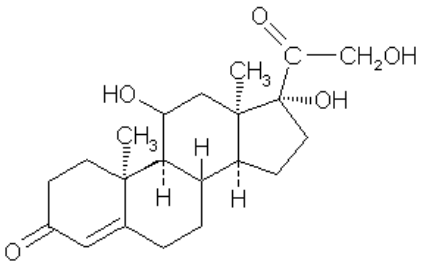
PRODUCT INFORMATION

Hysone 4
Hysone 20

Hydrocortisone

NAME OF THE MEDICINE

Active ingredient	:	Hydrocortisone
Chemical name	:	11β,17α,21-trihydroxypregn-4-ene-3,20-dione
Structural formula	:	

Molecular formula	:	$C_{21}H_{30}O_5$	Molecular weight	:	362.5
			CAS Registry no.	:	50-23-7

DESCRIPTION

Hydrocortisone, also known as cortisol, is 11β,17α,21-trihydroxypregn-4-ene-3,20-dione. It is a white or almost white, odourless crystalline powder. It is practically insoluble in water; sparingly soluble in ethanol (96%) and in acetone; slightly soluble in chloroform; very slightly soluble in ether. It melts at about 214°C, with decomposition.

Each Hysone 4 mg tablet contains 4 mg of hydrocortisone. The tablets also contain the following inactive ingredients: lactose monohydrate, maize starch, povidone and magnesium stearate.

Each Hysone 20 mg tablet contains 20 mg of hydrocortisone. The tablets also contain the following inactive ingredients: lactose monohydrate, maize starch, macrogol 8000, povidone and magnesium stearate.

PHARMACOLOGY

Hydrocortisone, which has salt-retaining properties, is believed to be the principal glucocorticoid secreted by the adrenal cortex. It is used as replacement therapy in adrenocortical deficiency states. It is also used for its potent anti-inflammatory effects in disorders of many organ systems.

Hydrocortisone is readily absorbed from the gastrointestinal tract, with peak blood concentrations being attained in about one hour. The biological half-life is about 100 minutes. It is more than 90% bound to plasma proteins.

Hydrocortisone is metabolised in the liver and most body tissues to hydrogenated and degraded forms such as tetrahydrocortisone and tetrahydrocortisol. These are excreted in the urine, mainly conjugated as glucuronides, together with a very small proportion of unchanged hydrocortisone.

INDICATIONS

Hydrocortisone is indicated for replacement therapy in Addison's disease or chronic adrenocortical insufficiency secondary to hypopituitarism.

CONTRAINDICATIONS

Patients with any uncontrolled infections; known hypersensitivity to hydrocortisone.

PRECAUTIONS

The use of Hysone in the treatment of conditions other than those specified in the Indications section is not advised, due to the marked effect of hydrocortisone on sodium retention.

Corticosteroids may mask some signs of infection, and new infections may appear during their use. There may be decreased resistance and inability to localise infection when corticosteroids are used. If an infection occurs during hydrocortisone therapy, consider stopping hydrocortisone if possible. In any case, the infection should be promptly controlled by suitable antimicrobial therapy.

Individuals on immunosuppressant therapy, including hydrocortisone, should avoid exposure to infections. For example, varicella and measles can prove serious or even fatal. The administration of an appropriate immunoglobulin may be indicated in individuals exposed to these infections during corticosteroid therapy.

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

Average and large doses of hydrocortisone can cause elevation in blood pressure, salt and water retention, and increased potassium excretion. Therefore, both dosage and salt intake should be carefully monitored in order to avoid the development of hypertension, oedema or weight gain.

Periodic checking of serum electrolyte levels is advisable during prolonged therapy; dietary salt restriction and potassium supplementation may be necessary. All corticosteroids increase calcium excretion.

Patients should not be vaccinated against smallpox whilst on corticosteroid therapy. Other immunisation procedures, particularly those involving the administration of live vaccines, e.g. BCG, should not be undertaken in patients who are taking corticosteroids, especially in high doses, because of the possible risks of neurological complications and a lack of antibody response.

The use of Hysone in patients with active tuberculosis should be restricted to those cases of fulminating or disseminated tuberculosis in which the corticosteroid is used for the management of the disease in conjunction with an appropriate anti-tuberculous regimen. If corticosteroids are indicated in patients with latent tuberculosis or tuberculin reactivity, close observation is necessary since reactivation of the disease may occur. During prolonged corticosteroid therapy, these patients should receive chemoprophylaxis.

Adverse effects to corticosteroids may be produced by too rapid withdrawal or by continued use of large doses.

There is an enhanced corticosteroid effect in patients with hypothyroidism and in those with cirrhosis.

Corticosteroids should be used cautiously in patients with ocular Herpes simplex because of possible corneal perforation. The lowest possible dose of corticosteroid should be used to control the condition being treated. When possible, the dosage should be gradually reduced.

Psychic derangements may appear when corticosteroids are used. These may range from euphoria, insomnia, mood swings, personality changes, and severe depression to frank psychotic manifestations. Existing emotional instability or psychotic tendencies may also be aggravated by corticosteroids.

Aspirin should be used cautiously in conjunction with corticosteroids in patients with hypoprothrombinaemia.

Corticosteroids should be used with caution in patients with nonspecific ulcerative colitis as there is a possibility of impending perforation, abscess, or other pyogenic infection.

Hydrocortisone should be used cautiously in the elderly and in post-menopausal women, in patients with diverticulitis, recent surgery including intestinal anastomoses, active or latent peptic ulcer, renal insufficiency, hypertension, osteoporosis, acute glomerulonephritis, vaccinia, varicella, exanthemata, Cushing's syndrome, antibiotic resistant infections, diabetes mellitus, congestive heart failure, chronic nephritis, thromboembolic tendencies, thrombophlebitis, convulsive disorders, metastatic carcinoma, impaired hepatic function, and vertebral collapse.

Growth and development of infants and children on prolonged corticosteroid therapy should be carefully observed.

Use in Pregnancy (Risk Category: A)

Category A: Drugs which have been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the fetus having been absorbed.

Use in Lactation

Corticosteroids appear in breast milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other unwanted effects. Mothers taking pharmacological doses of corticosteroids should be advised not to nurse.

INTERACTIONS WITH OTHER MEDICINES

Oral contraceptives may increase the half-life of corticosteroids. Barbiturates, phenytoin, rifampicin and other drugs which induce hepatic enzymes may shorten the elimination half-life of hydrocortisone.

Hydrocortisone can increase the loss of potassium. When administered concomitantly with potassium-depleting diuretics, patients should be observed closely for the development of hypokalaemia. Patients taking the combination of hydrocortisone and digoxin should also be closely monitored due to an increased sensitivity to digoxin.

ADVERSE EFFECTS

Fluid and electrolyte disturbances. Sodium retention, fluid retention, congestive heart failure in susceptible patients, potassium loss, hypokalaemic alkalosis, hypertension.

Musculoskeletal. Muscle weakness, steroid myopathy, loss of muscle mass, osteoporosis, vertebral compression fractures, aseptic necrosis of femoral and humeral heads, pathological fracture of long bones and spontaneous fractures, tendon rupture.

Gastrointestinal. Peptic ulcer with possible perforation and haemorrhage, perforation of the small and large bowel (particularly in patients with inflammatory bowel disease), pancreatitis, abdominal distension, ulcerative oesophagitis.

Dermatological. Impaired wound healing, thin fragile skin, bruising, petechiae and ecchymoses, facial erythema, increased sweating, subcutaneous fat atrophy, purpura, striae, hyperpigmentation of the skin and nails, hirsutism, acneform eruptions, other cutaneous reactions (such as allergic dermatitis, urticaria, angioneurotic oedema); reactions to skin tests may be suppressed.

Neurological. Convulsions, increased intracranial pressure with papilloedema (pseudotumour cerebri) usually after treatment, vertigo, headache, severe mental disturbances.

Endocrine. Menstrual irregularities, development of cushingoid state, suppression of growth in children, secondary adrenocortical and pituitary unresponsiveness, particularly in times of stress (e.g. trauma, surgery or illness), decreased carbohydrate tolerance, manifestations of latent diabetes mellitus, increased requirements for insulin or oral hypoglycaemic agents in diabetics.

Immunological. Clinically significant infections increase in frequency and severity during corticosteroid use.

Haematological. Corticosteroids will increase total WBC, with an increase in neutrophils and a decrease in monocytes, lymphocytes and eosinophils.

Ophthalmic. Posterior subcapsular cataracts, increased intraocular pressure, glaucoma, exophthalmos.

Metabolic. Hypertriglyceridaemia, hyperglycaemia, glycosuria, negative nitrogen balance due to protein catabolism.

Cardiovascular. Myocardial rupture following recent myocardial infarction.

Other. Hypersensitivity, thromboembolism, weight gain, increased appetite, nausea, malaise, necrotising angiitis, thrombophlebitis, aggravation or masking of infections, insomnia, syncopal episodes and anaphylactoid reactions.

DOSAGE AND ADMINISTRATION

Dosage requirements are variable and must be individualised on the basis of the disease and the response of the patient.

A typical dose in adults is hydrocortisone 30 mg daily in divided doses. Dosage may be increased if clinically necessary. Patients should be advised to take their hydrocortisone replacement therapy with meals or a glass of milk or antacid because the drug may increase gastric acidity. Approximately 2/3 of the dose should be taken in the morning and 1/3 at about 4pm. Some individuals may exhibit irritability or insomnia after initiation of therapy; in these the dosage should be reduced. Smaller doses may also be necessary in patients with hypertension, diabetes mellitus, or active tuberculosis.

Supplementary administration of fludrocortisone, 0.05 to 0.1 mg daily by mouth, is required to replace mineralocorticoid deficiency. Blood pressure and serum electrolyte measurements will give an indication of adequacy of mineralocorticoid dosage. Patients should be advised to ingest adequate sodium (3 to 4 g per day). The physician should be alert to complications of mineralocorticoid therapy, e.g. hypokalaemia, oedema, hypertension, cardiac enlargement, congestive heart failure.

Dosage of hydrocortisone should be increased during periods of intercurrent illness or surgery to about 75 to 150 mg/day. Fludrocortisone dosage should also be increased. Patients should be alerted to awareness of those occasions when excess sodium may be required, e.g. hot weather, gastrointestinal upsets.

After a favourable initial response, the proper maintenance dosage should be determined by decreasing the initial dosage in small amounts to the lowest dosage that maintains an adequate clinical response.

Patients should be observed closely for signs that may require dosage adjustment, including changes in clinical status resulting from remissions or exacerbations of the disease, individual drug responsiveness, and the effect of stress (e.g. surgery, infection, trauma). During stress it may be necessary to increase dosage temporarily.

If the drug is to be stopped after more than a few days of treatment, it usually should be withdrawn gradually.

OVERDOSAGE

Reports of acute toxicity and/or death following overdosage with glucocorticoids are rare. In the event of overdosage, no specific antidote is available; treatment is supportive and symptomatic.

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

PRESENTATION AND STORAGE CONDITIONS

Hysone 4 4 mg	:	Hydrocortisone 4 mg tablet: white, scored, marked H/4 on one side, G on reverse Packed in HDPE bottles of 50 tablets Store below 30°C.
Hysone 20 20 mg	:	Hydrocortisone 20 mg tablet: white, scored, marked H/20 on one side, G on reverse Packed in HDPE bottles of 60 tablets Store below 30°C.

NAME AND ADDRESS OF THE SPONSOR

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POISONS SCHEDULE OF MEDICINE

S4 (Prescription Only Medicine)

DATE OF FIRST INCLUSION IN THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS (THE ARTG)

21/10/1991

DATE OF MOST RECENT AMENDMENT

09/05/2017