AUSTRALIAN PRODUCT INFORMATION

COLIFOAM®

Hydrocortisone acetate

1 NAME OF THE MEDICINE

Hydrocortisone acetate

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

COLIFOAM contains hydrocortisone acetate 10% w/w.

Excipients with known effect:

COLIFOAM also contains methyl hydroxybenzoate and propyl hydroxybenzoate.

For the full list of excipients, see **Section 6.1 LIST OF EXCIPIENTS**.

3 PHARMACEUTICAL FORM

COLIFOAM is an enema, formulated as a lump free viscous, muco-adherent foam for rectal administration.

4 CLINICAL PARTICULARS

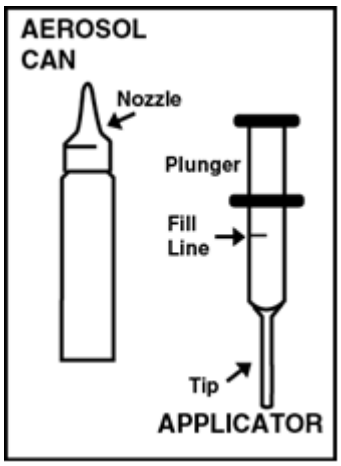
4.1 THERAPEUTIC INDICATIONS

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

4.2 DOSE AND METHOD OF 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 aerosol can vigorously for 60 seconds before each use. Hold aerosol can upright and insert its nozzle into the tip of the applicator. As a result the applicator will be on top of the aerosol can. Be sure the plunger is drawn all the way out. The aerosol can must be held upright to obtain proper flow of medication.

To fill the applicator, hold it by the barrel and press down gently on top of aerosol can until the foam has filled up approximately one quarter of the applicators body. Keep the plunger withdrawn during this procedure. Only a short press is needed to do this. Wait for few seconds until the foam has stopped expanding. These steps may be repeated until the foam has reached the fill line. When foam reaches fill line of the applicator, it is ready for use.

Caution: The aerosol can nozzle should never be inserted directly into the anus.

Remove applicator from aerosol can. Allow some foam to remain on the applicator tip. Hold applicator by barrel and gently insert tip sufficiently into the anus to ensure the foam is fully deposited into the rectum. With applicator in place, push plunger in order to expel foam, and then withdraw applicator. Some patients find the administration easier when standing with one leg raised or lying down on their side. Applicator parts should be pulled apart for thorough cleaning with warm water.

4.3 CONTRAINDICATIONS

- Hypersensitivity to the active substance and/or to any of the excipients
- Anal warts
- Fungal, viral, tuberculous or bacterial infections
- Obstruction
- Abscess
- Perforation
- Peritonitis
- Fresh intestinal anastomoses
- Extensive fistulae

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Do not insert any part of the aerosol can into the anus. The contents of the aerosol can are under pressure. Do not burn or puncture the aerosol can. Store below 25°C.

Treatment should be administered with caution in patients with severe ulcerative disease because of their predisposition to perforation of the bowel wall.

Caution should be used in patients with diabetes mellitus, it should be taken into consideration that they may need more insulin or oral anti-diabetics (see **Section 4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)**).

Stabilisation to corticoids should be done in a hospital when treating patients with myasthenia gravis.

Corticosteroids can cause elevation of blood pressure, salt and water retention in the blood, and increased urinary excretion of potassium. Therefore, patients with severe cardiac and/or renal insufficiency will require careful monitoring, and in patients with hypertension, regular blood pressure control is necessary.

Potentially severe psychiatric adverse reactions may occur with systemic steroids.

Particular care has to be taken in patients with existing or a previous history of severe affective disorders, e.g. depressive or manic-depressive illness and previous steroid psychosis.

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.

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.

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

Visual disturbance may be reported with systemic and topical corticosteroid use. Prolonged use of corticosteroids may produce posterior subcapsular cataracts, glaucoma with possible damage to optic nerves, and may enhance the establishment of secondary ocular infections due to fungi or viruses (see **Section 4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)**). COLIFOAM should not be used in patients with narrow- or wide-angle glaucoma.

Corticosteroid therapy has been associated with central serous chorioretinopathy (CSCR), which may lead to retinal detachment.

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.

Prolonged corticosteroid therapy

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. Abrupt cessation of therapy should be avoided.

Duration of treatment and dosage appear to be important factors in determining suppression of the hypothalamic-pituitary-adrenal (HPA) 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. 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 should be reinstituted. If the patient is receiving steroids already, dosage may have to be increased. 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 **Section 4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)**).

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.

Use in Hepatic Impairment

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.

Use in the Elderly

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

Paediatric Use

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

Effects on Laboratory Tests

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

Glucocorticoids can lead to positive results in doping tests.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

For systemic hydrocortisone, interactions with the following medicines are known:

- The effects of cardiac glycosides may be potentiated caused by potassium depletion
- When corticosteroids are administered concomitantly with other potassium depleting agents such as diuretic agents and amphotericin B (amphotericin), patients should be observed closely for development of hypokalaemia
- Macrolide antibiotics and ketoconazole may decrease corticosteroid clearance
- Anti-diabetic agents due to reduction of the blood-sugar lowering effect
- Salicylates and other NSAIDs which may increase the risk of gastrointestinal bleeding
- Antiretroviral agents due to the risk of adrenal suppression
- 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
- Phenytoin, phenobarbital (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 indometacin have been reported.
- Co-treatment with CYP3A4 inhibitors is expected to increase the risk of systemic side effects. The combination should be avoided unless the benefit outweighs the increased risk of systemic corticosteroid side effects, in which case patients should be monitored for systemic corticosteroid side effects
- Substances which are mainly metabolized by CYP3A4, CYP3A5, CYP3A7.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on Fertility

No data available.

Use in Pregnancy

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 birth weight 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.

Hydrocortisone should not be used extensively in pregnancy, this is in large amounts or for prolonged periods. This medicine should only be used in pregnancy if absolute necessary. The benefit of treatment for the mother must be carefully weighed against the potential risks for the fetus.

Use in Lactation

The drug is excreted in breast milk, therefore administration to breastfeeding mothers is not recommended. Otherwise, breast-feeding should be discontinued.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

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 white blood cell (WBC) 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 defence 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 (HPA) axis is one of the consequences of repeated administration of glucocorticoids; after termination of treatment a withdrawal syndrome may be experienced (see **Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE**).

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

Frequency not known reactions

Infections and infestations: Decreased resistance to infections*

Immunological: Hypersensitivity reactions including anaphylactic reaction, angioedema

Gastrointestinal: Proctalgia, Anorectal discomfort

Dermatological: Dermatitis allergic, urticaria, skin reactions (local, generalised) like blister, pruritus, rash

General: Application site reactions like erythema, irritation, burning, dryness

Post marketing

Eye disorders: vision blurred

Drugs of this class may cause systemic side effects (such as Cushing's Syndrome, decreased resistance to infections*), especially in long-term use, and if the medicine is not used as directed. The risk of systemic side effects when used at the correct dose by the local administration route is much lower than under systemic application.

Reporting Suspected Adverse Effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at http://www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

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.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of Action

COLIFOAM 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 muco-adherent base. Thus a patient can resume normal duties directly after use.

Clinical Trials

No data available.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

Limited data available on COLIFOAM 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.

Distribution
Corticosteroids in the circulation are extensively bound to plasma proteins.

Metabolism
Corticosteroids are metabolised in the liver and kidney. 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.

Excretion
Corticosteroids are excreted in the urine.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity
No data available.

Carcinogenicity
No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

- propane
- isobutane
- trolamine
- propylene glycol
- emulsifying wax
- cetyl alcohol
- steareth-10
- methyl hydroxybenzoate
- propyl hydroxybenzoate.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG).

The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25°C. Do not refrigerate.

6.5 NATURE AND CONTENTS OF CONTAINER

COLIFOAM is a foam enema supplied in an aerosol can filled with white, odourless, muco-adherent, expanding foam. Aerosol can is fitted with gold ferrule and white nozzle. Plastic applicator with plunger is also included in the carton and is used to administer COLIFOAM into the rectum.

One aerosol can contains 21.1 g of foam which is equivalent to approximately 14 applications. Each applicator full of COLIFOAM contains approximately 90 mg hydrocortisone acetate. One gram of foam contains 100 mg hydrocortisone acetate.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

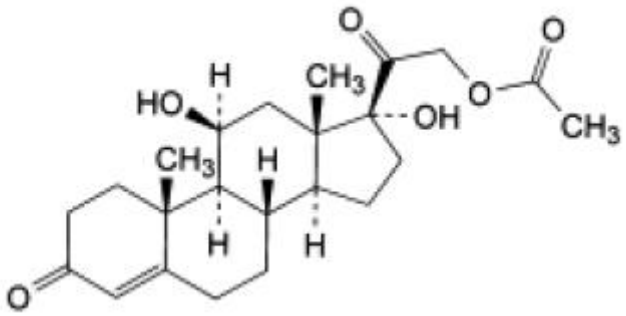
In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Hydrocortisone acetate occurs as white or almost white, crystalline powder. It is practically insoluble in water, slightly soluble in anhydrous ethanol and in methylene chloride.

The chemical name for hydrocortisone acetate is 11β,17-Dihydroxy-3,20-dioxopregn-4-en-21-yl acetate.

Chemical Structure



Chemical formula: $C_{23}H_{32}O_6$ Molecular weight: 404.5 g mol^{-1}

CAS number: 50-03-3

7 MEDICINE SCHEDULE (POISONS STANDARD)

S4 (Prescription Only Medicine)

8 SPONSOR

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Phone: 1800 314 527

9 DATE OF FIRST APPROVAL

28/11/2003

10 DATE OF REVISION

27/07/2020

Summary Table of Changes

Section Changed	Summary of New Information
4.5	Updated medicine names in line with International Harmonisation of Ingredient Names
6.7	Moved information on physicochemical properties from Section 2 to Section 6.7
8	Updated sponsor details

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