AUSTRALIAN PRODUCT INFORMATION – APOHEALTH HYDROCORTISONE 1% CREAM (HYDROCORTISONE)

1 NAME OF THE MEDICINE

Hydrocortisone acetate

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1.0% w/w hydrocortisone acetate in a water miscible, lanolin free cetomacrogol base.

Excipients with known effect

Chlorocresol 0.1% w/w is used as a preservative.

For the full list of excipients see **section 6.1 List of excipients.**

3 PHARMACEUTICAL FORM

APOHEALTH Hydrocortisone 1% Cream is a soft white cream with a faint odour of chlorocresol.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Topical corticosteroid therapy for the temporary relief of symptoms of non-infective inflammatory conditions of the skin (eg. minor skin irritations, itching and rashes due to eczema, dermatitis, contact dermatitis [such as rashes due to soap, detergent, cosmetics and jewellery], insect bites, itching anal and genital areas and sunburn).

4.2 DOSE AND METHOD OF ADMINISTRATION

Adults and children from 2 years of age: apply a thin layer to affected areas 2 - 4 times daily. Reduce the number of applications as the disorder subsides.

The cream should not be used under occlusive dressings or waterproof bandages unless advised to by a doctor.

This preparation should not be used for more than 7 days except on the advice of a doctor.

Rub in gently.

4.3 CONTRAINDICATIONS

- Tuberculous and fungal conditions of the skin, acute Herpes simplex, vaccinia, varicella and all viral infections.
- Untreated bacterial infections.
- Parasitic infestations (eg. scabies).
- In patients with markedly impaired circulation since skin ulceration has occurred in these patients following the use of corticosteroids.
- Hypersensitivity to any component of the cream.
- Not to be used in the eyes.
- Not to be used for acne or rosacea.
- The cream should not be used under occlusive dressings or waterproof bandages unless advised to by a doctor.
- Topical steroids should be used with caution and occlusive dressings should not be used in

patients with primary skin infections

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

FOR EXTERNAL USE ONLY. AVOID CONTACT WITH EYES.

This medicine should not be used in the eyes. Use of the cream near the eyes should be avoided. This is due to the risk of corticosteroid-induced open-angle glaucoma.

If irritation develops APOHEALTH Hydrocortisone 1% Cream should be discontinued and alternative therapy instituted. Prolonged and heavy doses of hydrocortisone may have an immunosuppressant effect and thus decrease resistance to infection as well as mask signs of it. If infection of the skin is present suitable antifungal or antibacterial agents should be used first. Any occlusive dressings should be discontinued. If the infection does not respond promptly to therapy, corticosteroid therapy should be discontinued until the infection has been controlled.

Where very large areas are treated for long periods (e.g. atopic dermatitis), the possibility of systemic absorption exists, particularly if an occlusive dressing is applied. Prolonged use of large quantities of topical corticosteroids may also result in atrophic striae or acne eruptions.

Due to the possible systemic absorption of topical steroids, there may be a need for periodic evaluation of hypothalamo-pituitary-adrenal (HPA)-axis suppression by using the urinary free cortisol test or the corticotrophin stimulation test. If the HPA-axis suppression is evident, withdrawal should be attempted and the frequency of application reduced.

Any corticosteroid therapy tends to elevate blood glucose levels in diabetic patients, and this should be monitored during treatment.

Corticosteroids should be used cautiously in patients with non-specific ulcerative colitis, diverticulitis, colon abscess or other pyogenic infection, colon obstruction, or extensive fistulas and sinus tracts, fresh intestinal anastomoses, active or latent peptic ulcers, renal insufficiency, hypertension, osteoporosis and myasthenia gravis.

Topical corticosteroids should be used with caution in the management of psoriasis, as exacerbation of the disease or pustular psoriasis may occur during or on withdrawal of topical corticosteroid therapy.

Topical corticosteroids should also be used with caution in patients with impaired T cell function or in those patients receiving other immunosuppressive therapy. The immunosuppressive effects of corticosteroids may be associated with impairment of the normal function of T cells and macrophages. The result of this impairment may be the activation of latent infection or exacerbation of intercurrent infections, including those caused by Candida, Mycobacterium, Toxoplasma, Strongyloides, Pneumocystis, Cryptococcus, Nocardia and Amoeba.

Patients on long term therapy, if there is a risk of immunosuppression, should not be given any live attenuated vaccines.

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.

Use in the elderly

No data available.

Paediatric use

Long term therapy in infants should be avoided as adrenal suppression may occur. The risk of systemic absorption, and hence systemic toxicity, is greater in children due to a larger skin surface to bodyweight ratio than adults. The preparation is not recommended for use in children under 2 years of age except on the advice of a doctor.

Manifestations of adrenal suppression in children include retardation of linear growth, delayed weight gain, low plasma cortisol concentrations and lack of response to corticotrophin stimulation (See Section 5.2 Pharmacokinetic Properties). Manifestations of intracranial hypertension include bulging fontanelles, headache, and bilateral papilloedema. Topical corticosteroid therapy in children should be limited to the minimum amount necessary for therapeutic efficacy; chronic topical corticosteroid therapy may interfere with growth and development. Parents should be advised not to use tight-fitting nappies or plastic pants on a child being treated in the diaper area, since such garments may constitute occlusive dressings.

Children have a greater surface to mass ratio than adults, and so may be at greater risk of adverse events from increased dosages.

Effects on laboratory tests

The use of corticosteroids has been shown to result in falsely elevated measurements of serum digoxin concentrations, but this occurred at dosages far greater than those likely to be delivered by topical therapy.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

There are many potential drug interactions with hydrocortisone, however most are quite unlikely with topical therapy, occurring mainly with prolonged or over-use.

Carbamazepine, phenytoin and rifampicin all induce hepatic enzymes and thus lead to increased metabolism of hydrocortisone.

Concomitant use of diuretics, which also deplete potassium ion concentration in the blood, may cause hypokalaemia.

All corticosteroids antagonise the effects of neuromuscular blocking agents, such as vecuronium.

Oral contraceptives have been shown to prolong the half-life of hydrocortisone and thus potentiate its anti-inflammatory effects.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

Long-term animal studies have not been performed to evaluate the effect on fertility of topical corticosteroids.

Use in pregnancy – Category A

Appropriate studies in humans have not been done. *In vivo* studies using pregnant animals have shown that application of large amounts of topical corticosteroids, especially the more potent ones, over prolonged periods may cause foetal abnormalities. Therefore, topical

corticosteroids should be used in pregnancy only when the potential benefits justify the possible risks to the foetus. The drugs should not be used on extensive areas, in large amounts or for prolonged periods in pregnant women.

Use in lactation

It is not known whether topical corticosteroids are distributed into milk; however, systemic corticosteroids are distributed into milk. Topical corticosteroids should be used with caution in nursing mothers.

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)

An itching or burning sensation may be experienced when using this medication.

Topical corticosteroids may cause adverse dermatological effects. Adverse dermatological effects are most likely to occur in intertriginous and facial areas. Local adverse corticosteroid effects occur most frequently with occlusive dressings, especially with prolonged therapy, and may require discontinuation of the dressings. Atrophy of the epidermis, subcutaneous tissue and dermal collagen; drying and cracking or tightening of the skin may occur. Epidermal thinning, telangiectasia, increased fragility of cutaneous blood vessels, pupura and atrophic striae are also reported.

Other adverse dermatologic effects of topical corticosteroids include acneform eruption, vesiculation, irritation, pruritis, hypertrichosis, rosacea-like eruptions on the face, erythema, hyperthesia, perioral dermatitis, burning or stinging sensation, folliculitis, and hypopigmentation.

Adverse dermatological effects usually improve when the drug is discontinued but may persist for long periods; atrophic striae may be permanent. In addition to the other adverse dermatological effects of topical corticosteroid therapy, maceration of the skin and milaria may occur, especially when occlusive dressings are used. Topically applied steroids are generally nonsensitising, but allergic contact dermatitis may occur rarely.

Topical corticosteroids should be used with caution in the management of psoriasis (see **Section 4.4 Special warnings and precautions for use**).

Topical corticosteroids should also be used with caution in patients with impaired T cell function or in those patients receiving other immunosuppressive therapy. The result of this impairment may be the activation of latent infection or exacerbation of intercurrent infections (see **Section 4.4 Special warnings and precautions for use**)

Any cardiovascular adverse events are unlikely with topical hydrocortisone therapy, however, prolonged prolific use may result in a transient hypertension as a result of fluid retention.

Long term corticosteroid use has resulted in Benign Intracranial Hypertension, with most reports occurring in children.

Corticosteroids have documented effects on serum lipids, including increased total cholesterol, increased low density lipoproteins and increased triglyceride levels.

Topical and systemic corticosteroid therapy has been implicated in posterior subcapsular cataract formation, elevated intraocular pressure, optic nerve damage and papilloedema.

Cataracts, although primarily reported with systemic corticosteroid use, have been reported with use of topical preparations.

Hydrocortisone has least potential for causing glaucoma, but reports have demonstrated this complication in patients using topical preparations on the face.

Post-marketing reports include the following adverse effect: Eye disorders: vision blurred

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 and Apotex Medical Information enquiries/Adverse Drug Reaction Reporting on 1800 195 055.

4.9 OVERDOSE

Acute ingestion or accidental poisoning, even in massive doses, is rarely a clinical problem. Treatment should be symptomatic and supportive. Excessive chronic exposure results in adverse systemic effects. In such cases the use of topical corticosteroid should be discontinued, with the consideration to tapering the dose. Emesis or activated charcoal is not usually indicated unless multiple ingestion is suspected. Support the patient as necessary and treat symptomatically.

For information on the management of overdose, contact the Poisons Information Centre on 131126 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

On topical application, corticosteroids produce anti-inflammatory, antipruritic and vasoconstrictor actions. The activity of the drugs is thought to result at least in part from binding with a steroid receptor. Corticosteroids decrease inflammation by stabilising leukocyte lysosomal membranes, preventing release of destructive acid hydrolyses from leukocytes; inhibiting macrophage accumulation in inflamed areas; reducing leukocyte adhesion to capillary endothelium; reducing capillary wall permeability and oedema formation; decreasing complement components; antagonizing histamine activity and release of kinin from substrates; reducing fibroblast proliferation, collagen deposition, and subsequent scar tissue formation; and possibly by other mechanisms as yet unknown.

Clinical trials

No data available.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

The rate and extent of hydrocortisone absorption through the skin varies among individual patients. Following topical application of a corticosteroid to most areas of normal skin, only minimal amounts of the lipophilic drug partitions into the predominantly aqueous dermo-epidermal layer (viable epidermis + dermis) and subsequently the systemic circulation.

Absorption is, however, markedly increased when the skin has lost its keratin layer or the rate limiting properties of the stratum corneum. Physical disruption of the stratum corneum,

inflammation and/or disease of the epidermal barrier (eg. psoriasis, eczema) may result in increased absorption. Hydrocortisone is absorbed to a greater degree from the skin behind and around the ear region, scrotum, axilla, eyelid, face and scalp than forearm, knees, elbow, palm and sole. Prolonged absorption persists even after the area of application has been washed, possibly because the drug is retained in the stratum corneum and/or the dermo-epidermal layer.

Children are at a greater risk of systemic absorption of topical steroids due to higher permeation properties of the skin and increased surface area to body mass ratio.

Distribution

Corticosteroids are rapidly distributed to all body tissues. They cross the placenta and may be excreted in small amounts in breast milk. Corticosteroids in the circulation are bound to plasma proteins in varying degrees, mainly to globulin and less so to albumin.

Metabolism

Hydrocortisone is metabolised in the liver and most tissues to biologically inactive compounds, mainly glucoronides and sulfates.

Excretion

The metabolites are excreted in urine, mainly conjugated as glucuronides, together with a very small proportion of unchanged hydrocortisone. Some of the topical corticosteroids and their metabolites are also excreted in the bile.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

There is no reliable evidence of induction of mutagenicity in humans by hydrocortisone.

Carcinogenicity

There is no reliable evidence of induction of carcinogenicity in humans by hydrocortisone.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

- Soft white paraffin
- liquid paraffin
- cetomacrogol 1000
- cetostearyl alcohol
- chlorocresol
- citric acid
- sodium citrate dihydrate
- purified water.

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.

6.5 NATURE AND CONTENTS OF CONTAINER

30 g tube.

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 is an odourless, white or almost white, crystalline powder. Hydrocortisone acetate 112 mg is approximately equivalent to 100 mg of hydrocortisone.

Hydrocortisone is a corticosteroid and is chemically described as 17-hydroxycorticosterone or 11,17,21-Trihydroxypregn-4-ene-3,20-dione. Hydrocortisone acetate is chemically described as hydrocortisone 21-acetate.

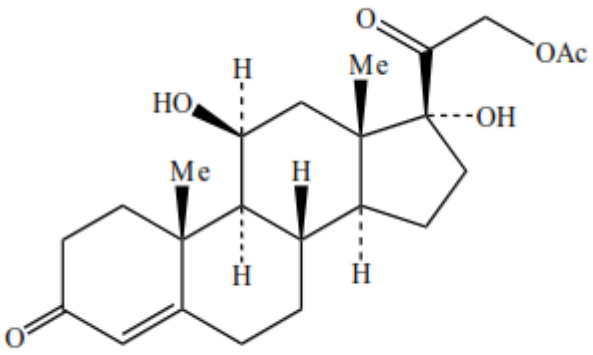
Solubility: Practically insoluble in water and in ether, soluble in ethanol (1 in 230) and in chloroform (1 in 200).

Molecular formula: $C_{23}H_{32}O_6$

Molecular weight: 404.5

CAS number 50-03-3

Chemical Structure



7 MEDICINE SCHEDULE (POISONS STANDARD)

S3 – Pharmacist Only Medicine.

8 SPONSOR

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9 DATE OF FIRST APPROVAL

30 October 2017

10 DATE OF REVISION

20 February 2019

Summary table of changes

Section Changed	Summary of new information
All	Reformatted product information; minor editorial changes
4.3, 4.4, 4.8	Safety related updates