

**Submissions to the Medicines Classification
Committee for the Reclassification of**

**Beclomethasone dipropionate aqueous
nasal spray
50 µg/metered dose**

(Beconase Allergy & Hayfever 12 Hour™)

Present Classification: Pharmacy-Only Medicine

Sought Classification: General Sale Medicine

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Sponsor: New Zealand Retailers Association (on behalf of Grocery Retailers)

Table of Contents

EXECUTIVE SUMMARY	3
PART A	4
A.1. International Non-proprietary Name (or British Approved Name or US Adopted Name) of the medicine	5
A.2. Proprietary name(s)	5
A.3. Name of company/organisation/individual requesting reclassification	5
A.4. Dose form(s) and strength(s) for which a change is sought	6
A.5. Pack size and other qualifications	6
A.6. Indications for which change is sought	6
A.7. Present classification of medicine	7
A.8. Classification sought	7
A.9. Classification status in other countries (especially Australia, UK, USA, Canada)	7
A.10. Extent of usage in New Zealand and elsewhere (e.g. sales volumes) and dates of original consent to distribute	8
A.11. Labelling or draft labelling for the proposed new presentation(s)	8
A.12. Proposed warning statements if applicable	8
A.13. Other products containing the same active ingredient(s) and which would be affected by the proposed change	9
PART B	10
B.1. A statement of the benefits to both the consumer and to the public expected from the proposed change	11
B.2. Ease of self-diagnosis or diagnosis by a pharmacist for the condition indicated	12
B.3. Relevant comparative data for like compounds	13
B.4. Local data or special considerations relating to New Zealand	15
B.5. Interactions with other medicines	15
B.6. Contraindications	16
B.7. Possible resistance	16
B.8. Adverse events - nature, frequency etc	16
B.9. Potential for abuse or misuse	18
REFERENCES	19
APPENDIX	21

Executive Summary

Beclomethasone Dipropionate is a glucocorticoid steroid and after topical application to the nasal mucosa it produces potent anti-inflammatory and vasoconstrictor effects. It is available as an aqueous suspension and used for temporary relief of seasonal Allergic Rhinitis and hayfever in adults and children aged 12 years and over.

Currently treatments to alleviate seasonal allergic rhinitis and hayfever available in the grocery channel are limited to oral antihistamines such as Fexofenadine (Telfast). When comparing the efficacy, rate of response to treatment and completeness of symptom control, topical corticosteroids are clearly the preferred first line treatment often giving sufferers immediate soothing effects⁹. These preferred topical nasal spray products are currently only available through pharmacies.

This reclassification application has chosen, Beconase Allergy & Hayfever 12 HourTM as the reference product. Beconase Allergy & Hayfever 12 HourTM has been registered in NZ as an aerosol formulation since 1974 as a Prescription Medicine. The aqueous formulation, called Beconase Aqueous Nasal Spray became available in 1983. The aerosol formulation was discontinued in 1995 and Beconase was reclassified to a Pharmacy Only Medicine in 1997 also changing in trade name to Beconase Hayfever.

The product is indicated for the prophylaxis and treatment of seasonal allergic rhinitis including hayfever. The purpose of this application is to seek reclassification of Beconase Allergy & Hayfever 12 HourTM, when labelled for use in adults and children over 12 years of age, from 'Pharmacy Only' medicine to 'General Sale' medicine. Beconase Allergy & Hayfever 12 HourTM is available as 'General Sale' in UK and 'Pharmacy Only' in Australia, and Prescription Medicine in Canada and USA^{3,4}.

The intention of this reclassification is to provide the consumer with the access to the preferred first line treatment for seasonal allergic rhinitis with the convenience and choice of purchasing the product for the short term treatment in an accessible environment which is not limited in hours of availability and/or location as it is at Pharmacy level. It is also an option for parents/caregivers who have pre-teen children who suffer from the effects of seasonal allergic rhinitis.

In addition, supermarkets generally open much longer hours than pharmacies⁸. Aside from those in malls, few pharmacies open on Sundays. Grocery stores are more prevalent in rural areas where there may be no other options for quick access to these medicines. The latest information sourced by the NZ Retailers Association still confirms that supermarkets opening hours are two times longer on average compared to pharmacies. This classification change enables access to consumers with after hour requirements.

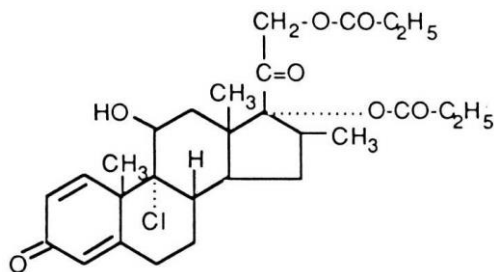
The safety and efficacy of Beclomethasone dipropionate nasal spray has been reviewed extensively and the safety profile of Beclomethasone dipropionate is well established. Side effects are also generally well tolerated. The proposed classification for Beclomethasone dipropionate is not expected to increase the potential risk of adverse events nor the potential for abuse or misuse.

Part A

A.1. International Non-proprietary Name (or British Approved Name or US Adopted Name) of the medicine

Name: Beclomethasone dipropionate

Chemical structure:



Molecular Formula: $C_{27}H_{23}ClO_7$

Molecular Weight: 521.042g/mol

CAS number: 5534-09-8

A.2. Proprietary name(s)

Beconase Allergy & Hayfever 12 Hour™

A.3. Name of company/organisation/individual requesting reclassification

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A.4. Dose form(s) and strength(s) for which a change is sought

Our proposal is to reclassify Beclomethasone dipropionate 50µg/metered dose aqueous suspension for nasal use, when labelled for use in adults and children over 12 years of age, from 'Pharmacy Only' medicine to 'General Sale' medicine.

A.5. Pack size and other qualifications

This reclassification request is to permit the Beconase Allergy & Hayfever 12 Hour™ to become a 'General Sale' medicine, when labelled for use in adults and children over 12 years of age. The product is an aqueous suspension delivered by a metering, atomising pump containing BDP 50µg/actuation. Each nasal spray bottle is packaged into a carton with an accompanying patient information leaflet (Appendix 3).

The current pack sizes and other qualifications for Beconase Allergy & Hayfever 12 Hour™ are outlined in Table 1.

Table 1: Beconase Allergy & Hayfever 12 Hour™ aqueous nasal spray pack size configurations

Medsafe File reference	Package	Contents	Current Classification:
TT50-2420/5	Spray bottle, metered, propylene.	200 dose units	Pharmacy only

A.6. Indications for which change is sought

This proposal does not increase the range of indications or dosage recommendations for the use of Beconase Allergy & Hayfever 12 Hour™ beyond those for existing treatments of seasonal allergic rhinitis and hayfever. The current approved indication is for the prophylaxis and treatment of seasonal allergic rhinitis including hayfever in Adults and children 12 years and over.

A.7. Present classification of medicine

Currently in NZ, there is only 1 classification for Beconase Allergy & Hayfever 12 Hour™ and conditions are provided below²:

Classification ²	Conditions (if any)
Pharmacy Only	for the treatment or prophylaxis of allergic rhinitis in adults and children over 12 years of age in aqueous nasal sprays delivering up to 50 micrograms per actuation when the maximum recommended daily dose is no greater than 400 micrograms (200 micrograms per nostril) in a pack containing 200 actuations or less

A.8. Classification sought

This application requests reclassification to 'General Sale' medicine status.

Classification	Conditions (if any)
General Sale	for the treatment or prophylaxis of allergic rhinitis in adults and children over 12 years of age in aqueous nasal sprays delivering up to 50 micrograms per actuation when the maximum recommended daily dose is no greater than 400 micrograms (200 micrograms per nostril) in a pack containing 200 actuations or less

A.9. Classification status in other countries (especially Australia, UK, USA, Canada)

Beclomethasone dipropionate aqueous nasal spray 50µg has been marketed on prescription since 1974 in approximately 70 countries. It has been available without prescription in a number of countries including Finland, Ireland, Poland, Switzerland, Sweden and South Africa for many years. In addition, in New Zealand it has been available since 1997 as a self select pharmacy only medicine due to the lack of requirement for supervised sales and it was recently de-scheduled to become a general sales medicine in the UK and a Pharmacy Medicine in Australia.

The conditions for General Sale in the UK are provided below³:

Country	Conditions (if any)
UK	Nasal administration in non-aerosol form. Prevention and treatment of allergic rhinitis in persons aged 18 years and over, for a maximum period of 3 months Max dose : 100mcg per nostril Max daily dose : 200mcg per nostril Max pack : 20,000mcg of beclomethasone dipropionate If symptoms are not controlled, or persist for longer than 2 weeks, medical advice must be sought.

A.10. Extent of usage in New Zealand and elsewhere (e.g. sales volumes) and dates of original consent to distribute

For over 25 years, Beclomethasone dipropionate in an aqueous nasal spray format has been widely utilized in over 30 countries with over 10 million patient years of exposure. During this time, Beclomethasone dipropionate has been shown to be extremely safe for use in the treatment of seasonal allergic rhinitis. The most common adverse events have been primarily associated with minor irritation of the nasal mucous membranes, events that are commonplace and anticipated with the use of nasal sprays.

Usage in New Zealand

The most up to date sales data indicates that from August 2012 - June 2014 (2 years) 21,156 units of Beconase Allergy & Hayfever 12 Hour™ Aqueous Nasal Spray 50 µg were sold across New Zealand on a Pharmacy Only Medicine basis. Previous sales data indicates that between August 1983 and October 1998, 1,505,500 units of 200 dose pack of Beconase Allergy & Hayfever 12 Hour Aqueous Nasal Spray™ 50µg were sold in New Zealand on a Prescription Medicine basis. An additional 100,800 units of 200 dose pack of Beconase Allergy & Hayfever 12 Hour™ were sold on a Restricted Medicine basis between September 1997 and October 1998.

A.11. Labelling or draft labelling for the proposed new presentation(s)

Directions for use, indications and warning statements will remain the same as that for the current aqueous nasal spray products currently marketed in New Zealand, the only change being the removal of the 'Pharmacy only medicine' statement.

There is no requirement for different dosing instructions or indications for 'General Sale'. It is important to ensure consistency of information so that consumers accustomed to using the product are not confused with conflicting information on packs bought in differing outlets.

A.12. Proposed warning statements if applicable

The warning / precautions statements contained on the current labelling will remain the same. Typical precautions listed below.

PRECAUTION:

- Do not use Beconase Allergy & Hayfever 12 Hour if you have ever had an allergic reaction to beclomethasone dipropionate, an allergic reaction to any other corticosteroid or any of the ingredients listed in this product.
- Do not use a larger dose or use your nasal spray more often than recommended in the instruction leaflet.
- See your doctor or pharmacist if symptoms are not relieved within 7 days.
- This product is not recommended for children under 12 years.
- If you have concerns about taking this medicine, ask your pharmacist or doctor.
- Do not use Beconase Allergy & Hayfever 12 Hour to treat any other conditions unless advised by your doctor to do so.

The above label warnings meet the labelling requirements stated in the Medsafe label statement database for nasal corticosteroids⁶.

A.13. Other products containing the same active ingredient(s) and which would be affected by the proposed change

Other intranasal corticosteroid sprays containing beclomethasone dipropionate 50 µg/metered dose which are presently registered as pharmacy only medicines in NZ¹ are:

Sponsor	Product	Approval date
Mylan New Zealand Ltd	Alanase Nasal spray solution, 50µg/dose	9/07/1991
Pharmacy Retailing (NZ) Ltd t/a Healthcare Logistics	Beconase Allergy & Hayfever 12 Hour Nasal spray suspension, 50µg/dose	1/04/1997
Novartis Consumer Health Australasia Pty Ltd (New Zealand)	Otrinese Hayfever Relief Nasal spray suspension, 50µg/dose	2/03/2006

Part B

B.1. A statement of the benefits to both the consumer and to the public expected from the proposed change

Beclomethasone dipropionate nasal spray has been available in NZ market since 1974. Currently it is available for self-selection by patients in the pharmacy setting. It has been available at this level of classification since 1997 with no significant safety concerns have arisen.

Seasonal Allergic Rhinitis is associated with impairments in how people function in their everyday lives and can create difficulties at work or school¹⁰.

In Australia alone it is estimated that 500,000 sick days every year are attributed to the symptoms of this condition¹¹. Effective management of seasonal allergic rhinitis and hayfever can therefore have a significant effect on quality of life and work performance¹⁰.

Recent research conducted amongst Australian allergy sufferers has revealed that many are obtaining inadequate symptom relief with the current products that they self-select in the pharmacy. The consensus from this research is that consumers will put up with what they have access to and are reluctant to bother their GP or pharmacist for advice on a more suitable, or more effective, product.

This unfortunate situation is perpetuated by the products available to consumers. Currently a limited range of medications for the symptomatic control of seasonal allergic rhinitis are available as General Sales Medicines. Whilst these medications do confer some benefits to sufferers, they are not regarded as the first-choice treatment option. Intranasal corticosteroids, currently held as Pharmacy Medicines, are the first-choice treatment option because they provide superior symptom control as well as prophylactic benefits with no increase in risk from adverse events.

Changing the classification of Beclomethasone dipropionate to General Sales Medicine would provide an alternative treatment option to consumers. Moreover, patients would be able to find these products in the same place that they find their current products. Presented with a new treatment choice, consumers would have an increased chance of successfully controlling their symptoms and in doing so avoid the negative health consequences that result from inadequate symptom management.

Taking into consideration the safeguard of adequate labelling (via packaging and Product Information Leaflets) to provide clear and simple instructions for the use of these products, it is difficult to argue that their rescheduling from Pharmacy Medicines to General Sales Medicines will pose any added risk to public health and safety to consumers. On the contrary, there are tremendous public health benefits in having safe, efficacious first-line agents available without the limitation of pharmacy opening hours which are generally short compared to operating hours of supermarkets. This can limit the access of consumers to required medication. A study in New Zealand by the NZ Retailers Association concluded that supermarkets were open for 101.5 hours per week on average and pharmacies were open 55.1 hours per week on average in the same areas examined⁸. The latest survey by the NZ Retailers Association still confirms that supermarkets opening hours are two times longer on average compared to pharmacies.

Providing greater access through reclassification of Beclomethasone dipropionate, especially for after hours emergencies and in more rural areas of New Zealand where pharmacy access can be difficult, will potentially reduce the number of physician visits and result in a subsequent reduction in medical costs for a condition that can be effectively self-managed and referred to physicians if necessary (as indicated in the product information).

This change will mean that consumers in New Zealand will have the same access to Beclomethasone dipropionate nasal spray as consumers in the United Kingdom.

B.2. Ease of self-diagnosis or diagnosis by a pharmacist for the condition indicated

The indication for use and dose form proposed in this reclassification application for Beconase Allergy & Hayfever 12 Hour™ nasal spray is essentially identical to those for nasal spray currently available as 'Pharmacy Only'.

Hayfever is a common allergic disease, affecting an estimated 10% to 15% of the population¹². The condition is easily self-diagnosed by the characteristic symptoms of rhinorrhoea, sneezing and nasal stuffiness, as well as possible itching of the eyes, nose, ears and/or palate. Seasonal allergic rhinitis is easy to distinguish from other forms of rhinitis because it tends to occur only in spring or summer with the release of pollens from flowers, weeds, grasses and trees. Hayfever is also a self-limiting disorder which requires no special investigations, and is unlikely to mask a more serious underlying disease.

Indeed, hayfever has long been recognised as being appropriate for self-diagnosis, as reflected by the extensive range of oral antihistamine and intranasal decongestant products which have been marketed for many years worldwide on an OTC basis. The symptoms of seasonal allergic rhinitis are also well documented in the consumer information leaflet accompanying Beconase Allergy & Hayfever 12 Hour™ (Appendix 3).

The labelling directs consumers to seek medical advice and consult doctor or pharmacist before use if use coincides with the commencement of any other medications. Consumers are also advised to seek medical advice if the symptoms persist after 7 days. We believe that consumers recognize that prolonged pain/congestion is a sign of something more serious as such and are able to adequately evaluate this and seek appropriate medical treatment.

The labelling clearly states that the product is for short term use (consumers are directed to seek advice from a doctor or pharmacist if use continues for more than 6 months) and only, 1-2 sprays per nostril, twice daily when necessary for adults and children over 12 years of age.

The easily recognisable and short-term nature of the indications for use ensures that neither medical diagnosis nor on-going medical management are required.

B.3. Relevant comparative data for like compounds

Antihistamines

Oral antihistamines have been used for many years for the prevention and treatment of seasonal allergic rhinitis. A number of these are available as Pharmacy Medicines for 10-day treatment and as General Sale Medicines for short-term, 5-day treatment e.g., loratadine (Claratyne™) and cetirizine hydrochloride (Zyrtec™). They can be used to treat some of the histamine-mediated symptoms of rhinitis, such as nasal itching, sneezing and watery rhinorrhoea, by blockade of histamine H1-receptors¹³.

Even though H1 antihistamines are effective at reducing the neurally mediated symptoms of itch, sneeze, and rhinorrhoea they have little objective effect on nasal blockage^{13,14}. The reason for this is that histamine is not the main cause of nasal obstruction following allergen challenge; here other mediators such as prostaglandins, leukotrienes and kinins play a significant role¹⁶.

Newer antihistamine plus decongestant combinations such as Clarinase™ are reputed to relieve nasal congestion arising from the late-phase inflammatory response. However, unlike intranasal corticosteroids, they do not treat the underlying inflammation that leads to nasal congestion.

Antihistamines vary widely in their onset of activity. Generally, the onset of the antihistaminic effect begins within one hour and is greatest 5–7 hours after oral administration of the compound¹⁷.

Symptoms of sedation, drowsiness, fatigue, performance impairment and somnolence are the most problematic adverse effects of the first-generation antihistamines. Second-generation antihistamines clearly cause less sedation and impairment than their predecessors, but none of them are entirely devoid of CNS activity. Indeed, all antihistamines possess the potential to cause a degree of somnolence as a function of the histaminergic mechanisms involved in the control of CNS arousal¹⁸.

Topical anti-histamines, such as levocabastine aqueous nasal spray (Livostin™ nasal spray and eye drops) and azelastine HCl (AZEP™ Hayfever relief) are also Pharmacy Medicines. Topical intranasal agents are reported as having a slightly more rapid onset of action than oral preparations and are quite effective in relieving pruritis, sneezing, and rhinorrhoea. However, like H1-receptor antagonists administered orally, they are not highly effective in relieving nasal blockage¹⁷.

Mast cell stabilisers

Mast cell stabilisers, such as sodium cromoglycate (Rynacrom™), reduce nasal itching, sneezing, hypersecretion and nasal blockage in seasonal allergic rhinitis. Mast cell stabilisers inhibit the release of histamine and other mediators of inflammation from sensitised mast cells. These medications prevent the early- and late-phase reactions of AR, but do not relieve pre-existing symptoms. As such, they are prophylactic agents and need to be started before the onset of symptoms for maximum effect. They reduce the symptoms of AR, but are clearly less effective than nasal corticosteroids¹³.

Sodium cromoglycate is effective immediately, but for effective use it must be used 4–6 times a day. This need for frequent dosing (which can lead to poor patient compliance) is its major disadvantage.²

Topical decongestants

Topical decongestants, such as ephedrine nasal drops, can provide symptomatic relief from nasal congestion associated with vasomotor rhinitis and the common cold. They contain sympathomimetic drugs, which exert their effect by vasoconstriction of the mucosal blood vessels, which in turn reduces oedema of the nasal mucosa. They are of limited value because they can give rise to rebound congestion (rhinitis medicamentosa) when their effects wear off. This is because secondary vasodilation causes a subsequent temporary increase in nasal congestion¹⁹.

The more potent sympathomimetic drugs oxymetazoline (Logicin™), phenylephrine and xylometazoline (Otrivin™) are more likely to cause a rebound effect. All of these agents can cause a hypertensive reaction if used during treatment with a monoamine oxidase inhibitor.

Intranasal corticosteroids

Topical corticosteroids are effective in reducing nasal blockage, itching, sneezing and rhinorrhoea in all forms of rhinitis. They have effects on cells and mediators involved in both early- and late-phase reactions. They have proved to be more effective in symptomatic control of AR than sodium cromoglycate, antihistamines and decongestants¹³. When formulated as aqueous nasal sprays, they can have an immediate soothing effect⁹ and are well tolerated, with a low incidence of side effects²⁰. It may be three to four days before the maximum benefits of the anti-inflammatory effect of the corticosteroid are attained.

Oral antihistamine preparations have been the mainstay of prevention and treatment of allergic rhinitis for many years. A number of these products are freely available in New Zealand as Pharmacy and/or General Sale Medicines (dependent on pack size), including AVIL™ (pheniramine, HMR), CLARATYNE™ (loratadine, Schering-Plough), PHENERGAN™ (promethazine, RPR), POLARAMINE™ (dextrochlorpheniramine, Schering-Plough) and TELFAST™ (fexofenadine, HMR). Although these products are particularly effective in the suppression of sneezing they are less effective for rhinorrhoea and have little influence on nasal blockage. Moreover, most antihistamines produce a degree of dose-related sedation, although the newer agents claim to be non-sedating at therapeutic doses. Some of the newer antihistamines have been associated with cardiac toxicity when taken in higher doses or concomitantly with medicines metabolised via the cytochrome p₄₅₀ system. Some antihistamines also have well-documented interactions with other commonly used medicines. In particular, they potentiate the effects of alcohol.

Several intranasal decongestants are marketed in New Zealand as Pharmacy Medicines for the short term treatment of nasal blockage associated with allergic rhinitis. These agents have a rapid onset of action, providing initially effective symptomatic relief. However, the disadvantages of some of these products for consumers are that rebound hyperaemia may occur, and continued use may cause rhinitis medicamentosa.

Intranasal corticosteroid preparations such as Beconase Allergy & Hayfever 12 Hour™ have a potent anti-inflammatory effect on the nasal mucosa and have been used worldwide, including in New Zealand, for over 25 years for the prevention and treatment of seasonal allergic rhinitis. Topically administered corticosteroids have been shown to provide effective relief for nasal congestion, sneezing, rhinorrhoea

and nasal itching. These agents also have low oral bioavailability, so the swallowed portion of an intranasal dose does not produce detectable systemic levels or the unwanted effects and/or drug interactions of the oral antihistamines and intranasal decongestants.

The role of intranasal corticosteroids has evolved over time from second-line to first-line treatment of seasonal allergic rhinitis and prevention of symptom recurrence. The results of a meta-analysis of 16 randomised controlled trials involving 2267 subjects indicate that intranasal corticosteroids are more effective than oral antihistamines for alleviating most nasal symptoms of allergic rhinitis, and suggest no difference between these treatment modalities for relief of associated eye symptoms²¹. The authors recommend intranasal corticosteroids for cost-effective first-line treatment of allergic rhinitis, and suggest a role for oral antihistamines as ancillary treatment, especially for eye symptoms or nasal itch if inadequately controlled by intranasal corticosteroids.

The results of clinical studies in over 1900 patients with seasonal allergic rhinitis and an additional 1500 patients with perennial rhinitis have demonstrated that beclomethasone dipropionate is significantly superior to placebo in terms of effectiveness. Beclomethasone dipropionate has also been shown to provide equivalent efficacy to other intranasal corticosteroids in the treatment of the symptoms of rhinitis and rhinorrhoea. Ocular symptoms have also been shown to correlate well with objective nasal cytology findings and nasal rhinomanometry measurements. The wealth of data from clinical trials and the published literature, as well as the availability of the prescription product for over 20 years is supportive of the efficacy of the product.

B.4. Local data or special considerations relating to New Zealand

A review of current literature shows that beclomethasone dipropionate in doses up to 160 µg/d in children as young as 6 years old^{22,23} and doses up to 320 µg/d in adolescent children is safe for administration and offers significant and effective relief of symptoms of allergic rhinitis in paediatric populations^{24,25}. Whilst in the UK Beconase Allergy & Hayfever 12 HourTM for general sale is indicated for use in persons aged 18 years and over, Beconase Allergy & Hayfever 12 HourTM would continue to be indicated for use in persons aged 12 years and above due to the established safety and efficacy of the product in the adolescent population.

B.5. Interactions with other medicines

There have been no clinically significant reports of drug interactions with beclomethasone dipropionate to date.

B.6. Contraindications

Beconase Allergy & Hayfever 12 Hour™ is contraindicated in patients with a history of hypersensitivity to any of its components. Infections of the nasal passages and paranasal sinuses should be appropriately treated but do not constitute a specific contraindication to treatment with intranasal Beclomethasone dipropionate.

B.7. Possible resistance

Not applicable as it is not expected that short term use of Beconase Allergy & Hayfever 12 Hour™ will cause any resistance to develop.

B.8. Adverse events - nature, frequency etc

Between January 2000 and March 2014 there have only been 16 total AE reports where Beconase Allergy & Hayfever 12 Hour™ was reported as a medication being taken in the reported case in Australia and New Zealand⁵

The most commonly reported AEs were:

- Dizziness
- Dyspnoea
- Headache
- Rash
- Nausea

The majority of events reported were not clinically serious and were reversible on discontinuing therapy.

According to the New Zealand National Poisons Centre, between 1 July 2002 and 14 July 2014 (12 years) there were a total of 77 exposure calls made to them regarding products containing beclomethasone dipropionate. Of these, 4 were classified as chronic (using the product for longer than recommended). This ranged from a few days to over a month. 73 of the calls were classified as acute and of those, 36 were child exploratory (28 ingestions and 8 inhalation/nasal). The circumstances ranged from the child sucking on the end of nozzle through to actively administering it to another child.

There was 1 intentional call. This was a multiple substance overdose call where the patient took every substance they had available to them including their nasal spray and there were 40 therapeutic error calls (where 'therapeutic error is defined as being wrong dose, wrong substance, wrong patient or wrong route of administration). Of these, 5 were eye exposures (often mistaking the product for eye drops), 3 ingestions, 31 inhalation/nasal exposures (usually involving wrong dose eg. 2 sprays instead of 1) and there was 1 skin exposure.

The main area of concern with intranasal corticosteroids is growth suppression which remains a debated issue. Certainly it is agreed that oral steroids can affect growth and suppress the hypothalamic-pituitary-

axis (HPA). It is suspected that inhaled and intranasal may do this also, although systemic levels are obviously lower and therefore the risk of suppression is likely to be lower.

In 1998 the FDA tightened its labelling on inhaled and intranasal corticosteroids to include mandatory statements regarding growth suppression in the precautions and paediatric sections on all these products. At that time there were 8 reports of growth suppression with intranasal steroid use and 12 reports with inhaled steroids. They assessed the international literature on the subject and found only a few good studies examining growth suppression. Problems with studies included inaccurate height measurement, difficulties in adjusting for puberty, the possibility of later growth recovery after stopping steroids, and difficulties in developing a model to predict final adult height.

The FDA then concluded, "The finding of growth inhibition was robust". However, they could not predict the effects of intranasal or inhaled corticosteroids on final adult height, nor the impact of different products on growth. They recommended that growth needs to be monitored with treatment adjusted if growth is suppressed. They commented that more studies are required. The FDA went on to say that they are not suggesting that inhaled/intranasal corticosteroids are unsafe in children and are not considering restricting use in children. However they wanted properly labelled medications to promote their safest use.

The New Zealand Medicines Adverse Reactions Committee (MARC) has also considered the issue. The MARC examined recent literature on growth suppression with inhaled and intranasal steroids and the FDA decision at their June 2000 meeting. They concluded that long term well-controlled studies are required to confirm whether there is growth suppression, and whether it has an impact on adult height.

Other clinically serious events of interest with respect to non-prescription use of a drug are severe hypersensitivity reactions and, in the case of a corticosteroid, systemic effects. Intranasal beclomethasone dipropionate is contra-indicated in patients with a history of hypersensitivity to any of its components. Approximately 10% of all spontaneously reported adverse events are suggestive of hypersensitivity reactions. The majority of these are skin reactions, although in some cases oedema or puffiness of the lips, eyes or face were also noted. However, the relationship of all of these reactions to use of intranasal beclomethasone dipropionate is difficult to assess in a population that is typically atopic and prone to conditions such as allergic rhinitis, asthma, eczema, and food or environmental allergies.

In a number of cases, concomitant medications appear to be a more likely cause of the reaction, or the time to onset is inappropriately long (months or years) for a causal relationship¹⁴. Allergic reactions to the preservatives in the aqueous nasal spray (phenylethyl alcohol and benzalkonium chloride) may occur very rarely. More severe hypersensitivity reactions with systemic manifestations are extremely rare and no fatal anaphylactic-type reactions have been reported. Thus, true allergic reactions to beclomethasone dipropionate are likely to be rare and usually mild and transient.

Potentially serious local effects such as nasal septal perforation (NSP) and mucosal atrophy are more commonly associated with aerosol than aqueous spray formulations of corticosteroids, possibly due to the higher speed of drug delivery with the nasal spray. Spontaneous data reveals a low reporting rate of NSP with beclomethasone dipropionate.

Although beclomethasone dipropionate is not intended for use in children under 12 years of age, its safety in this population is of importance in the context of accidental or intentional overdose by children. Review of events reported in children reveals no safety issues specific to this group of patients. Similarly, there is no evidence of any difference in safety profile between patients over 65 years of age and younger adults.

Use in pregnancy

Administration of medicines during pregnancy should only be considered if the expected benefit to the mother is greater than any possible risk to the foetus. There is inadequate evidence of safety of beclomethasone dipropionate in human pregnancy. In animal reproduction studies adverse effects typical of potent corticosteroids are only seen at high systemic exposure levels; direct intranasal application ensures minimal systemic exposure.

Lactation:

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 intranasal 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.

Overdose

The only harmful effect that follows inhalation of larger 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 BECONASE Allergy & Hayfever 12 Hour should be continued at the recommended dose. HPA function recovers in a day or two²⁶.

Given the above safety data and warning statements on the label, adverse effects with short-term use beclomethasone dipropionate nasal spray are rare. beclomethasone dipropionate should not be considered as just another Seasonal Allergic Rhinitis treatment but rather a safe, proven nasal spray which is internationally acknowledged for self-medication.

B.9. Potential for abuse or misuse

Beclomethasone dipropionate has a low potential for harm from inappropriate use because of a combination of the inherent characteristics of the active ingredient and the dosage form and administration method of the product. Beclomethasone dipropionate has low oral bioavailability, so the swallowed portion of an intranasal dose does not produce detectable systemic levels or any unwanted interactions with oral antihistamines or intranasal decongestants.

The most likely harmful effect that would be expected to follow inhalation of large amounts of beclomethasone dipropionate over a short time period is suppression of hypothalamic-pituitary-adrenal (HPA) function. HPA function recovers in one to two days. If treatment is discontinued there may be a delay before relief of symptoms is obtained after recommencing treatment.

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Appendix

Appendix 1. Current box packaging label of 'Beconase Allergy & Hayfever 12 Hour'



Appendix 2. Current bottle label of Beconase Allergy and Hayfever 12 Hour

PHARMACY MEDICINE
KEEP OUT OF REACH OF CHILDREN

beclomethasone dipropionate

BECONASE[®]

Allergy & Hayfever **12** HOUR

TWICE DAILY EFFECTIVE RELIEF AND PREVENTION

200 SPRAYS

NON DROWSY NASAL SPRAY

50 mcg per spray
AUST R 72346

Please read the enclosed leaflet carefully before use. Dosage: Adults and children 12 years and over, two sprays into each nostril twice a day. For the short term (3-6 months) prevention or treatment of hayfever and allergies. Shake gently before use. Discard 3 months after first using. Store below 30°C.

GlaxoSmithKline
CONSUMER HEALTHCARE
82 Hughes Avenue, Ermington,
NSW 2115, Australia
& Auckland, New Zealand.

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Exp. 06-2015



PHARMACY MEDICINE
KEEP OUT OF REACH OF CHILDREN

beclomethasone dipropionate
BECONASE
Allergy & Hayfever
12 HOUR

TWICE DAILY
EFFECTIVE RELIEF
AND PREVENTION
200 SPRAYS NON-DROWSY
0.1mg per spray ALIST R 22945
NASAL SPRAY

CONSUMER MEDICINE INFORMATION

WHAT IS IN THIS LEAFLET?

Please read this leaflet carefully before you use Beconase Allergy & Hayfever 12 Hour.

This leaflet answers some common questions about Beconase Allergy & Hayfever 12 Hour. It does not contain all of the available information. It does not take the place of talking to your doctor or pharmacist.

All medicines have risks and benefits. If you have any concerns about taking this medicine, ask your pharmacist or doctor.

Keep this leaflet with the medicine. You may need to read it again.

WHAT BECONASE ALLERGY & HAYFEVER 12 HOUR IS USED FOR

Beconase Allergy & Hayfever 12 Hour contains a corticosteroid called beclomethasone dipropionate which treats inflamed tissue. The tiny amounts sprayed into your nose help to reduce swelling and irritation.

Beconase Allergy & Hayfever 12 Hour can be used to treat and prevent seasonal allergic rhinitis (hayfever) and perennial allergic rhinitis (due to airborne allergens) in adults and children aged 12 years and over.

When you have rhinitis, the inside of your nose becomes swollen and itchy. This usually occurs during spring and summer when it is caused by breathing pollens from grasses or trees. This condition is called hayfever. Some people get problems all year round and this is called Perennial Rhinitis. It is often due to house dust mites or animals such as cats or dogs.

When you spray Beconase Allergy & Hayfever 12 Hour into your nose it helps to relieve itching, sneezing and a blocked or runny nose.

Ask your pharmacist or doctor if you have any questions or if you aren't sure why Beconase Allergy & Hayfever 12 Hour has been recommended for you.

Beconase Allergy & Hayfever 12 Hour is non-drowsy, and is not addictive.

BEFORE YOU USE BECONASE ALLERGY & HAYFEVER 12 HOUR

When you must not use it

- Do not use Beconase Allergy & Hayfever 12 Hour if you have ever had an allergic reaction to beclomethasone dipropionate, an allergic reaction to any other corticosteroid or any of the ingredients listed at the end of this leaflet.

Read the side effects section to find out the symptoms of an allergic reaction.

- Do not use Beconase Allergy & Hayfever 12 Hour after the expiry date (EXP) printed on the pack. If you use it after the expiry date has passed, it may not work as well.

- Do not use Beconase Allergy & Hayfever 12 Hour if the packaging is torn or shows signs of tampering. If you're not sure whether you should be using Beconase Allergy & Hayfever 12 Hour, talk to your pharmacist or doctor.

Before you start to use it

You must tell your pharmacist or doctor if you:

- Are pregnant or planning to become pregnant
- Are breastfeeding
- Have recently had nasal ulcers, injury or surgery to your nose
- Have a tendency to nose bleeds
- Have a nasal or sinus infection

Taking other medicines

Tell your doctor if you are taking any other medicines, including medicines you buy without a prescription from a pharmacy, supermarket or health food shop.

Some medicines may affect the way other medicines work. Your doctor or pharmacist will be able to tell you what to do when using Beconase Allergy & Hayfever 12 Hour with other medicines.

HOW TO USE BECONASE ALLERGY & HAYFEVER 12 HOUR

How much to use

If your Beconase Allergy & Hayfever 12 Hour is new and you have not used it before, or if you have not used it for one week or more, you should prime the bottle by spraying a few times into the air before use.

For adults and children aged 12 and over, the usual dose is two sprays into each nostril twice daily. Beconase Allergy & Hayfever 12 Hour quickly starts to reduce inflammation and swelling in your nose, although it may take a few days to significantly improve symptoms. Therefore to prevent the onset of symptoms, start to use Beconase Allergy & Hayfever 12 Hour a few days before expected exposure to one of your 'usual' triggers.

It may take a few days for this medicine to work and it is very important that you use it regularly. If you stop the treatment when you feel better, your symptoms may return as the medication wears off. If your symptoms include watery eyes and they trouble you, advise your pharmacist or doctor.

Once your symptoms have improved you may be able to halve the dose to one spray into each nostril twice a day. If symptoms get worse again, the dosage may be increased to two sprays into each nostril twice a day. Try to use the lowest dose to control your symptoms.

Do not use a larger dose or use your nasal spray more often than recommended in the instruction leaflet. Do not use more than 2 sprays in each nostril twice daily (4 sprays).

See your doctor or pharmacist if symptoms are not relieved within 7 days.

This product is not recommended for children under 12 years. Do not use for more than 6 months without the advice of a doctor or pharmacist.

If you use too much (overdose)

If you or someone else accidentally uses too much Beconase Allergy & Hayfever 12 Hour on one occasion, there is nothing to worry about. However, if you use too much of it over a long time (months or years) you may start to get unwanted side effects inside your nose and body.

Discuss any worries you may have about this with your doctor or pharmacist.

In case of overdose or poisoning contact a doctor or the Poisons Information Centre. In Australia call 13 11 26. In New Zealand call 0800 764 766.

USING THE SPRAY

1. Shake the bottle and remove the cap. Prime the bottle by pumping the spray a few times until a fine mist is produced.
 2. Blow your nose gently.
 3. Close one nostril as shown. Hold the bottle and put the nozzle in the other nostril. Tilt your head forward slightly and keep the bottle upright.
 4. Start to breathe in slowly through your nose. While you are breathing in, squirt a spray of fine mist into your nostril by pressing down firmly on the collar with your fingers.
 5. Breathe out through your mouth. Repeat step 4 to take a second spray in the same nostril.
 6. Remove the nozzle from this nostril and breathe out through your mouth.
 7. Repeat steps 3 to 6 for the other nostril.
- AFTER USING THE SPRAY, WIPE THE NOZZLE CAREFULLY WITH A CLEAN TISSUE OR HANDKERCHIEF AND REPLACE THE CAP.



HOW LONG TO USE THE SPRAY?

Your pharmacist or doctor will tell you how long to use your Becomase Allergy & Hayfever 12 Hour for. Do not use the spray for more than 6 months without the advice of your doctor or pharmacist.

If you forget to use the spray if you miss a dose just use the next one when it is due.

WHILE YOU ARE USING BECOMASE ALLERGY & HAYFEVER 12 HOUR

Things you must do:

Tell your doctor or pharmacist that you are using Becomase Allergy & Hayfever 12 Hour if you are about to be started on any new medicines. Tell your pharmacist or doctor if, for any reason, you have not used your medicine exactly as recommended. Use Becomase Allergy & Hayfever 12 Hour only in your nose.

Things you must not do:

Do not give this medicine to anyone else, even if their symptoms seem similar to yours.

Do not use Becomase Allergy & Hayfever 12 Hour to treat any other conditions unless advised by your doctor to do so.

SIDE EFFECTS

Check with your pharmacist or doctor as soon as possible if you have any problems while using Becomase Allergy & Hayfever 12 Hour, even if you do not think the problems are related to the medicine or are not listed in this leaflet.

See your doctor or pharmacist if:

- You develop signs or symptoms of a nasal or sinus infection such as fever, pain or swelling, or discoloured nasal discharge
- You have eye pain or visual disturbances.

Like other medicines, Becomase Allergy & Hayfever 12 Hour can cause some side effects. If they occur, they are most likely to be minor and temporary. However, some may be serious and may need medical attention.

The most commonly reported side-effects are:

- Painful nose or throat
- Nose bleed
- Bad taste or smell

If any of these side effects persist, or are troublesome, see your doctor.

Stop using your spray and contact your doctor immediately if you develop any of the following:

- Rash
- Wheezing
- Breathlessness
- Swelling of the lips/mouth

These could be symptoms of an allergic reaction to the spray. If you think you are having an allergic reaction to Becomase Allergy & Hayfever 12 Hour, TELL YOUR DOCTOR IMMEDIATELY or go to the emergency department at your nearest hospital.

This is not a complete list of all possible side effects. Others may occur in some people and there may be some side effects not yet known.

Tell your pharmacist or doctor if you notice anything else that is making you feel unwell, even if it is not on this list.

Ask your doctor or pharmacist if you don't understand anything in this list. Do not be alarmed by this list of possible side effects. You may not experience any of them.

AFTER USING BECOMASE ALLERGY & HAYFEVER 12 HOUR

Storage

Keep this medicine where young children cannot reach it.

Keep Becomase Allergy & Hayfever 12 Hour below 30°C. Protect it from frost and light.

Do not refrigerate. Do not store it, or any other medicine in a bathroom or near a sink.

Heat and dampness can destroy some medicines.

Keep your Becomase Allergy & Hayfever 12 Hour in its pack until it is time to take it.

If you take the product out of its packaging it may not keep well.

Disposal

If your doctor tells you to stop using Becomase Allergy & Hayfever 12 Hour, or the product has passed its expiry date, ask your pharmacist what to do with any Becomase Allergy & Hayfever 12 Hour left over.

PRODUCT DESCRIPTION

What Becomase Allergy & Hayfever 12 Hour looks like

Becomase Allergy & Hayfever 12 Hour is contained in a plastic bottle fitted with a metering pump, a nasal adaptor and a dust cover. Each bottle contains around 200 sprays.

Ingredients

Becomase Allergy & Hayfever 12 Hour contains the active ingredient bedomethasone dipropionate. It also contains the following inactive ingredients:

Dispersible cellulose, Sodium carboxymethylcellulose, Anhydrous glucose, Polysorbate 80, Hydrochloric acid (to adjust pH), Purified water, Benzalkonium chloride, Phenylethyl alcohol

Further information

Please call GlaxoSmithKline's toll-free infoline in Australia on 1800 028 533, or in New Zealand on 0800 540 144.

Or if you have any more questions or are unsure about anything, ask your pharmacist or doctor.

Becomase Allergy & Hayfever 12 Hour has an Australian Registration number of AUST R 72345.

Do not throw this leaflet away. You may need to read it again.

MANUFACTURERS/SUPPLIER/DISTRIBUTOR

Becomase Allergy & Hayfever 12 Hour is supplied by GlaxoSmithKline Consumer Healthcare 82 Hughes Avenue, Ermington NSW 2115, Australia & Auckland, New Zealand.

Becomase Allergy & Hayfever 12 Hour Aqueous Nasal Spray is a trademark of the GlaxoSmithKline Group of Companies. This leaflet was prepared in January 2005.

Becomase Allergy & Hayfever 12 Hour gives you highly effective hayfever and allergy treatment and prevention. For relief from:

- SNEEZING
- ITCHY NOSE
- RUNNY NOSE
- NASAL CONGESTION

Becomase Allergy & Hayfever 12 Hour protects from all major allergens including:

- POLLEN/GRASSES
- DUST MITES
- PET HAIR
- MOULD SPORES

УПАКОВКА
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Allergy & Hayfever 12 Hour

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Page 2