COLIFOAM

1. Product Name

Colifoam, 10% w/w, foam enema.

2. Qualitative and Quantitative Composition

One gram of foam enema contains 100 mg of hydrocortisone acetate.

Each applicator full of Colifoam contains approximately 90 mg hydrocortisone acetate.

For the full list of excipients, see section 6.1.

3. Pharmaceutical Form

Colifoam is a foam enema supplied in an aerosol can filled with white, odourless, muco-adherent, expanding foam.

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

Dose

The dosage is one applicator full containing approximately 90 to 100 mg hydrocortisone acetate. 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 into the rectum.

Special populations

Hepatic impairment

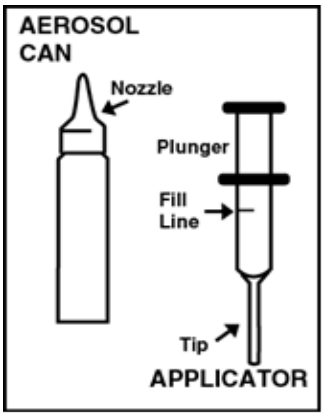
A reduction of dosage may be necessary in treating chronic active liver disease with the medicine (see section 4.4).

Method of administration

Shake aerosol can vigorously for 60 seconds before 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 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 Keep the plunger withdrawn during this procedure.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 the 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

Contraindicated in patients with:

- hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- 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

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).

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

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 section 4.8). Colifoam should not be used in patients with narrow- or wide-angle glaucoma.

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.

General

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 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. 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). 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.

Special populations

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 medicine. Major adverse reactions such as vertebral collapse, diabetes, hypertension, cataracts and Cushing's syndrome occur in about 30% of patients.

Paediatric population

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.

Laboratory tests

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

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

Glucocorticoids can lead to positive results in doping tests.

4.5 Interaction with other medicines and other forms of interaction

The active substance hydrocortisone is absorbed up to 5% in the gastrointestinal tract. 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 potassium depleting agents such as diuretic agents and amphotericin B, patients should be observed closely for development of hypokalaemia.
- Macrolide antibiotics and ketoconazole may decrease corticosteroid clearance.
- Anti-diabetics may have a reduced effect on lowering blood sugar.
- 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, 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.
- 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 metabolised by CYP3A4, CYP3A5, and CYP3A7.

4.6 Fertility, pregnancy and lactation

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 foetus 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 foetus 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 foetus.

Breast-feeding

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

This medicine has no influence on the ability to drive and use machines.

4.8 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 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).

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, urticarial, skin reactions (local, generalised) like blister, pruritus, and rash

General

Application site reactions like erythema, irritation, burning, and dryness

*Drugs of this class may cause systemic side effects (such as Cushing 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 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

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 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: Corticosteroid acting locally. ATC code: A07EA02

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 mucoadherent base. Thus a patient can resume normal duties directly after use.

The use of topically applied steroids in the treatment of ulcerative colitis, proctosigmoiditis and granular proctitis is well known. Hydrocortisone acetate has anti-inflammatory activity resulting, at least in part, from binding with a steroid receptor.

It has a membrane sealing effect and inhibits of accumulation of neutrophiles and macrophages in the region of inflammation. Furthermore, it reduces the migration of leukocytes and mastocytes into the tissue, inhibits the activity of lymphatic tissue and the secondary reaction of connective tissue (anti-proliferative, anti-oedematous effect).

5.2 Pharmacokinetic properties

Absorption

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 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.

Bioavailability

The topically applied steroid acts mainly locally. After rectal administration, bioavailability of hydrocortisone acetate ranges between 2% and 3% in healthy subjects, and between 4% and 5% in patients.

5.3 Preclinical safety data

None stated.

6. Pharmaceutical Particulars

6.1 List of excipients

Colifoam also contains:

- Propane
- Isobutane
- Trolamine
- Propylene glycol
- Emulsifying wax
- Cetyl alcohol
- Steareth-10
- Methyl hydroxybenzoate
- Propyl hydroxybenzoate.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store at or below 25°C.

Keep away from sources of ignition (e.g. smoking) as the aerosol can contains flammable propellant.

6.5 Nature and contents of container and special equipment for administration

A white aluminium aerosol can with metered valve and aerosol actuator.

Pack size of one aerosol can containing 15g of foam enema, which is equivalent to approximately 14 applications.

6.6 Special precautions for disposal and other handling

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.

7. Medicines Schedule

Prescription Medicine

8. Sponsor Details

Viatris Ltd
PO Box 11-183
Ellerslie
AUCKLAND
www.viatris.co.nz
Telephone 0800 168 169

9. Date of First Approval

4 November 1982

10. Date of Revision of the Text

13 December 2021

Summary table of changes

Section changed	Summary of new information
8	Sponsor name updated.