1. NAME OF THE MEDICINAL PRODUCT

Rhinocort Aqua, 64 mcg/dose

Budesonide (INN)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Table 1. Dosage Forms and Strengths

Dosage Form	Budesonide Strength
Suspension (Nasal Spray)	64 mcg

3. PHARMACEUTICAL FORM

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

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

- Relieves symptoms of seasonal or perennial allergic rhinitis (nasal congestion, runny nose, sneezing and itchy nose)
- Treatment of allergic rhinoconjunctivitis (nasal congestion, runny nose, sneezing, itchy nose, itchy and watery eyes)
- Prevention of allergic rhinitis

Under the Supervision of a Healthcare Professional

- Treatment of nasal polyps and prevention of nasal polyps after polypectomy
- Relieves symptoms of vasomotor rhinitis

4.2 Posology and Method of Administration

Some symptoms may get better on the first day of treatment. It may take up to two weeks of daily use to feel the most symptom relief.

For prevention, start therapy before anticipated exposure to the allergens

64 mcg per spray Dose Formulation

Allergic Rhinitis and Vasomotor Rhinitis

Adults and Children 12 years and over:

- Once daily, use up to 2 sprays in each nostril (256 mcg total daily dose) while sniffing gently. (Alternatively, total daily dose of 256 mcg may be administered in twice daily divided doses of 1 spray in each nostril in the morning and evening).
- Once allergy symptoms improve, reduce dose to 1 spray in each nostril daily

Children aged 6 to less than 12 years:

- An adult should supervise use in children under age 12
- Once daily, use 1 spray in each nostril (total dose 128 mcg) while sniffing gently
- If symptoms do not improve, dose can be increased up to 2 sprays per nostril (up to 256 mcg total daily dose) (Alternatively, total daily dose of 256 mcg may be administered in twice daily divided doses of up to 1 spray in each nostril in the morning and evening).
- Once allergy symptoms improve, reduce dose to 1 spray in each nostril daily
- Talk to your child's physician if your child needs to use the spray for longer than two months a year

Treatment and Prevention of Nasal Polyps

Adults and Children 12 years and over:

- Twice daily, use 1 spray in each nostril (256 mcg total daily dose) while sniffing gently

4.3 Contraindications

Hypersensitivity to budesonide or to any of the ingredients

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 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.
- Consult a physician before use if you are using a steroid medicine for conditions such as asthma, allergies or skin rash.
- Consult a physician before use if you have ever been diagnosed with glaucoma, cataracts or have an eye infection, or if you have diabetes.
- Stop use and consult a physician if you have any change in vision.
- Consult a physician before use if you have or have been exposed to someone who has tuberculosis, chicken pox or measles.
- Consult a physician if you develop signs or symptoms of an infection such as persistent fever.
- Consult a physician if you have severe or frequent nosebleeds, recent nose ulcers, nose surgery or have a nose injury that has not healed.
- If symptoms persist or get worse, or if new symptoms occur, patients should stop use and consult a physician

4.5 Interactions with Other Medicinal Products and Other Forms of Interactions

CYP3A4 Inhibitors

Concomitant use of inhaled budesonide and cytochrome P450 inhibitors particularly isoenzyme CYP3A4 (i.e., cobicistat-containing products, ketoconazole, ritonavir, atazanavir, clarithromycin, indinavir, itraconazole, nefazodone, nelfinavir, saquinavir, telithromycin) increases 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. Short term use (1 to 2 weeks) of ketoconazole concomitantly with budesonide is not associated with clinically significant drug interaction.

4.6 Pregnancy and Lactation

There are no adequate well-controlled clinical studies in pregnant or breastfeeding women.

Pregnancy

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.

Lactation

Budesonide is excreted in breast milk. However, due to negligible systemic exposure, minimal exposure to nasal budesonide in breast-fed infants is expected. 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 concentration of budesonide in breast milk is less than plasma concentration.

Fertility
There are insufficient data available to determine whether intranasal administration of budesonide has the potential to impair fertility.
This product should not be used during pregnancy or lactation unless the potential benefit of treatment to the mother outweighs the possible risks to the developing fetus or breastfeeding infant. Ask a physician before use if you are pregnant or breastfeeding.

4.7 Effects on Ability to Drive or Use Machines
There is no evidence that budesonide has an effect on the ability to drive or use machines.

4.8 Undesirable Effects
Adverse drug reactions (ADRs) identified during clinical trials and post-marketing experience with budesonide are listed below by System Organ Class (SOC). The frequencies are defined in accordance with current guidance, 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) and not known (cannot be estimated from the available data).

ADRs are presented by frequency category based on 1) incidence in adequately designed clinical trials or epidemiology studies, if available or 2) when incidence is unavailable, frequency category is listed as Not known.

System Organ Class (SOC)	Frequency	Adverse Drug Reaction (Preferred Term)
Immune system disorders	Uncommon	Hypersensitivity (Immediate and delayed hypersensitivity reactions including erythema, urticaria, rash, dermatitis, angioedema and pruritus)
	Rare	Anaphylactic reaction
Endocrine disorders	Rare	Signs and symptoms of systemic corticosteroid effects, including adrenal suppression and growth retardation
Eye disorders	Rare	Vision, blurred

	Not known	Cataract Raised intraocular pressure or Glaucoma
Respiratory, thoracic and mediastinal disorders	Common	Epistaxis Haemorrhagic secretion Nasal discomfort (sneezing, stinging and dryness)
	Rare	Dysphonia Nasal septum perforation Nasal ulcer
Musculoskeletal and connective tissue disorders	Uncommon	Muscle spasms
General disorders and administration site conditions	Very rare	Mucosal ulceration
Injury, poisoning and procedural complications	Rare	Contusion*

* based on mechanistic plausibility and extrapolation from other budesonide/corticosteroid formulations.

In rare cases, signs or symptoms of systemic glucocorticosteroid side effects such as Cushing's syndrome, Cushingoid features, psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children), may occur with intranasal glucocorticosteroids, probably depending on dose, exposure time, concomitant and previous corticosteroid exposure, and individual sensitivity (see section 4.4).

Paediatric population

Growth retardation has been reported in children receiving intranasal steroids.

4.9 Overdose

No overdose-associated ADRs have been identified for budesonide nasal spray from review of the post-marketing safety data and from the literature.
Acute overdose with intranasal budesonide, even in excessive doses, is not expected to be a clinical problem.
Keep out of reach of children. In the event of overdose, get medical help right away.

5 PHARMACOLOGICAL PROPERTIES

Budesonide

Chemical Name	(11β,16α)-16,17-(Butylidenebis(oxy))-11,21-dihydroxypregna-1,4-diene-3,20-dione
Molecular Weight	430.54 g/mol

5.1 Pharmacodynamic Properties

Budesonide is a corticosteroid with mainly glucocorticoid activity. It is used intranasally for the prophylaxis and treatment of allergic rhinitis. Corticosteroids are generally considered the most effective medications for the management of inflammatory diseases. Intranasal corticosteroids are quickly metabolized to less active metabolites, minimally absorbed, and have been associated with few systemic adverse effects. Studies have shown that control of allergic rhinitis symptoms by intranasal corticosteroids is dependent on local activity.

Glucocorticoid potency is closely related to their glucocorticoid receptor (GR) binding affinity within the target cell. This receptor binding triggers a cascade of biochemical reactions within the target cell, thereby affecting the rate of protein synthesis. This is responsible for the anti-inflammatory effect of glucocorticoids. Upon GR activation, there is a decrease in the production of cytokines and other inflammatory mediators such as kinins, histamine, and platelet activating factor. Corticosteroids also reduce the number of circulating T lymphocytes and inhibit activation of other T lymphocytes. The inhibition of T lymphocytes and cytokine production reduce the recruitment and influx of circulating eosinophils, macrophages, and basophils into the nasal epithelium.

5.2 Pharmacokinetic properties

5.2.1. ABSORPTION

Budesonide is moderately lipophilic and systemic exposure is primarily due to its rapid absorption through the nasal mucosa. The systemic bioavailability of budesonide following intranasal administration is 6 to 16% while its pulmonary bioavailability is 28%.
Metered doses of budesonide 400 mcg to 1600 mcg given as single or repeated doses reach peak plasma concentrations of 0.51 nmol/L to 5.37 nmol/L and 2.03 nmol/L to 6.40 nmol/L, respectively. No consistent differences in the peak plasma concentrations between the epimers of budesonide, 22R and
22S, have been reported.

Following inhalation, the mean time to peak plasma concentration of budesonide is achieved within 1 to 2 hours.

5.2.2. DISTRIBUTION

Budesonide is distributed widely into tissues with plasma protein binding averaging between 85 and 90%. The epimers of budesonide have large volumes of distribution – 424L for 22R-budesonide and 245 L for 22S budesonide. 22R-budesonide has a larger volume of distribution than the 22S epimer due to its greater lipophilicity. At steady state, the active, unbound form of budesonide has a volume of distribution of approximately 3 L/kg in both adults and children.

5.2.3. METABOLISM

Although budesonide is rapidly and extensively absorbed through the lungs, it is not biotransformed in the lung or gastrointestinal tract. Budesonide is metabolized in the liver primarily via oxidative and reductive pathways. Budesonide undergoes an extensive degree (~90%) of biotransformation on first passage by CYP3A4 enzymes to metabolites of low glucocorticosteroid activity. Major metabolites, 6β-hydroxybudesonide and 16α-hydroxyprednisolone, have similar half-lives but are relatively inactive compared to budesonide having less than 1% of its glucocorticoid and anti-inflammatory activity.

5.2.4. ELIMINATION

Budesonide is excreted primarily as metabolites in the urine and feces. No intact budesonide has been detected in the urine.
Budesonide systemic clearance is 0.92 to 1.4 L/min. The half-life of unchanged budesonide following both inhalation and intravenous administration averages between 2 to 4 hours.

5.2.5. SPECIAL POPULATION

5.2.5.1. Pediatrics

The bioavailability of budesonide in children with asthma is reported to be 25.4±10.4% for the 22R epimer and 29.6±12.4% for the 22S epimer after inhalation of the nominal dose. Total systemic availability in 3- to 6-year old children is approximately 6% of the labeled dose and a peak plasma concentration of 2.6 nmol/L is achieved within 10 to 30 minutes after inhalation. The volume of distribution in children with asthma is reported at 3.11 kg/L and 4.8 kg/L for the 22R and 22S epimer of budesonide, respectively. At steady state, the volume of distribution has been reported to be 55 L when administered via nebulization. Systemic clearance is approximately 50% higher than in healthy adults. Total plasma clearance is higher for the 22R epimer than for the 22S epimer (2.0 L/kg・h versus 1.51 L/kg・h, $P<0.001$) while terminal elimination half-life is 2.3 hours.

5.2.5.2. Elderly

There are no budesonide pharmacokinetic data available in elderly patients.

5.3 Pre-Clinical Safety Data
Summary: Preclinical data reveal no special hazard for humans based on conventional studies of single and repeated dose toxicity, genotoxicity, carcinogenicity and toxicity to reproduction and development.

6 PHARMACEUTICAL PARTICULARS
6.1 List of Excipients
Microcrystalline cellulose and carboxymethylcellulose sodium
Glucose anhydrous
Polysorbate 80
Disodium edetate
Potassium sorbate
Hydrochloric acid
Purified water

6.2 Incompatibilities
Not applicable

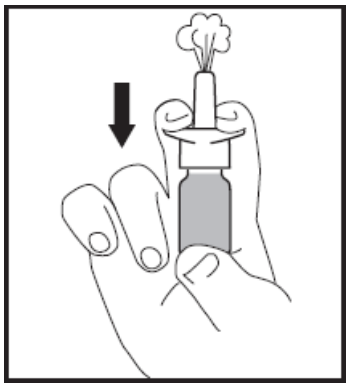
6.3 Shelf Life
The expiry date is indicated on the packaging.

6.4 Special Precautions for Storage
Do not store above 30°C. Do not freeze.

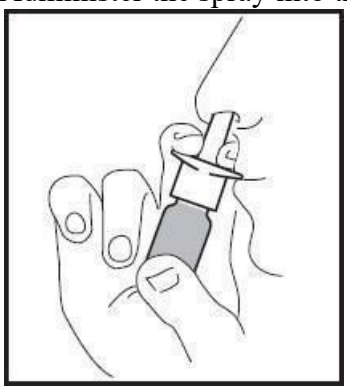
6.5 Nature and Contents of Container
Brown glass bottles provided with a spray pump and nasal applicator. One bottle contains 120 doses respectively.

6.6 Instructions for Use, Handling and Disposal
UNLESS INSTRUCTED OTHERWISE, DO NOT DISPOSE OF UNUSED MEDICINES BY EMPTYING THEM INTO YOUR SINK, TOILET OR STORM DRAIN.
Read the information before using Rhinocort Aqua nasal spray.
Follow the directions carefully. Before using Rhinocort Aqua nasal spray for the first time shake the bottle and then pump several times (5-10 times) into the air, so that a uniform mist is obtained (see picture). If not used daily the pump must be loaded again. After the first time it is sufficient to pump just once (1) into the air.

1. Blow your nose. Shake the bottle. Remove the protective cap.
2. Hold the bottle as shown in the pictures.



3. Insert the tip into your nostril and pump the number of doses prescribed. Administer the spray into the other nostril in the same way.



4. Replace the protective cap. Do not use Rhinocort Aqua nasal spray more often than prescribed.

Children
Children should only use Rhinocort Aqua nasal spray under supervision by an adult to ensure that the dose is correctly administered, and that the dosage is according to the doctor's prescription.

Cleaning
Clean the upper plastic parts regularly. Remove the protective cap and lift off the white nasal applicator. Wash the plastic parts in warm water. Allow the plastic part to air-dry completely before replacing them.
Do not try to clean the nasal applicator by using a pin or sharp object.
Rhinocort Aqua nasal spray does not give immediate relief. Generally, it will take a few days to achieve full effect. It is therefore very important that Rhinocort Aqua is used regularly.

7 PRODUCT REGISTRATION HOLDER

JNTL (Malaysia) Sdn. Bhd.,
Lot 3 & 5, Jalan Tandang,46050 Petaling Jaya, Selangor, Malaysia.

Manufactured by: McNeil AB, Helsingborg, Sweden.

8 MARKETING AUTHORIZATION NUMBER

MAL20000013AZ

9 DATE OF REVISION OF THE TEXT

12 June 2025 (Based on Sweden SmPC dated 9 Nov 2020; France SmPC dated 13 Nov 2019; UK SmPC dated 17 Nov 2020; CCDS version 2.0 dated 5 March 2020)