

ALANASE



1. Product Name

ALANASE, 50 micrograms per actuation, nasal spray solution.

ALANASE 100, 100 micrograms per actuation, nasal spray solution.

2. Qualitative and Quantitative Composition

Each 100 mg spray delivered by the nasal applicator contains 50 micrograms or 100 micrograms of beclometasone dipropionate.

Excipient with known effect:
Benzalkonium chloride

For the full list of excipients, see section 6.1.

3. Pharmaceutical Form

ALANASE aqueous nasal spray (50 micrograms per actuation) is an almost white opaque suspension of microfine beclometasone dipropionate delivered by a metering, atomising pump.

ALANASE 100 aqueous nasal spray (100 micrograms per actuation) is an almost white opaque suspension of microfine beclometasone dipropionate delivered by a metering, atomising pump.

4. Clinical Particulars

4.1 *Therapeutic indications*

ALANASE aqueous nasal spray (50 micrograms per actuation) is indicated for the short-term prevention and treatment of seasonal allergic rhinitis (hay fever).

ALANASE 100 aqueous nasal spray (100 micrograms per actuation) is indicated for the prevention and treatment of seasonal and perennial allergic rhinitis and vasomotor rhinitis.

ALANASE 100 can significantly delay the recurrence of nasal polyps in those patients who have undergone nasal polypectomy. In those polyps that do recur, ALANASE 100 can suppress their increase in size.

4.2 *Dose and method of administration*

Dose

ALANASE and ALANASE 100 should be shaken before use.

ALANASE (50 micrograms per actuation)

For adults and children over 12 years of age:

Initially one or two sprays into each nostril twice a day (morning and night), then after 2 to 3 days, one spray into each nostril twice a day.

Do not use ALANASE (50 micrograms per actuation) for children under 12 years of age without first consulting with a doctor.

If hayfever symptoms do not improve within 7 days of treatment with ALANASE, consult with a doctor.

ALANASE 100 (100 micrograms per actuation)

For adults and children over 6 years of age:

The recommended dosage is one spray into each nostril twice daily.

For some patients, a dosage regimen of 50 micrograms into each nostril three or four times daily may be preferred. Total daily administration should not normally exceed 400 micrograms.

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.

Special populations

Paediatric

For children under six years old, there are insufficient clinical data to recommend use.

Method of administration

ALANASE and ALANASE 100 nasal sprays are for administration by the intra-nasal route only.

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 (see Paediatric use), cataract, glaucoma 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 ALANASE and ALANASE 100 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 contraindication to treatment with ALANASE and ALANASE 100.

Although ALANASE and ALANASE 100 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.

ALANASE and ALANASE 100 contain benzalkonium chloride which may cause bronchospasm.

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.

Paediatric Use

Continuous long-term treatment of children is not recommended.

4.5 Interaction with other medicines and other forms of interaction

Beclomethasone 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. ALANASE and ALANASE 100 deliver beclomethasone dipropionate directly to the nasal mucosa and so minimise systemic exposure.

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

Breast-feeding

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

4.7 Effects on ability to drive and use machines

Adverse effects of beclomethasone include blurred vision which could affect the ability to drive or use machines (see section 4.8).

4.8 Undesirable effects

Adverse reactions are listed below by system organ class and frequency. Frequencies are defined as: very common ($\geq 1/10$), common ($\geq 1/100$ and $< 1/10$), uncommon ($\geq 1/1000$ and $< 1/100$), rare ($\geq 1/10,000$ and $< 1/1000$) and very rare ($< 1/10,000$) including isolated reports. 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 Event	Frequency
Immune system disorders	Hypersensitivity reactions including:	
	Rash, urticaria, pruritis, erythema.	Common
	Angioedema	Very rare
	Dyspnoea and/or bronchospasm	Very rare
	Anaphylactoid/anaphylactic reactions	Very rare
Nervous system disorders	Unpleasant taste, unpleasant smell.	Common
Eye disorders	Glaucoma, raised intraocular pressure, cataract.	Very rare
	Vision, blurred (see section 4.4)	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 used at high doses for prolonged periods (see section 4.4).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions <https://nzphvc.otago.ac.nz/reporting/>.

4.9 Overdose

The only harmful effect that follows inhalation of large amounts of the medicine over a short time period is suppression of Hypothalamic-Pituitary-Adrenal (HPA) function. No special emergency action need be taken. Treatment with ALANASE and ALANASE 100 nasal spray should be continued at the recommended dose. HPA function recovers in 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.

For further advice on management of overdose please contact the National Poisons Information Centre (0800 POISON or 0800 764 766).

5. Pharmacological Properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Decongestants and other nasal preparations for topical use

ATC code: R01AD01

Mechanism of action

Following topical administration beclometasone 17, 21-dipropionate (BDP) produces potent anti-inflammatory and vaso-constrictor 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 mucociliary 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 (< 50 picograms/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 (20 L) but more extensive for B-17-MP (424 L). 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 120 L/hour) with corresponding terminal elimination half-lives of 0.5 hours and 2.7 hours. Following oral administration of tritiated BDP, approximately 60% of the dose was excreted in the faeces within 96 hours mainly as free and conjugated polar metabolites. Approximately 12% of the dose was excreted as free and conjugated polar metabolites in the urine.

5.3 Preclinical safety data

No clinically relevant findings were observed in preclinical studies.

6. Pharmaceutical Particulars

6.1 List of excipients

- benzalkonium chloride
- phenethyl alcohol
- polysorbate
- dispersible cellulose
- glucose (anhydrous)

- purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

ALANASE and ALANASE 100 should be protected from light and stored below 25°C. Do not refrigerate.

Discard three months after first using the spray.

6.5 Nature and contents of container

Amber glass bottles fitted with a metering, atomising pump and nasal applicator. Both dosage strengths provide 200 actuations.

6.6 Special precautions for disposal

Not applicable.

7. Medicines Schedule

ALANASE: Pharmacy only medicine.

ALANASE 100: Prescription medicine.

8. Sponsor Details

Mylan New Zealand Ltd
PO Box 11183
Ellerslie
AUCKLAND
Telephone 09-579-2792

9. Date of First Approval

ALANASE: 9 July 1991

ALANASE 100: 1 4 February 1992

10. Date of Revision of the Text

6 August 2019

Summary table of changes

Section	Summary of new information
-	Minor editorial updates

2	Naming benzalkonium chloride as an excipient with known effects
4.4	Added statement concerning benzalkonium chloride
4.5	Added interactions with CYP3A inhibitors
4.7	Added statement based on blurred vision as an adverse effect
4.8	Added blurred vision as an adverse effect
4.9	Added statement concerning the treatment of overdose
5.2	Added data on oral administration