NEW ZEALAND DATA SHEET

BUTACORT

1. Product Name

BUTACORT, 50 micrograms or 100 micrograms per actuation, aqueous nasal suspension.

2. Qualitative and Quantitative Composition

BUTACORT 50: Each actuation contains 50 micrograms of budesonide.

BUTACORT 100: Each actuation contains 100 micrograms of budesonide.

For the full list of excipients, see section 6.1.

3. Pharmaceutical Form

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

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

4. Clinical Particulars

4.1 Therapeutic 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 100 Aqueous Nasal Spray is also indicated for the symptomatic relief of nasal polyposis.

4.2 Dose and method of 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.

4.3 **Contraindications**

Hypersensitivity to any ingredient listed in section 6.1

Severe nasal infections, especially candidiasis.

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

4.4 **Special warnings and precautions for use**

**Clinical response**

The full effect of BUTACORT in allergic rhinitis is not achieved until at least 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 BUTACORT is prescribed for patients already using corticosteroids, care should be taken to ensure that the daily dosage of BUTACORT is included when determining total daily corticosteroid dose.

**Continuous, long term use**

In continuous long term treatment, care should be exercised to avoid the development of nasal mucosal atrophy. 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 section 4.4), 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 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.

**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 section 4.3).

**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.

**Reduced liver function**

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.

**Adrenocortical function**

Topical corticosteroids may be absorbed in amounts that can have systemic effects. Use of higher than recommended doses may suppress HPA function. However, at recommended doses, BUTACORT does not cause any clinically important changes in basal cortisol levels. Similar effects have been noted with inhaled budesonide, whilst still retaining the physiological circadian rhythms of plasma cortisol. This indicates that the HPA axis suppression represents a physiological adaption in response to budesonide, not necessarily adrenal insufficiency. This is further supported by inhaled and intranasal budesonide studies, which found that, at recommended doses, there was no clinically relevant effect on the response to stimulation with ACTH (predictor for clinically manifest adrenal insufficiency).

Clinically important disturbances of the HPA axis and/or adrenal insufficiency induced by stress may be related to budesonide in specific patient populations, particularly patients administering concomitant medication metabolised by CYP3A4 (see section 4.5). Monitoring for signs of adrenal dysfunction is advisable in this patient group.

**Paediatric use**

Controlled clinical studies have shown that intranasal corticosteroids may cause a reduction in growth velocity in paediatric patients. Whilst no long term studies are available for intranasal budesonide, long term studies in a clinical practice environment suggest that children treated with orally inhaled budesonide on average achieve their adult target height. However, in a long-term double-blind study, in which the budesonide dose was generally not titrated to the lowest effective dose, children treated with inhaled budesonide became on average 1.2 cm shorter as adults than those randomised to placebo.

Rare individuals may be exceptionally sensitive to intranasal corticosteroids. Height measurements (e.g. via stadiometry) should be performed to identify patients with increased sensitivity. The potential growth effects of prolonged treatment should be weighed against the clinical benefits and the availability of safe and effective non-corticosteroid alternatives. To minimize the systemic effects of intranasal corticosteroids, each patient should be titrated to his/her lowest effective dose (see section 4.2).
The continuous long term use of budesonide nasal spray in children is not recommended due to the possibility of reduced growth velocity. Studies of children with seasonal allergic rhinitis did not extend beyond four weeks of treatment.

Safety and effectiveness of intranasal budesonide in children below 6 years of age 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.

**Laboratory variables**

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

**4.5 Interaction with other medicines and other forms of interaction**

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 (e.g. itraconazole, clarithromycin, erythromycin) may inhibit the metabolism of, and therefore increase systemic exposure to budesonide. As a result of the CYP3A4 inhibition caused by such medications there may be an increased risk of developing Cushing’s syndrome.

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**

Category A: Results from a large prospective epidemiological study and from world-wide post marketing experience indicate that inhaled budesonide during pregnancy has no adverse effects on the health of the foetus or new born child. As with other medications the administration of budesonide during pregnancy requires that the benefits for the mother be weighed against the risks for the foetus.

Intranasal glucocorticosteroids such as budesonide should be considered because of the lower systemic effects, compared to oral glucocorticosteroids.

**Use in lactation**

Budesonide is excreted in breast milk. However, due to the relatively low doses used via the intranasal route the amount of budesonide present in the breast milk, if any, is likely to be low. Breastfeeding can be considered if the potential benefit outweighs any potential risks.

**4.7 Effects on ability to drive and use machines**

Not relevant.

**4.8 Undesirable 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 section 4.4). Growth suppression has been reported in association with administration of intranasal corticosteroids. Whilst no long-term studies are available for intranasal budesonide, long-term studies in a clinical practice environment suggest that children treated with orally inhaled budesonide
on average achieve their adult target height. However, in a long-term double-blind study, in which the budesonide dose was generally not titrated to the lowest effective dose, children treated with inhaled budesonide became on average 1.2 cm shorter as adults than those randomised to placebo. (see section 4.4).

Adverse events reported during studies with budesonide aqueous nasal sprays:

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

**Nose and throat:**
Nasal irritation, itching of throat and larynx, sore throat, dry mucous membranes, dry mouth, increased sputum, haemorrhagic secretion, epistaxis (nose bleeding), sneezing after spraying, nasal crust, sinusitis.

**Respiratory:**
Cough, dyspnoea.

**Central Nervous System:**
Headache, dizziness, tiredness.

**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.

**Immune system:**
Immediate and delayed hypersensitivity reactions, including urticaria, rash, dermatitis, angioedema and pruritus.

**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.

**Reporting of suspected adverse reactions**

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/.

**4.9 Overdose**

Acute overdosage with BUTACORT, even in excessive doses, is not expected to be a clinical problem.
In the unlikely event of prolonged excessive use of BUTACORT, 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 further advice on management of overdose please contact the National Poisons Information Centre (0800 POISON or 0800 764 766).

5. Pharmacological Properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Decongestants and other nasal preparations for topical use, ATC code: R01AD05.

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.

5.2 Pharmacokinetic properties

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

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

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

Budesonide is metabolised in the liver by cytochrome P450 3A to more polar metabolites with low glucocorticoid activity (i.e. 100-fold lower than the parent compound). The metabolites are inactive and excreted mainly via the kidneys. No intact budesonide has been found in the urine. Budesonide has a high systemic clearance (approximately 1.2L/min) and the plasma half-life after i.v. dosing averages 2-3 hours.

5.3 Preclinical safety data

Carcinogenicity/mutagenicity

The carcinogenic potential of budesonide has been evaluated in mouse and rat at oral doses up to 200 and 50 micrograms/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 micrograms/kg/day, those receiving 25 and 50 micrograms/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.

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.

6. Pharmaceutical Particulars

6.1 List of excipients
BUTACORT aqueous nasal suspension also contains

- glucose (anhydrous),
- dispersible cellulose,
- potassium sorbate,
- disodium edetate,
- polysorbate,
- hydrochloric acid,
- purified water.

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
2 years.

6.4 Special precautions for storage
BUTACORT 50 micrograms/dose and 100 micrograms/dose should be protected from the light and stored at or below 25°C. Do not refrigerate.

Discard three months after first using the spray.

6.5 Nature and contents of container
Round amber glass bottle fitted with a metering, atomising pump and nasal applicator. The pump is fitted with a 50 microliters valve and a nasal adaptor. Both dosage strengths provide 200 actuations.

6.6 Special precautions for disposal
Any unused medicine or waste material should be disposed of in accordance with local requirements.

7. Medicines Schedule

BUTACORT 50: Pharmacy Medicine

BUTACORT 100: Prescription Medicine.

8. Sponsor Details

Mylan New Zealand Ltd
PO Box 11183
Ellerslie
9. Date of First Approval

4 August 1994

10. Date of Revision of the Text

19 July 2018

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