayfever when taken prior to allergen challenge. After which, with regular use, BDP can continue to prevent allergy symptoms from reappearing.

5.2 Pharmacokinetic properties

Absorption
Following intranasal administration of BDP in healthy males, the systemic absorption was assessed by measuring the plasma concentrations of its active metabolite B-17-MP, for which the absolute bioavailability following intranasal administration is 44% (95% CI 28%, 70%). After intranasal

administration, <1% of the dose is absorbed by the nasal mucosa. The remainder, after being cleared from the nose, either by drainage or mucocilary clearance, is available for absorption from the gastrointestinal tract. Plasma B-17-MP is almost entirely due to conversion of BDP absorbed from the swallowed dose.

Following oral administration of BDP in healthy males, the systemic absorption was also assessed by measuring the plasma concentrations of its active metabolite B-17-MP, for which the absolute bioavailability following oral administration is 41% (95% CI 27%, 62%).

Following an oral dose, B-17-MP is absorbed slowly with peak plasma levels reached 3-5 hours after dosing.

Metabolism
BDP is cleared very rapidly from the circulation and plasma concentrations are undetectable (< 50pg/ml) following oral or intranasal dosing. There is rapid metabolism of the majority of the swallowed portion of BDP during its first passage through the liver. The main product of metabolism is the active metabolite (B-17-MP). Minor inactive metabolites, beclometasone -21-monopropionate (B-21-MP) and beclometasone (BOH), are also formed but these contribute little to systemic exposure.

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

Elimination
The elimination of BDP and B-17-MP are characterised by high plasma clearance (150 and 120l/h) with corresponding terminal elimination half-lives of 0.5h and 2.7h. Following oral administration of tritiated BDP, approximately 60% of the dose was excreted in the faeces within 96 hours mainly as free and conjugated polar metabolites. Approximately 12% of the dose was excreted as free and conjugated polar metabolites in the urine.

5.3 Preclinical safety data

No clinically relevant findings were observed in preclinical studies. See sections 4.3 to 4.9 above.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzalkonium Chloride Solution
Phenylethyl alcohol
Polysorbate 80
Glucose
Microcrystalline cellulose and carmellose sodium
Hydrochloride Acid (if necessary – to adjust pH)
Purified Water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Three years unopened.
Use within three months of first opening.

6.4 Special precautions for storage

Store below 30°C.
Protect from light. Keep bottle in the outer carton.
Do not refrigerate.
Discard three months after first using the spray.

6.5 Nature and contents of container

Beclometasone Dipropionate Aqueous Nasal Spray is supplied in high density polyethylene bottles of 30ml capacity containing a nominal 200 doses. Each bottle is fitted with a metering pump with a built in nasal adaptor designed to deliver a nominal 100 milligrams of suspension per spray.

6.6 Special precautions for disposal

None stated.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Teva UK Limited,
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Whistler Drive,
Castleford,
WF10 5HX,
United Kingdom.

8 MARKETING AUTHORISATION NUMBER(S)

PL 00289/1626

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12/04/2023