PACKAGE INSERT – AEROMIDE NASAL 100

SCHEDULING STATUS

S2

PROPRIETARY NAME (and dosage form)

AEROMIDE NASAL 100

aqueous nasal spray

COMPOSITION

Each metered dose contains 100 μg micronised budesonide.
Contains: glucose anhydrous, sodium carboxymethylcellulose/microcrystalline cellulose, polysorbate 80, disodium edetate, hydrochloric acid, purified water and potassium sorbate 0,12 % *m/v* as preservative.

PHARMACOLOGICAL CLASSIFICATION

A 21.5.1 Corticosteroids and Analogues.

PHARMACOLOGICAL ACTION

Pharmacodynamic properties

Budesonide is a non-halogenated corticosteroid, which has a local anti-inflammatory effect on the nasal mucosa.

Pharmacokinetic properties

Absorption

Studies in healthy adults indicate that after local application of budesonide into the nasal mucosa, budesonide is systemically absorbed. The systemic availability of budesonide with reference to a metered dose has been reported to be approximately 30 %.

After the administration of a metered dose of 400 µg by means of an aqueous pump spray, a mean plasma concentration of 0,99 nmol/L is found in approximately 38 min.

Distribution

Budesonide is widely distributed into tissues. It has a plasma protein binding of 88,3 % and among plasma proteins it is mainly bound to albumin. Following intravenous administration, the volume of distribution of unchanged budesonide was reported to be 2,69 L/kg.

Metabolism and elimination

In vitro studies with human liver homogenate indicate that budesonide is rapidly and extensively metabolised by the cytochrome P450 system, especially by the CYP3A enzymes. Two major metabolites have been identified, 6β-hydroxybudesonide formed by hydroxylation and 16α-hydroxyprednisolone formed via side-chain cleavage. Both metabolites have very little biological activity (1/10 - 1/100 of budesonide). Budesonide has been identified to be a substrate of the intestinal drug efflux pump, P-glycoprotein.

The plasma clearance of unchanged budesonide was reported to be 83,7 ± 27,5 L/h, whereas those of its epimers 22R and 22S have been reported to be 117 ± 40 L/h and 67 ± 19 L/h, respectively. Following inhalation, the plasma half-lives of both epimers are approximately the same, i.e. 2,7 h. In children with asthma, the systemic clearance of both budesonide epimers was found to be approximately 50 % higher than in healthy adults.

In healthy volunteers, 31,8 % of an inhaled [^{3}H] budesonide dose was recovered in the urine and 15,1 % in the faeces.

INDICATIONS

Prophylactic treatment of seasonal and perennial allergic rhinitis.

CONTRAINDICATIONS

Hypersensitivity to budesonide or any excipient.

Fungal and viral nasal infections.

Active or quiescent pulmonary tuberculosis.

Children under the age of 12 years.

WARNINGS AND SPECIAL PRECAUTIONS

In continuous long-term treatment, the nasal mucosa should be inspected regularly e.g. 6 months.

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

Corticosteroids may mask signs of infection and may suppress the immune system and patients are thus more susceptible to infection.

In these cases adequate anti-infective therapy should promptly be instituted and a careful benefit risk consideration concerning the administration of corticosteroids is necessary.

Consideration should also be given to the possibility of opportunistic infections.

Caution is advised in viral infections such as varicella and measles and in untreated fungal and bacterial infections (e.g. tuberculosis) of the respiratory system. The effect on quiescent tuberculosis is unknown.

Persons who are using medicines that suppress the immune system such as **AEROMIDE NASAL 100** are more susceptible to infections than healthy individuals.

Systemic effects including hypothalamic-pituitary-adrenal (HPA) axis suppression may occur. Care should be taken when a systemic corticosteroid is replaced with a topical corticosteroid as this can cause adrenal insufficiency.

Patients being introduced to **AEROMIDE NASAL 100** as a substitute for oral corticosteroids:

Patients should be advised to inform subsequent medical practitioners of their prior use of corticosteroids. These patients may have adreno-cortical suppression. Gradual, stepwise withdrawal of the systemic corticosteroids (e.g. 2,5 mg prednisolone equivalent per 1-2 weeks) may be attempted after about 10 days of combined therapy with oral and inhaled corticosteroids. After withdrawal from systemic corticosteroid treatment, the recovery of the hypothalamic-pituitary-adrenal axis can last for

some months. Too rapid withdrawal may result in deterioration of disease control. During this time patients may have adrenal insufficiency following trauma, surgery, infections or other physical stress conditions. In these cases and following the onset of a severe asthma attack, systemic corticosteroid treatment has to be resumed immediately. Due to a decreased systemic corticosteroid effect, some patients may experience increased symptoms from other allergic diseases. Temporary resumption of systemic corticosteroids may be necessary to treat these conditions.

Moderate liver impairment (Child-Pugh classification B) could affect the metabolism of **AEROMIDE NASAL 100**; caution should thus be exercised.

Chronic overdosing (exceeding the maximum recommended dose) may cause adrenal suppression, resulting in decreased production of corticosteroids and relative deficiency during periods with pronounced physical stress (severe infections, trauma, surgical operations, etc.). It may be advisable to supplement with systemic corticosteroids.

The body height of children receiving prolonged treatment with **AEROMIDE NASAL 100** should be regularly monitored.

If growth is slowed, therapy should be reassessed with a view to reducing the dose of **AEROMIDE NASAL 100**, if possible, to the lowest dose at which effective control of symptoms is achieved.

Caution is advised in patients with diabetes mellitus, osteoporosis and peptic ulcer disease.

Rare instances of nasal septum perforation, cataracts, glaucoma, and increased intraocular pressure have been reported, following the intranasal application of corticosteroids. Therefore, close follow-up is warranted in patients with any change in vision and with a history of glaucoma and/or cataracts.

Because of the inhibitory effect of corticosteroids on wound healing, patients who have experienced recent nasal septum ulcers, nasal surgery or nasal trauma should not use a nasal corticosteroid like **AEROMIDE NASAL 100** nasal spray suspension until healing has occurred.

AEROMIDE NASAL 100 nasal spray suspension contains 9,50 mg of glucose per maximum recommended daily dose.

Effects on ability to drive and use machines:

No studies on the effects on the ability to drive and use machines have been performed. However, patients should be advised that they may experience undesirable effects such as dizziness, or behavioural changes during treatment with **AEROMIDE NASAL 100** spray suspension. Therefore, caution should be recommended when driving a car or operating machinery. If patients experience dizziness or behavioural changes they should avoid potentially hazardous tasks such as driving or operating machinery.

INTERACTIONS

Efficacy and systemic side effects may be enhanced by the concomitant administration of oral or parenteral corticosteroids.

CYP3A3/4 inhibitors

Serum level and/or toxicity of **AEROMIDE NASAL 100** may be increased (e.g. ketoconazole, itraconazole, clotrimazole, ritonavir, cyclosporine, ethinylestradiol, troleandomycin, clarithromycin, cimetidine, diltiazem, indinavir).

CYP3A3/4 inducers

Serum level and/or toxicity of **AEROMIDE NASAL 100** may be decreased (e.g. carbamazepine, phenytoin, phenobarbital, rifampicin).

Cimetidine

Decreased clearance and increased bioavailability of **AEROMIDE NASAL 100**.

PREGNANCY AND LACTATION

Safety in pregnancy and lactation has not been established.

Budesonide crossed the placenta in animal studies.

Corticosteroids such as **AEROMIDE NASAL 100** are teratogenic in animals.

Infants born of mothers who have received substantial doses of corticosteroids should be observed for hypoadrenalism.

AEROMIDE NASAL 100 appears in breastmilk. Safety has not been demonstrated in breastfeeding.

DOSAGE AND DIRECTIONS FOR USE

Adults and children 12 years of age and older

The initial dose is 2 actuations (100 μg per actuation) into each nostril in the morning or 1 actuation into each nostril morning and evening. The maximum daily dose should not exceed 400 μg. The maintenance dose may be reduced to the lowest dose that adequately controls symptoms.

Administration

NB Before using **AEROMIDE NASAL 100** for the first time, shake the bottle, remove the protective cap and spray several times (5 to 10 times) into the air until a uniform mist is obtained (see **fig. 1**). The loading effect remains for approximately twenty four hours. If a longer period of time passes before the next dose is taken, the pump will need to be loaded with medicine again. This time it will be sufficient to spray just once into the air.

Instructions for use:

1. Blow your nose.
2. Shake the bottle vigorously.
3. Remove the protective cap.
4. Hold the bottle upright, place your index and middle finger onto the wings of the actuator and support the bottom of the bottle with your thumb. (See **Fig. 1**)



Fig 1.

5. Insert the tip of the actuator into your nostril and spray the number of doses prescribed. (See **Fig. 2**)



Fig 2.

6. Administer the spray into the other nostril in the same way.

7. Wipe the tip of the actuator with a clean tissue after use. Replace the protective cap. Keep the bottle in an upright position.

Cleaning:

Clean the upper plastic parts at least once a week or at any time the medicine is not coming out as it should. Remove the protective cap and lift off the nasal actuator. Wash the plastic parts in warm water. Allow the plastic parts to air dry completely before replacing them. The actuator should not be unblocked with a pin or other sharp object. After cleaning, the pump will need to be loaded with medicine again, before use.

Note:

The full effect of **AEROMIDE NASAL 100** spray suspension is not achieved until after a few days.

SIDE EFFECTS

Infections and infestations

Less frequent: nasal candidiasis, oropharyngeal candidiasis

Immune system disorders

Less frequent: hypersensitivity

The following side effect has been reported but the frequency is unknown: anaphylactic reaction

Endocrine disorders

The following side effects have been reported but the frequency is unknown: Hypercorticoidism, adrenal suppression

Psychiatric disorders:

Less frequent: psychotic disorder, aggression, depression, irritability, anxiety

The following side effects have been reported but the frequency is unknown: abnormal behaviour (in children), nervousness, restlessness

Nervous system disorders

Less frequent: dizziness or light-headedness

The following side effect has been reported but the frequency is unknown: headache

Eye disorders

Less frequent: glaucoma, increased intraocular pressure, cataract

Respiratory, thoracic and mediastinal disorders

Frequent: mild and transient burning, dryness or other irritation inside the nose, dysphonia

Less frequent: crusting/scab inside the nose or epistaxis (especially if the spray is improperly aimed towards the nasal septum, rather than onto the turbinates), rhinorrhoea, nasal congestion, sneezing, mucosal ulceration, throat irritation, oropharyngeal pain, dry throat, cough, nasal septum perforation

Gastrointestinal disorders

Less frequent: diarrhoea, nausea or vomiting, dysgeusia

Skin and subcutaneous tissue disorders

Less frequent: dermatitis, rash, urticaria (hives), pruritus

The following side effect has been reported but the frequency is unknown: angioedema

Musculoskeletal, connective tissue and bone disorders

Less frequent: myalgia, arthralgia

The following side effect has been reported but the frequency is unknown: growth retardation, bone density decreased

General disorders:

Less frequent: lethargy, fatigue

The following side effect has been reported but the frequency is unknown: thirst

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

Occasional overdosing will not give any obvious symptoms in many cases but it will decrease the plasma cortisol level.

There is an increased risk of infection at higher doses.

IDENTIFICATION

A white opalescent viscous (thixotropic) suspension, which requires vigorous shaking before use.

PRESENTATION

Amber glass bottle containing 10 ml of suspension (200 doses) fitted with a pump spray, nasal actuator and protective cap. The bottle is packed in an outer carton.

STORAGE CONDITIONS

Store at or below 25 °C.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER

41/21.5.1/0238

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