

# DATA SHEET

## ELTAIR FORTE AQUEOUS

### **budesonide**

100mcg/dose

### **Presentation**

ELTAIR FORTE AQUEOUS nasal spray is a uniform, white, liquid suspension packed in a 12mL amber glass bottle fitted with a metered dose pump.

### **Uses**

#### *Actions*

Budesonide is a non-halogenated corticosteroid. In investigations in animals and man, budesonide has shown a favourable relationship between local anti-inflammatory activity and systemic glucocorticoid side effects over a wide dose range. This favourable relation between therapeutic effect and systemic side effects is due to budesonide's high glucocorticoid receptor affinity and high first-pass metabolism with a short half-life.

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.

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

#### *Pharmacokinetics*

Due to extensive first pass metabolism in the liver, the oral bioavailability of budesonide is low (approximately 10%). After nasal administration of a large dose (1mg) of budesonide from a metered dose aerosol the systemically available fraction is approximately 15%.

Negligible biotransformation occurs in human nasal mucosa.

After nasal application of 100mcg, budesonide peak plasma concentrations of approximately 1nmol/L were observed with 45 minutes.

The volume of distribution of budesonide in adult man is  $301.3 \pm 41.7L$  and in children is 3.1 to 4.8L/kg indicating a high tissue affinity. Plasma protein binding is  $88.3 \pm 1.5\%$  in humans.

Budesonide is metabolised in the liver to more polar metabolites with low glucocorticoid activity (ie. 100 fold lower than the parent compound).

The plasma half-life of budesonide in humans after nasal inhalation is  $2.9 \pm 0.4$  hours and the plasma clearance of unchanged budesonide is  $55.2 \pm 7.8$ L/hour.

### ***Indications***

Budesonide is indicated for the prophylaxis and treatment of seasonal and perennial allergic rhinitis, vasomotor rhinitis and symptomatic relief of nasal polyposis.

## **Dosage and Administration**

**Adults and Children (6 years and older):** Initially, total daily dose 400mcg given as 100mcg into each nostril morning and evening, or as a single daily application of 200mcg into each nostril in the morning. For patients with only mild symptoms, a total daily dose of 200mcg may be sufficient.

After a good therapeutic response has been achieved, the daily dosage may be reduced to a total daily dose of 200mcg.

In seasonal allergic rhinitis, treatment ideally should start before exposure to the allergen.

Patients should be advised to clear nasal passages of secretions prior to use and not to exceed recommended dose.

For long-term treatment the lowest dose which keeps the patient symptom-free should be used.

Continuous long term use in children is not recommended.

## **Contraindications**

History of hypersensitivity to preparations containing budesonide. Severe nasal infections, especially candidiasis. Persons with recurrent nasal bleeding or haemorrhagic diatheses.

## **Warnings and Precautions**

**Clinical response:** The full effect of **ELTAIR FORTE AQUEOUS** is not achieved until at least 2 to 3 days of treatment.

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

**Transfer from oral corticosteroids:** Caution should be observed when transferring patients previously treated with systemic corticosteroids to **ELTAIR FORTE AQUEOUS**, particularly if adrenal function deficiency may be present. During transfer patients may need supplementary systemic steroids during periods of stress.

**Concomitant corticosteroid therapy:** Should **ELTAIR FORTE AQUEOUS** be prescribed for patients already using corticosteroids for oral inhalation, care should be taken to ensure that the combined daily intake via all routes of administration is considered when determining total daily corticosteroid dose.

Intranasal corticosteroids may cause a reduction in growth velocity when administered to paediatric patients (See Paediatric Use)

**Continuous, long term use:** In continuous, long term treatment, the nasal mucosa should be inspected at least twice a year.

**Severe nasal obstruction/congestion:** In some patients with severe nasal obstruction and congestion, concomitant treatment with local decongestants for 2-3 days should be considered, either before commencing or together with, 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, therapeutic advantages should be weighed against possible undesirable effects.

**Infection:** If infection of the respiratory tract, nasal passages, or paranasal sinuses is present or occurs during administration of **ELTAIR FORTE AQUEOUS**, adequate antibacterial therapy should be promptly instituted.

**Wound healing:** Because of the inhibitory effect of corticosteroids on wound healing, patients who have experienced recent nasal septal ulcers, nasal surgery or trauma should not use a nasal corticosteroid until healing has occurred.

**Use in pregnancy:** Administration during pregnancy should be avoided unless there are compelling reasons. In pregnant animals, administration of budesonide causes abnormalities of foetal development. The relevance of these findings to man has not been established. If treatment with corticosteroids during pregnancy is unavoidable, inhaled corticosteroids should be preferred because of their lower systemic effect compared with equipotent antiasthmatic doses of oral corticosteroids.

**Use during lactation:** There is no information available on the passage of budesonide into breast milk. It is recommended, therefore, that breast-feeding be discontinued in women receiving budesonide.

**Paediatric Use:** **ELTAIR FORTE AQUEOUS** is not recommended for use in children under six years of age. Controlled clinical studies have shown that intranasal corticosteroids may cause a reduction in growth velocity in paediatric patients. This effect has been observed in the absence of laboratory evidence of hypothalamic-pituitary-adrenal (HPA) axis suppression, suggesting that growth velocity is a more sensitive indicator of systemic corticosteroid exposure in paediatric patients than some commonly used tests of HPA axis function. The long-term effects of this reduction in growth velocity associated with intranasal corticosteroids, including the impact on final adult height, are unknown. The potential for "catch up" growth following discontinuation of treatment with intranasal corticosteroids has not been adequately studied. The growth of paediatric patients receiving intranasal corticosteroids, should be monitored routinely (e.g. via stadiometry). The potential growth effects of prolonged treatment should be weighed against clinical benefits obtained and the availability of safe and effective non corticosteroid treatment alternatives. To minimize the systemic effects of intranasal corticosteroids, each patient should be titrated to his/her lowest effective dose.

**Carcinogenicity, Mutagenicity:** The mutagenic potential of budesonide was evaluated in 6 different test systems. No mutagenic or clastogenic properties were found.

**Operation of motorised vehicle or machinery:** Presumed to be safe or unlikely to produce an effect on the ability to drive or use machinery.

## Adverse Effects

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

Adverse effects reported during studies with budesonide nasal presentations:

### **More Common (more than 1%):**

*Nose and Throat:* Nasal irritation, haemorrhagic secretion or nose bleeding, dry mucous membranes, sneezing after spraying, nasal crust.

*Central Nervous System:* Headache.

### **Less Common (less than 1%):**

*Nose and Throat:* Itching, strong smell of spray, bad taste, itching of throat and larynx, sore throat, dry mouth, earache.

*Respiratory:* Cough.

*Gastrointestinal:* Loss of appetite, stomach disorder, nausea.

*Skin and Appendages:* Skin itching.

*Central Nervous System:* Tremor, tiredness, sedation.

**Rare (less than or equal to 0.2%):** Ear itching, joint aches.

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

## Interactions

Budesonide is primarily metabolised by the enzyme CYP3A4, a subfamily of cytochrome P450. The interaction between budesonide and inhibitors of CYP3A4 such as ketoconazole and itraconazole may result in increased systemic exposure to budesonide.

Inhibition of CYP3A4 increases the risk of Cushing's syndrome, a condition due to hyperadrenocorticism.

## Overdosage

Budesonide 400mcg/day does not suppress the HPA axis as assessed by morning plasma cortisol and synacthen tests. The dose of intra-nasal budesonide, which may cause suppression of the HPA axis, is not known. In the unlikely event of adrenal suppression due to pro-longed excessive use of

**ELTAIR FORTE AQUEOUS**, treatment should be discontinued, although normalisation of the HPA-axis may be a slow process.

## **Pharmaceutical Precautions**

Store below 25°C. Keep out of reach of children.

## **Medicine Classification**

Prescription Medicine.

## **Package Quantities**

**ELTAIR FORTE AQUEOUS**: 100mcg/spray, 200 sprays.

## **Further Information**

Budesonide is 16,17-Butylidene bis (oxy)-11,21-dihydroxypregna-1,4-diene-3,20-dione. It has a molecular formula and weight of  $C_{25}H_{34}O_6$  and 430.55 respectively.

Other ingredients are: Purified water, Dispersible cellulose, Hydroxypropylmethyl cellulose, Sodium lauril sulphate, Polyethylene glycol 400, Butylated hydroxy Anisole, Sodium citrate, Citric acid monohydrate, Potassium sorbate and Disodium edetate.

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## **Date of Preparation**

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