

NEW ZEALAND DATA SHEET

BUTACORT

***Budesonide (50 µg & 100 µg per actuation)
Aqueous Nasal Suspension***



Presentation

Budesonide aqueous spray 50µg and 100µg per metered actuation.

50 µg/actuation: An almost white opaque suspension, almost odourless. Amber glass bottle fitted with a metered pump device delivering 50 µg budesonide per actuation. Delivery of valve: 50 µl (each 50 µl contains 50 µg of budesonide).

100 µg/actuation: An almost white opaque suspension, almost odourless. Amber glass bottle fitted with a metered pump device delivering 100 µg budesonide per actuation. Delivery of valve: 50 µl (each 50 µl contains 100 µg of budesonide).

Uses

Actions

Budesonide is a potent non-halogenated corticosteroid. In investigations in animals and humans, budesonide has shown a favourable relation between local anti-inflammatory activity and systemic glucocorticoid effect over a wide dosage range. This favourable relations ratio is due to budesonide's high glucocorticoid receptor affinity and high first pass metabolism with 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 400 micrograms 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.

The maximal plasma concentration after nasal application of 100 µg budesonide is less than 0.2 nmol/L and is reached within 45 minutes. The volume of distribution of budesonide in adult humans is 301.3 ± 41.7 L and in children is 3.1 to 4.8 L/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 (i.e. 100-fold lower than the parent compound). The plasma half-life of budesonide in humans after nasal inhalation is 2.9 ± 0.4 hours, and the plasma clearance of unchanged budesonide is 55.2 ± 7.8 L/h.

Indications

BUTACORT 50 Aqueous Nasal Spray is indicated for the short-term prevention and treatment of seasonal allergic rhinitis (hayfever).

BUTACORT 100 Aqueous Nasal Spray is indicated for the prevention and treatment of seasonal and perennial allergic rhinitis and vasomotor rhinitis.

BUTACORT Aqueous Nasal Sprays are also indicated for the symptomatic relief of nasal polyposis.

Dosage and Administration

BUTACORT 50:

For adults and children over 12 years:

Initially one or two sprays into each nostril twice a day (morning and night), then after 2 to 3 days, one spray into each nostril twice a day.

BUTACORT 100:

For adults and children over 6 years:

Initially one or two sprays into each nostril in the morning, then after 2 to 3 days, one spray into each nostril in the morning.

For patients with only mild initial symptoms, a total daily dose of 200 micrograms may be sufficient.

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.

Patient Instructions:

Patients should be instructed in the correct use of BUTACORT. Patients should be informed that full response may not occur until after 2-3 days of treatment. Patients should also be advised to clear nasal passages of secretions prior to use and not to exceed the recommended dose. In seasonal allergic rhinitis, treatment ideally should start before exposure to the allergen. Do not use for more than 6 months except on medical advice.

Contraindications

Hypersensitivity to any ingredient.

Severe nasal infections, especially candidiasis.

Persons with haemorrhagic diatheses or with a history of recurrent nasal bleeding.

Warnings and Precautions

Clinical Response:

The full effect of BUTACORT 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 BUTACORT, particularly if adrenal function deficiency may be present. During transfer patients may need supplementary systemic steroids during periods of stress.

Concomitant Corticosteroid Therapy:

Should BUTACORT 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.

Continuous, long term use:

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

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 (see Paediatric Use), cataract, glaucoma and more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children).

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, the 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 BUTACORT, adequate antibacterial therapy should be promptly instituted (see Contraindications).

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.

Paediatric Use:

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 noncorticosteroid treatment alternatives. To minimize the systemic effects of intranasal corticosteroids, each patient should be titrated to his/her lowest effective dose.

Use during Pregnancy and Lactation:

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 humans 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.

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.

Carcinogenicity/Mutagenicity:

The carcinogenic potential of budesonide has been evaluated in mouse and rat. 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. No oncogenic effect was noted in the mouse.

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

Do not use BUTACORT 50 for children under 12 years of age without first consulting with a doctor.

If hayfever symptoms do not improve within 7 days of treatment with BUTACORT 50, consult with a doctor.

Adverse Effects

Adverse local reactions following budesonide use are mild and usually transient. Systemic side effects may occur, particularly at high doses prescribed for prolonged periods (see Warnings and Precautions)..

Adverse events reported during studies with budesonide aqueous nasal sprays:

More Common (more than 1%):

Nose and haemorrhagic dry mucous throat:

Nasal irritation, secretion or nose bleeding, 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.

Cases of growth suppression have been reported for intranasal corticosteroids (see Warnings and Precautions).

Interactions

The metabolism of budesonide is primarily mediated by CYP3A4, a subfamily of cytochrome P450. Inhibitors of this enzyme, e.g ketoconazole, may therefore increase systemic exposure to budesonide. As a result of

the CYP3A4 inhibition caused by such medications as ketoconazole there may be an increased risk of developing Cushing's syndrome.

The influence of cimetidine on budesonide kinetics and dynamics after concomitant oral and intravenous administration is of minor clinical importance. Information about other possible interactions with budesonide is presently not available.

Overdosage

Budesonide 400 micrograms/day does not suppress the HPA axis as assessed by morning plasma cortisol and synacthen tests. The dose of intranasal budesonide which may cause suppression of the HPA axis is not known. In the unlikely event of adrenal suppression due to prolonged excessive use of BUTACORT, treatment should be discontinued.

Pharmaceutical Precautions

BUTACORT 50 µg/dose and 100 µg/dose should be protected from the light and stored below 25°C. Do not refrigerate.

Discard three months after first using the spray.

Medicine Classification

BUTACORT 50: Pharmacy Medicine

BUTACORT 100: Prescription Medicine.

Package Quantities

Round amber glass bottle fitted with a metering, atomising pump and nasal applicator. The pump is fitted with a 50 µl valve and a nasal adaptor. Both dosage strengths provide 200 actuations.

Further Information

List of excipients: glucose (anhydrous), dispersible cellulose, potassium sorbate, disodium edetate, polysorbate, hydrochloric acid and purified water.

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