

## **DATA SHEET**

### **COLIFOAM RECTAL FOAM**

*Hydrocortisone Acetate BP*

#### **DESCRIPTION**

The product is administered into the rectum where the hydrocortisone exerts an anti-inflammatory effect on the mucosa. The medication is kept in contact with the inflamed mucosa due to the mucoadherent base. Thus a patient can resume normal duties directly after use.

#### **PHARMACOLOGY**

Corticosteroids in the circulation are extensively bound to plasma proteins, metabolised in the liver and kidney, and excreted in the urine. Hydrocortisone is metabolised by reduction at both hepatic and extrahepatic sites with the formation of tetrahydrocortisol and tetrahydrocortisone being formed in the liver. Further metabolism by conjugation reactions to form sulfate esters or glucuronides occur in the liver and to some extent in the kidney. Limited data available on Colifoam Rectal Foam indicate that the amount of hydrocortisone absorbed is comparable to that secreted endogenously. Up to 50% of the administered dose may be absorbed from some rectal preparations of hydrocortisone acetate used in patients with proctitis.

#### **INDICATIONS**

Topical treatment of inflammation occurring in the rectal mucosa, e.g. ulcerative colitis, proctosigmoiditis and granular proctitis.

#### **CONTRAINDICATIONS**

Hypersensitivity to propane, isobutane, triethanolamine, propylene glycol, emulsifying wax, cetyl alcohol, steareth-10, methyl hydroxybenzoate and propyl hydroxybenzoate. Anal warts, anal infections, in common with topical steroids, where usually fungal or bacterial infections are involved.

#### **WARNINGS & PRECAUTIONS**

##### **Stress and intercurrent illness**

In patients on long-term corticosteroid therapy subject to stress from trauma or infection, steroid dosage should generally be increased to cover the stressful period. For mild infections without fever no increase is necessary. For more serious infections the dose of glucocorticoid should be doubled normal dose.

##### **Adrenocortical insufficiency**

Drug induced secondary adrenocortical insufficiency may result from too rapid withdraw of corticosteroids and may be minimised by gradual reduction of dosage (see Precautions). This type of relative insufficiency may persist for months after discontinuation of therapy, therefore in any situation of stress occurring during that period, hormone therapy may need to be reinstated. If the patient is receiving steroids already, dosage may have to be increased.

### **Infection**

Corticosteroids may mask some signs of infection (e.g. fever and inflammation), and new infections may appear during their use. There may be decreased resistance and inability to localise infection when corticosteroids are used. Susceptibility to infection is not specific for any particular bacterial or fungal pathogen.

### **Ophthalmological complications**

Prolonged use of corticosteroids may produce posterior subcapsular cataracts or glaucoma with possible damage to optic nerves, and may enhance the establishment of secondary ocular infections due to fungi or viruses (see Adverse Reactions).

Do not insert any part of the aerosol container into the anus. The contents of the container are under pressure. Do not burn or puncture the aerosol container. Store below 25 deg. C. During prolonged corticosteroid therapy adrenal suppression and atrophy may occur and secretion of corticotrophin may be suppressed. Abrupt withdrawal of corticosteroid therapy may precipitate acute adrenal insufficiency and muscle weakness, hypotension, hypoglycaemia, headache, nausea, vomiting, restlessness and muscle and joint pain. Muscle weakness and stiff joints may persist for three to six months after discontinuation of treatment. In some cases, withdrawal symptoms may stimulate a clinical relapse of the disease for which the patient has been under treatment.

Duration of treatment and dosage appear to be important factors in determining suppression of the pituitary! adrenal axis response to stress on cessation of steroid treatment. The patient's liability to depression is also variable. Some patients may recover normal function rapidly. In others, the production of hydrocortisone in response to the stress of infections, surgical operations or accidents may be insufficient and death results. Therefore, withdrawal of corticosteroids should always be gradual to avoid a drug induced secondary adrenocortical insufficiency. In addition, during any situation of stress, hormone therapy should be reinstated. Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticoid should be administered concurrently. If sudden withdrawal is necessary, corticotrophin (20 units) given daily by intravenous infusion during eight hours for three to five successive days is usually sufficient to prevent withdrawal symptoms. During long courses of treatment, laboratory and metabolic studies should be done. Fluid retention should be watched for, via a fluid balance chart and daily weighing. Sodium intake may need to be reduced to less than 1 g daily and potassium supplements may be necessary. The possibility of development of osteoporosis should be an important consideration in initiating and managing corticosteroid therapy, especially in postmenopausal women (see Adverse Reactions).

Caution should be used in patients with diabetes mellitus (see Adverse Reactions).

Patients should not be vaccinated with live vaccines while on corticosteroid therapy. Other immunisation procedures should not be undertaken in patients on corticosteroid therapy, especially on high doses, because of possible hazards of neurological complications and lack of antibody response. Immunisation procedures may be undertaken in patients receiving corticosteroids as replacement therapy.

Close observation is necessary in patients with latent tuberculosis or tuberculin reactivity as reactivation of the disease may occur. Chemoprophylaxis is indicated during prolonged corticosteroid therapy.

**Impaired hepatic function.** Use with caution in patients with impaired hepatic function. A reduction of dosage may be necessary in treating chronic active liver disease with the drug. Major adverse reactions such as vertebral collapse, diabetes, hypertension, cataracts and Cushing's syndrome occur in about 30% of patients.

## **DRUG INTERACTIONS**

Aspirin should be used cautiously in conjunction with corticosteroids in hypoprothrombinaemia. Phenytoin, phenobarbitone, ephedrine and rifampicin may enhance the metabolic clearance of corticosteroids, resulting in decreased blood levels and lessened physiological activity, thus requiring adjustment in corticosteroid dosage. These interactions may interfere with dexamethasone suppression tests which should be interpreted with caution during administration of these drugs.

False negative results in the dexamethasone suppression test in patients being treated with indomethacin have been reported.

The prothrombin time should be checked frequently in patients who are receiving corticosteroids and coumarin anticoagulants at the same time because of reports that corticosteroids have altered the response to these anticoagulants. Studies have shown that the usual effect produced by adding corticosteroids is inhibition of response to coumarins, although there have been conflicting reports of potentiation not substantiated by studies.

When corticosteroids are administered concomitantly with potassium depleting diuretics, patients should be observed closely for development of hypokalaemia.

### **Laboratory tests**

Corticosteroids may affect the nitroblue tetrazolium test for bacterial infection and produce false negative results.

### **Use in pregnancy (Category A)**

In animal experiments, systemic corticosteroids have been found to cause malformations of various kinds (cleft palate, skeletal malformations) and abortion. These findings do not seem to be relevant to humans. Reduced placental weight and birthweight have been recorded in animals and humans after long-term treatment. Since the possibility of suppression of the adrenal cortex in the newborn baby after long-term treatment must be considered, the needs of the mother must be carefully weighed against the risk to the fetus when prescribing these drugs. The short-term use of corticosteroids antepartum for the prevention of respiratory distress syndrome does not seem to pose a risk to the fetus or the newborn infant. Maternal pulmonary oedema has been reported with tocolysis and fluid overload.

### **Use in lactation**

The drug is excreted in breast milk; therefore administration to breastfeeding mothers is not recommended.

### **Use in children**

Children on long-term steroids must be carefully observed for potential serious reactions such as obesity, growth retardation, osteoporosis and adrenal suppression.

### **Use in the elderly**

Caution is recommended for elderly patients, as they are more susceptible to adverse reactions.

## **ADVERSE REACTIONS**

Adverse reactions from corticosteroids are those resulting from withdrawal or from prolonged use of high doses.

### **More common reactions**

**Cardiovascular.** The mineralocorticoid activity of a steroid may lead to salt and water

retention which can also result in hypertension. Hypokalaemia can lead to arrhythmias and cardiac arrest.

**Central nervous system.** Large doses can cause behavioural personality changes ranging from nervousness, insomnia, euphoria or mood swings to psychotic episodes, which can include both manic and depressive states, paranoid states and acute toxic psychosis.

It is no longer believed that previous psychiatric problems predispose to behavioural disturbances during therapy with glucocorticoids. Conversely, the absence of a history of psychiatric illness is no guarantee against the occurrence of psychosis during hormonal therapy.

**Dermatological.** Impaired wound healing; facial plethora. An acneform eruption on the face, chest and back; red striae on the thighs, buttocks and shoulders. Several months of high dose therapy often results in thinning of skin. Corticosteroid induced purpura resembles senile purpura. This purpura usually occurs on exterior surfaces, dorsum of the hand and radial aspect of the forearm.

**Endocrine.** Menstrual irregularities. Cushing's syndrome may result from prolonged elevation of plasma glucocorticoid levels. The endocrine effects of the glucocorticoids involve the hypothalamic-pituitary-adrenal (HPA) axis, the genitals, the parathyroid and the thyroid. There are also metabolic effects, primarily involving carbohydrates. Suppression of growth may occur in children.

Antagonism occurs between the parathyroids and hypercorticism. Latent hyperparathyroidism may be unmasked by the administration of corticosteroids. Hypoparathyroidism may be manifested by phosphate retention occurring in renal failure caused by adrenal insufficiency.

**Biochemical.** All glucocorticoids increase gluconeogenesis. Glucose tolerance and sensitivity to insulin are decreased, but provided pancreatic islet function is normal, carbohydrate metabolism will not be noticeably deranged. Steroid diabetes has been reported to develop in one-fifth of patients treated with high glucocorticosteroid dosage.

High dose corticosteroid therapy may induce marked hypertriglyceridaemia with milky plasma.

**General.** Retardation of growth by long-term corticosteroid treatment in children.

**Haematological.** Corticosteroids will increase the total WBC (white blood cell) count, with an increase in neutrophils and a decrease in monocytes, lymphocytes and eosinophils.

**Immunological.** The frequency and severity of clinical infections increase during glucocorticoid therapy.

**Musculoskeletal.** Osteoporosis and vertebral compression fractures in patients of all ages. Osteoporosis is an indication for withdrawal of therapy.

Myopathy, characterised by weakness of the proximal musculature of the arms and legs or their associated shoulder and pelvic muscles, is occasionally reported in patients taking large doses of corticosteroids. It may occur soon after treatment is begun and be sufficiently severe to prevent ambulation. It is an indication for withdrawal of therapy. Avascular aseptic necrosis of bone has often been described and preferentially involves the femoral and humeral head.

**Ocular.** Increased intraocular pressure and glaucoma occur with corticosteroid treatment. The rise in intraocular pressure may lead to blindness. The incidence of posterior subcapsular cataract in patients undergoing long-term therapy with corticosteroids is

approximately 10%. A correlation with the duration of treatment and the total dose is clear.

#### Less common reactions

**Gastrointestinal, pancreatic.** Peptic ulceration is an occasional complication. The high incidence of haemorrhage and perforation in these ulcers and the insidious nature of their development make them severe therapeutic problems. Some investigators believe the available evidence does not support the conclusion that steroids cause ulcers. Others feel that only patients with rheumatoid arthritis have an increased incidence of ulcers. It has been proposed that the glucocorticoids alter the mucosal defense mechanism.

**Neurological.** Latent epilepsy can be rendered manifest by corticosteroid treatment. Long-term treatment may result in benign intracranial hypertension.

#### Severe or life-threatening reactions

Suppression of the hypothalamic-pituitary-adrenal axis is one of the consequences of repeated administration of glucocorticoids; after termination of treatment a withdrawal syndrome may be experienced (see Precautions).

In some cases acute adrenal insufficiency after a period of glucocorticoid treatment has proved fatal.

### **DOSAGE AND ADMINISTRATION**

The dosage is one applicator full containing approximately 90 to 100 mg hydrocortisone acetate, as directed by the doctor. The usual dosage rate is one applicator full once or twice daily for two to three weeks, and every second day thereafter, applied as directed above into the rectum.

**Directions for use.** Shake foam container vigorously for 60 seconds before use. Hold container upright and insert into opening of the tip of the applicator. Be sure applicator plunger is drawn all the way out. Container must be held upright to obtain proper flow of medication.

To fill, press down gently on container cap. When foam reaches fill line of the applicator, it is ready for use.

**Caution.** The aerosol container should never be inserted directly into the anus.

Remove applicator from container. Allow some foam to remain on the applicator tip. Hold applicator by barrel and gently insert tip into anus. With applicator in place, push plunger in order to expel foam, then withdraw applicator. (Applicator parts should be pulled apart for thorough cleaning with warm water.)

### **OVERDOSAGE**

A single overdose of a corticosteroid would not be expected to produce acute symptoms. Hypercorticoid effects are not anticipated unless there has been repeated administration of high doses.

**Symptoms.** Systemic effects of chronic overdosage with steroids include effects on sodium and water retention, increased appetite, mobilisation of calcium and phosphorus with osteoporosis, nitrogen depletion, hyperglycaemia, effects on tissue repair, increased susceptibility to infection, adrenal insufficiency, adrenal cortex hyperactivity, mental and

neurological disturbances and muscular weakness.

**Treatment.** In case of an acute overdose, maintain adequate fluid intake and monitor electrolytes in serum and urine, with particular attention to sodium and potassium balance. In case of chronic toxicity, slowly withdraw drug. Treat electrolyte imbalance if necessary.

### **PRESENTATION**

Aerosol, 10% (100 mg/g) (white, odourless, mucoadherent foam): 21.1 g (equiv. greater than or equal to 14 applications) (with plastic applicator and illustrated patient instructions).

### **PHARMACEUTICAL PRECAUTIONS**

Store below 25°C.

### **SHELF LIFE**

3 years

### **MEDICINE CLASSIFICATION**

Prescription Medicine

### **NAME AND ADDRESS**

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### **DATE OF PREPARATION**

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