PRODUCT INFORMATION- RHINOCORT HAYFEVER & ALLERGY ORIGINAL (BUDESONIDE) NASAL SPRAY

1 NAME OF THE MEDICINE

Budesonide

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

RHINOCORT is an aqueous nasal suspension containing 32 µg budesonide per actuation as the active ingredient. RHINOCORT also includes disodium edetate, potassium sorbate, glucose anhydrous, dispersible cellulose polysorbate 80 and purified water as inactive ingredients. The pH of the solution may have been adjusted by hydrochloric acid, if required.

3 PHARMACEUTICAL FORM

Budesonide is formulated for intranasal administration and is available as a nasal spray

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

For short term (3-6 months) prophylaxis or treatment of seasonal allergic rhinitis in adults and children aged 12 years and over and perennial allergic rhinitis in adults 18 years and over.

4.2 DOSE AND METHOD OF ADMINISTRATION

Seasonal allergic rhinitis (adults and children 12 years and over) and pernnial allergic rhinitis (adults 18 years and over) There is no evidence that efficacy improves when the recommended dose is exceeded.

Initially

Total daily dose, 256 micrograms given as either a single daily application of 128 micrograms into each nostril in the morning, or divided into two applications of 64 micrograms into each nostril, morning and evening.

Maintenance – individualisation of dosage

When a satisfactory therapeutic response has been achieved, the maintenance dose should be titrated to the minimum effective dose. This may be a total daily dose of 128 micrograms given as 64 micrograms into each nostril in the morning, however clinical trials suggest that a maintenance dose of 32 micrograms in each nostril in the morning may be sufficient in some patients.

Patients should be informed that full response may not occur until after 2-3 days of treatment (in rare cases not until after 2 weeks). Ideally, in seasonal allergic rhinitis treatment should start before exposure to the allergen.

Patient instructions

Patients should be instructed in the correct use of RHINOCORT. An instruction leaflet is included in each pack of RHINOCORT. Patients should also be advised to clear secretions from nasal passages prior to use and not to exceed the recommended dose.

4.3 CONTRAINDICATIONS

1. Hypersensitivity to any ingredient.
2. Hypersensitivity to other corticosteroids.
3. Severe nasal infections, especially candidiasis.
4. Persons with haemorrhagic diatheses or with a history of recurrent nasal bleeding.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

If symptoms persist, worsen or if new symptoms occur, patients should stop use and consult a physician

Clinical response

The full effect of RHINOCORT in allergic rhinitis is not achieved until after 2 to 3 days of treatment (in rare cases not until after 2 weeks).

Concomitant treatment

Concomitant treatment may sometimes be necessary to counteract potential eye symptoms caused by the allergy.

Concomitant corticosteroid therapy

If RHINOCORT is administered to patients already using corticosteroids, care should be taken to ensure that the daily dosage of RHINOCORT is included when determining total daily corticosteroid dose.

Consult a physician before use if you are using a steroid medicine for conditions such as asthma, allergies or skin rash.

Severe nasal obstruction/congestion

In some patients with severe nasal obstruction and congestion, concomitant treatment with local decongestants should be considered for 2-3 days only. The decongestant should be administered a few minutes before budesonide. Nasal polypectomy may be indicated initially for patients with nasal obstruction due to nasal polyposis.

Tuberculosis

Whenever corticosteroid administration is required in patients with quiescent or active tuberculosis, the therapeutic advantages should be weighed against possible undesirable effects.

Consult a physician before use if patient has been exposed to someone who has tuberculosis, chicken pox or measles.

Infection

If infection of the respiratory tract, nasal passages or paranasal sinuses is present or occurs during administration of RHINOCORT, adequate antibacterial therapy should be promptly instituted (see also Contraindications, 2).

Consult a physician if you develop signs or symptoms of an infection such as a persistent fever.

Wound healing

Because of the inhibitory effect of corticosteroids on wound healing, patients who have experienced recent nasal septal ulcers, nasal surgery or nose injury that has not healed should not use a nasal corticosteroid until healing has occurred.

Adrenocortical function

Dose-related suppression of plasma and urinary cortisol has been observed in healthy volunteers after short-term administration of RHINOCORT. However, at recommended doses, RHINOCORT does not cause any clinically important changes in basal cortisol levels nor in the response to stimulation with ACTH in patients with rhinitis.

Use in hepatic impairment

Reduced liver function may affect the elimination of glucocorticosteroids. The pharmacokinetics after oral ingestion of budesonide were affected by compromised liver function as evidenced by a doubled systemic availability. The relevance of this finding to intranasally administered budesonide has not been established.

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.

Stop use and consult a physician if you have any change in vision. Consult a physician before use if you have ever been diagnosed with glaucoma, cataracts or have an eye infection or if you have diabetes.

Use in the elderly

No data available

Paediatric use

RHINOCORT is not recommended for use in children below 12 years of age.
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 and more rarely, a range of psychological or behavioral effects including psychomotor hyperactivity, sleep

disorders, anxiety, depression or aggression (particularly in children)

This product may slow the growth rate in some children when used in combination with other steroids.

Effects on laboratory tests

No data available

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

The metabolism of budesonide is primarily mediated by CYP3A, a subfamily of cytochrome P450. After oral administration of ketoconazole, a potent inhibitor of cytochrome P450 3A, the mean plasma concentration of budesonide increased by more than seven fold. Concomitant administration of other known inhibitors of this enzyme, (eg itraconazole, clarithromycin, erythromycin, ritonavir, atazanavir, indinavir, nefazodone, nelfinavir, saquinavir, telithromycin, itaconazole) may inhibit the metabolism of, and increase the concentration of budesonide in the plasma leading to increased risk of systemic side-effects such as Cushing's syndrome and adrenal suppression. If used, close monitoring of patients is advised for any systemic effects. Otherwise, the combination should be avoided unless the benefit outweighs the risk. Cimetidine, primarily an inhibitor of cytochrome P450 1A2, caused a slight decrease in budesonide clearance and corresponding increase in its oral bioavailability.

4.6 FERTILITY, PREGNANCY AND LACTATION

Use in pregnancy – Pregnancy Category A

It is not known if budesonide can cross the placenta but due to its relatively low molecular weight, placental transfer may be possible. When given at therapeutic doses, systemic exposure after intranasal administration is low. As with other drugs the administration of budesonide during pregnancy requires that the benefits for the mother be weighed against the risks for the foetus. Inhaled glucocorticosteroids such as budesonide, should be considered because of the lower systemic effects, compared to oral glucocorticosteroids.

Ask a physician before use if you are pregnant.

Use in lactation

Budesonide is excreted in breast milk. However, due to the relatively low doses used via the intranasal route the amount of drug present in the breast milk, if any, is likely to be low. The infant daily dose of inhaled budesonide is around 0.3% of the maternal daily dose. There is a linear relationship between budesonide concentration in plasma and breast milk, where the concentration of budesonide in breast milk is less than plasma concentration. Breastfeeding can be considered if the potential benefit outweighs any potential risks.

Ask a physician before use if you are breastfeeding.

Effects on fertility

There are insufficient data available to determine whether intranasal administration of budesonide has the potential to impair fertility.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

There is no evidence that budesonide has an effect on the ability to drive or use machines.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Adverse local reactions following intranasal budesonide use are mild and usually transient. Systemic corticosteroid side-effects have not been reported during clinical studies of intranasal budesonide in adults.

Adverse events reported during studies with intranasal budesonide:

Common (more than 1%)

Nose and throat	Nasal irritation, itching of throat and larynx, sore throat, dry mucous membranes, dry mouth, sneezing after spraying, increased sputum, haemorrhagic secretion, epistaxis (nose bleeding), nasal crust, sinusitis.
Respiratory	Cough, dyspnoea, asthma, epistaxis, oropharyngeal pain, upper respiratory tract infection, rhinitis
Central Nervous System	Headache, dizziness, tiredness, pyrexia
Skin and appendages	Rash
Gastrointestinal	Abdominal discomfort
Injury, poisoning and procedural complication	Head injury

Uncommon (less than 1%)

Nose and throat	Strong smell of spray, bad taste, earache.
Gastrointestinal	Loss of appetite, stomach disorder, nausea.
Skin and appendages	Skin itching
Central Nervous System	Tremor, sedation
Infection	Urinary tract infection
Immune system	Immediate and delayed hypersensitivity reactions including urticaria, rash, dermatitis, angioedema and pruritus
Injury, poisoning and procedural complications	Injury

Rare (less than or equal to 0.2%)

Ear itching, joint aches, sexual dysfunction.

Very rare cases of ulcerations of the mucous membrane, nasal septal perforations and anaphylactic reactions have been reported following the use of intranasal corticosteroids.

Laboratory variables

All changes in haematology, biochemistry and urinalysis were within the normal range and were not considered clinically significant.

Post Marketing Data

Adverse drug reactions (ADRs) identified during Post-marketing experience with budesonide are included in the following table. The frequencies are provided according to the following convention:

Very common	≥1/10
Common	≥1/100 and < 1/10
Uncommon	≥1/1,000 and <1/100
Rare	≥1/10,000 and <1/1,000
Very rare	<1/10,000
Not known (cannot be estimated from the available data)	

Adverse Drug Reactions Identified During Post-Marketing Experience with Budesonide by Frequency Category Estimated from Spontaneous Reporting Rates

SOC	
Frequency Category	Adverse Event Preferred Term
Immune System Disorders	
Very rare	*Anaphylactic reaction*
Uncommon	*hypersensitivity*
Respiratory, Thoracic and Mediastinal Disorders	
Common	*Haemorrhagic secretion and Epistaxis*
Common	*Nasal discomfort (nasal irritation)*
Very rare	*Nasal septum perforation*
Skin and subcutaneous tissue disorders	
Uncommon	Angioedema[a]
Uncommon	Dermatitis[a]
Uncommon	Erythema[a]
Uncommon	Pruritus[a]
Uncommon	Rash[a]
Uncommon	Urticaria[a]
Eye disorders	
Rare	*Vision blurred*
General Disorders and Administration Site Conditions	
Very rare	*Mucosal ulceration (ulcerations of the mucous membrane)*

a: Immediate and delayed hypersensitivity reactions

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration 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 at: https://www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

Acute overdosage with RHINOCORT, even in excessive doses, is not expected to be a clinical problem.

In the unlikely event of prolonged excessive use of RHINOCORT which could possibly lead to adrenal suppression, treatment should be discontinued. Overdosage may give rise to signs of Cushing's syndrome, such as increased bodyweight, lethargy, hypertension, hirsutism, cutaneous striae, personality change, ecchymosis, oedema, polyuria and polydipsia. In severe cases, the dosage of the corticosteroid should be gradually withdrawn to prevent the possibility of adrenal failure.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

Keep out of reach of children. In the event of overdose, seek medical attention immediately.

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

The mechanism of action of intranasally administered budesonide has not yet been completely defined, however budesonide has been shown to counteract the mainly "IgE", mediated lung anaphylaxis in guinea pigs.

Clinical trials

The therapeutic efficacy of intranasal budesonide has been evaluated in placebo-controlled clinical trials of seasonal and perennial allergic rhinitis of 3-6 weeks duration.

Overall, the results of these clinical trials showed that intranasal budesonide administered once daily provides statistically significant reduction in the severity of nasal symptoms of seasonal and perennial allergic rhinitis including runny nose, sneezing, and nasal congestion. In some studies, improvement versus placebo has been shown to occur within 24 hours of initiating treatment with intranasal budesonide. Maximum benefit can take up to 2 weeks after initiation of treatment.

Studies in animals and humans have shown an advantageous ratio between topical anti-inflammatory activity and systemic glucocorticoid effect over a wide dose range.

Budesonide is approximately twice as potent as beclomethasone dipropionate as shown in the skin blanching test for anti-inflammatory activity of topical steroids in humans. Budesonide has, however, less systemic effect than beclomethasone dipropionate, as measured by

depression of morning plasma cortisol and effect on differential WBC count. The improved ratio of topical anti-inflammatory activity to systemic effect of budesonide is due to high glucocorticoid receptor affinity combined with a high first pass metabolism and a short half-life.

Pre-treatment for one week with intranasal budesonide 400 micrograms daily in asymptomatic patients with seasonal rhinitis, significantly inhibited the immediate reaction to allergen challenge.

5.2 PHARMACOKINETIC PROPERTIES

The systemic availability of budesonide from RHINOCORT, with reference to the metered dose, is 33%. Negligible biotransformation occurs in human nasal mucosa.

Absorption

After nasal application of 256 micrograms budesonide peak plasma concentrations of approximately 0.63 nmol/L in adults and 1.53 nmol/L in children were observed within 45 minutes. The area under the curve (AUC) after administration of 256 µg budesonide from RHINOCORT is 2.7 nmol.h/L in adults and 5.5 nmol.h/L in children.

Distribution

Budesonide has a volume of distribution of approximately 3 L/kg. Plasma protein binding averages 85-90%.

Metabolism

Budesonide is metabolised in the liver by cytochrome p450 3A to more polar metabolites with low glucocorticoid activity (ie 100 fold lower than the parent compound). The metabolites are inactive and excreted mainly via the kidneys. No intact budesonide has been detected in the urine. Budesonide has a high systemic clearance (approximately 1.2 L/min) and the plasma half-life after i.v. dosing averages 2-3 hours.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available

Carcinogenicity

The carcinogenic potential of budesonide has been evaluated in mouse and rat at oral doses up to 200 and 50 µg/kg/day, respectively. No oncogenic effect was noted in the mouse. One study indicated an increased incidence of brain gliomas in male Sprague-Dawley rats given budesonide, however the results were considered equivocal.

Further studies performed in male Sprague-Dawley and Fischer rats showed that the incidence of gliomas in the budesonide treated rats was low and did not differ from that in the reference glucocorticoid groups or the controls. It was concluded that treatment with budesonide does not increase the incidence of brain tumours in the rat.

In male rats dosed with 10, 25 and 50 µg/kg/day, those receiving 25 and 50 µg/kg/day showed an increased incidence of primary hepatocellular tumours. This was observed in all three steroid groups (budesonide, prednisolone, triamcinolone acetonide) in a repeat study in male Sprague-Dawley rats thus indicating a class effect of corticosteroids.

The mutagenic potential of budesonide was evaluated in 6 different test systems. No mutagenic or clastogenic effects of budesonide were found.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Refer to Section 2 - Qualitative and quantitative composition

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine. Refer to section 4.5: Interactions with other medicines and other forms of interactions.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 30°C. Do not freeze.

6.5 NATURE AND CONTENTS OF CONTAINER

RHINOCORT Nasal Spray is available in a brown glass bottle, with pump spray equipment and nasal adaptor. Each bottle contains either 60 or 120 actuations approximately, with 32 micrograms of budesonide per actuation.

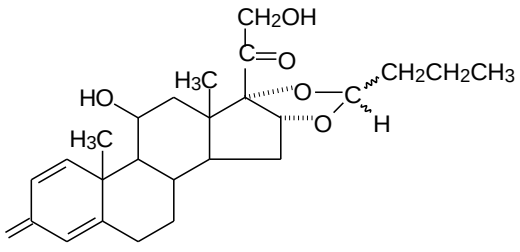
6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

The active ingredient, budesonide, is a non-halogenated glucocorticoid structurally related to 16α hydroxyprednisolone. Budesonide is a white to off-white powder, freely soluble in chloroform, sparingly soluble in ethanol and practically insoluble in water and heptane. Budesonide melts between 224°C and 231.5°C with decomposition.

Chemical structure



Chemical Name: 16α, 17α-22 R, S-propylmethylenedioxypregna-1, 4- diene-11β, 21-diol-3, 20-dione; MW 430.5

CAS number 51333-22-3

7 MEDICINE SCHEDULE (POISONS STANDARD)

Pharmacy Medicine (S2)

8 SPONSOR

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9 DATE OF FIRST APPROVAL

25 June 2003

10 DATE OF REVISION

16 February 2021

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
All	Reformatted product information
4.4	Additional warnings
4.8	Addition of adverse effects and changes to post marketing data
4.6	Updates to fertility