HYDROCORTISONE - hydrocortisone tablet
Physicians Total Care, Inc.

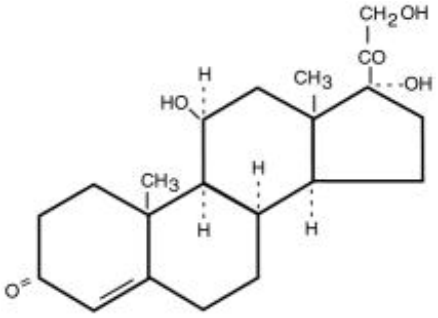
Rev. 07/03

Rx Only

DESCRIPTION

Glucocorticoids are adrenocortical steroids, both naturally occurring and synthetic, which are readily absorbed from the gastrointestinal tract.

Hydrocortisone is a white to practically white, odorless, crystalline powder, very slightly soluble in water. The molecular weight is 362.47. It is designated chemically as 11B, 17,21-trihydroxy-pregn-4-ene-3,20-dione. The molecular formula is $C_{21}H_{30}O_5$ and the structural formula is:



Hydrocortisone is believed to be the principal hormone secreted by the adrenal cortex.

Each tablet for oral administration contains 20 mg of hydrocortisone.

Inactive Ingredients: Anhydrous Lactose, Colloidal Silicon Dioxide, Magnesium Stearate, Microcrystalline Cellulose, and Sodium Starch Glycolate.

CLINICAL PHARMACOLOGY

Naturally occurring glucocorticoids (hydrocortisone and cortisone), which also have salt-retaining properties, are used as replacement therapy in adrenocortical deficiency states. They are also used for their potent anti-inflammatory effects in disorders of many organ systems.

Glucocorticoids cause profound and varied metabolic effects. In addition, they modify the body's immune responses to diverse stimuli.

INDICATIONS AND USAGE

1. *Endocrine Disorders* Primary or secondary adrenocortical insufficiency (hydrocortisone or cortisone is the first choice; synthetic analogs may be used in conjunction with mineralocorticoids where applicable; in infancy mineralocorticoid supplementation is of particular importance) Congenital adrenal hyperplasia Nonsuppurative thyroiditis Hypercalcemia associated with cancer
2. *Rheumatic Disorders* As adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in: Psoriatic arthritis Rheumatoid arthritis, including juvenile rheumatoid arthritis (selected cases may require low-dose maintenance therapy): Ankylosing spondylitis Acute and subacute bursitis Acute nonspecific tenosynovitis Acute gouty arthritis Post-traumatic osteoarthritis Synovitis or osteoarthritis Epicondylitis
3. *Collagen Diseases* During an exacerbation or as maintenance therapy in selected cases of: Systemic lupus erythematosus Acute rheumatic carditis Systemic dermatomyositis (polymyositis)
4. *Dermatologic Diseases* Pemphigus Bullous dermatitis herpetiformis Severe erythema multiforme

(Stevens-Johnson syndrome) Exfoliative dermatitis Mycosis fungoides Severe psoriasis Severe seborrheic dermatitis

5. *Allergic States* Control of severe or incapacitating allergic conditions intractable to adequate trials of conventional treatment: Seasonal or perennial allergic rhinitis Bronchial asthma Contact dermatitis Atopic dermatitis Serum sickness Drug hypersensitivity reactions
6. *Ophthalmic Diseases* Severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa, such as: Allergic conjunctivitis Keratitis Allergic corneal marginal ulcers Herpes zoster ophthalmicus Iritis and iridocyclitis Chorioretinitis Anterior segment inflammation Diffuse posterior uveitis and choroiditis Optic neuritis Sympathetic ophthalmia
7. *Respiratory Disease* Symptomatic sarcoidosis Loeffler's syndrome not manageable by other means Berylliosis Fulminating or disseminated pulmonary tuberculosis when used concurrently with appropriate antituberculosis chemotherapy Aspiration pneumonitis
8. *Hematologic Disorder* Idiopathic thrombocytopenic purpura in adults Secondary thrombocytopenia in adults Acquired (autoimmune) hemolytic anemia Erythroblastopenia (RBC anemia) Congenital (erythroid) hypoplastic anemia
9. *Neoplastic Disease* For palliative management of: Leukemias and lymphomas in adults Acute leukemia of childhood
10. *Edematous States* To induce a diuresis or remission of proteinuria in the nephrotic syndrome, without uremia, of the idiopathic type or that due to lupus erythematosus
11. *Gastrointestinal Diseases* To tide the patient over a critical period of the disease in: Ulcerative colitis Regional enteritis
12. *Miscellaneous* Tuberculous meningitis with subarachnoid block or impending block when used concurrently with appropriate antituberculous chemotherapy Trichinosis with neurologic or myocardial involvement

CONTRAINDICATIONS

Systemic fungal infections Hypersensitivity to this product

WARNINGS

Persons who are on drugs which suppress the immune system are more susceptible to infections than healthy individuals. Chickenpox and measles, for example, can have a more serious or even fatal course in non-immune children or adults on corticosteroids. In such children or adults who have not had these diseases, particular care should be taken to avoid exposure. How the dose, route and duration of corticosteroid administration affects the risk of developing a disseminated infection is not known. The contribution of the underlying disease and/or prior corticosteroid treatment to the risk is also not known. If exposed to chickenpox, prophylaxis with varicella zoster immune globulin (VZIG) may be indicated. If exposed to measles, prophylaxis with pooled intramuscular immunoglobulin (IG) may be indicated. (See the respective package inserts for complete VZIG and IG prescribing information). If chickenpox develops, treatment with antiviral agents may be considered.

In patients on corticosteroid therapy subjected to unusual stress, increased dosage of rapidly acting corticosteroids before, during, and after the stressful situation is indicated.

Drug-induced secondary adrenocortical insufficiency may result from too rapid withdrawal of corticosteroids and may be minimized by gradual reduction of dosage. 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 mineralo-corticoid should be administered concurrently.

Corticosteroids may mask some signs of infection, and new infections may appear during their use. There may be decreased resistance and inability to localize infection when corticosteroids are used.

Moreover, corticosteroids may affect nitroblue-tetrazolium test for bacterial infection and produce false negative results.

In cerebral malaria, a double-blind trial has shown that the use of corticosteroids is associated with prolongation of coma and higher incidence of pneumonia and gastrointestinal bleeding.

Corticosteroids may activate latent amebiasis. Therefore, it is recommended that latent or active amebiasis be ruled out before initiating corticosteroid therapy in any patient who has spent time in the tropics or any patient with unexplained diarrhea.

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.

Usage in pregnancy: Since adequate human reproduction studies have not been done with corticosteroids, use of these drugs in pregnancy or in women of childbearing potential requires that the anticipated benefits be weighed against the possible hazards to the mother and embryo or fetus. Infants born of mothers who have received substantial doses of corticosteroids during pregnancy should be carefully observed for signs of hypoadrenalism.

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

Average and large doses of hydrocortisone or cortisone can cause elevation of blood pressure, salt and water retention, and increased excretion of potassium. These effects are less likely to occur with synthetic derivatives except when used in large doses. Dietary salt restriction and potassium supplementation may be necessary. All corticosteroids increase calcium excretion.

Administration of live virus vaccines, including smallpox, is contraindicated in individuals receiving immunosuppressive doses of corticosteroids. If inactivated viral or bacterial vaccines are administered to individuals receiving immunosuppressive doses of corticosteroids, the expected serum antibody response may not be obtained. However, immunization procedures may be undertaken in patients who are receiving corticosteroids as replacement therapy, e.g., for Addison's disease.

The use of hydrocortisone tablets in 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 antituberculous regimen.

If corticosteroids are indicated in patients with latent tuberculosis or tuberculin reactivity, close observation is necessary as reactivation of the disease may occur. During prolonged corticosteroid therapy, these patients should receive chemoprophylaxis.

Literature reports suggest an apparent association between use of corticosteroids and left ventricular free wall rupture after a recent myocardial infarction; therefore, therapy with corticosteroids should be used with great caution in these patients.

PRECAUTIONS

General: Following prolonged therapy, withdrawal of corticosteroids may result in symptoms of the corticosteroid withdrawal syndrome including fever, myalgia, arthralgia, and malaise. This may occur in patients even without evidence of adrenal insufficiency.

There is an enhanced effect of corticosteroids 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 under treatment, and

when reduction in dosage is possible, the reduction should be gradual.

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

Aspirin should be used cautiously in conjunction with corticosteroids in hypoprothrombinemia.

Steroids should be used with caution in nonspecific ulcerative colitis, if there is a probability of impending perforation, abscess, or other pyogenic infection, diverticulitis, fresh intestinal anastomoses, active or latent peptic ulcer, renal insufficiency, hypertension, osteoporosis, and myasthenia gravis. Signs of peritoneal irritation following gastrointestinal perforation in patients receiving large doses of corticosteroids may be minimal or absent. Fat embolism has been reported as a possible complication of hypercortisonism.

When large doses are given, some authorities advise that corticosteroids be taken with meals and antacids taken between meals to help to prevent peptic ulcer.

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

Steroids may increase or decrease motility and number of spermatozoa in some patients.

Phenytoin, phenobarbital, ephedrine, and rifampin may enhance the metabolic clearance of corticosteroids, resulting in decreased blood levels and lessened physiologic activity, thus requiring adjustment in corticosteroid dosage.

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 courmarins, although there have been some 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 hypokalemia.

Information for Patients: Persons who are on immunosuppressant doses of corticosteroids should be warned to avoid exposure to chickenpox or measles. Patients should also be advised that if they are exposed, medical advice should be sought without delay.

ADVERSE REACTIONS

Fluid and Electrolyte Disturbances

Sodium retention Fluid retention Congestive heart failure in susceptible patients Potassium loss Hypokalemic alkalosis Hypertension

Musculoskeletal

Muscle weakness Steroid myopathy Loss of muscle mass Osteoporosis Vertebral compression fractures Aseptic necrosis of femoral and humeral heads Pathologic fracture of long bones Tendon rupture

Gastrointestinal

Peptic ulcer with possible perforation and hemorrhage Perforation of the small and large bowel, particularly in patients with inflammatory bowel disease Pancreatitis Abdominal distention Ulcerative esophagitis

Dermatologic

Impaired wound healing Thin fragile skin Petechiae and ecchymoses Erythema Increased sweating May suppress reactions to skin tests Other cutaneous reactions, such as allergic dermatitis, urticaria, angioneurotic edema

Neurologic
Convulsions Increased intracranial pressure with papilledema (pseudotumor cerbri) usually after treatment Vertigo Headache Psychic disturbances

Endocrine
Menstrual irregularities Development of cushingoid state Suppression of growth in children Secondary adrenocortical and pituitary unresponsiveness, particularly in times of stress, as in trauma, surgery, or illness Decreased carbohydrate tolerance Manifestations of latent diabetes mellitus Increased requirements for insulin or oral hypoglycemic agents in diabetics Hirsutism

Ophthalmic
Posterior subcapsular cataracts Increased intraocular pressure Glaucoma Exophthalmos

Metabolic
Negative nitrogen balance due to protein catabolism

Cardiovascular
Myocardial rupture following recent myocardial infarction (see **WARNINGS**)

Other
Hypersensitivity Thromboembolism Weight gain Increased appetite Nausea Malaise

OVERDOSAGE

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

The intraperitoneal LD_{50} of hydrocortisone in female mice was 1740 mg/kg.

DOSAGE AND ADMINISTRATION

For oral administration

DOSAGE REQUIREMENTS ARE VARIABLE AND MUST BE INDIVIDUALIZED ON THE BASIS OF THE DISEASE AND THE RESPONSE OF THE PATIENT.

The initial dosage varies from 20 to 240 mg a day depending on the disease being treated. In less severe diseases doses lower than 20 mg may suffice, while in severe diseases doses higher than 240 mg may be required. The initial dosage should be maintained or adjusted until the patient's response is satisfactory. If satisfactory clinical response does not occur after a reasonable period of time, discontinue hydrocortisone tablets and transfer the patient to other therapy.

After a favorable 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 might require 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.

HOW SUPPLIED

Hydrocortisone Tablets USP 20 mg: White, round, scored tablets; imprinted "West-ward 254".

Bottles of 30 tablets (NDC 54868-1743-3),
Bottles of 50 tablets (NDC 54868-1743-0),

Bottles of 60 tablets (NDC 54868-1743-2),
Bottles of 100 tablets (NDC 54868-1743-1).

Store at 20-25°C (68-77°F) [See USP Controlled Room Temperature]. Protect from light and moisture.

Dispense in a tight, light-resistant container as defined in the USP using a child-resistant closure.

Manufactured by:
West-ward Pharmaceutical Corp.
Eatontown, N.J. 07724
Revised July 2003

PRINCIPAL DISPLAY PANEL
Hydrocortisone Tablets, 20 mg

HYDROCORTISONE

hydrocortisone tablet

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:54868-1743(NDC:0143-1252)
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
HYDROCORTISONE (UNII: WI4X0X7BPJ) (HYDROCORTISONE - UNII:WI4X0X7BPJ)	HYDROCORTISONE	20 mg

Inactive Ingredients	
Ingredient Name	**Strength**
CELLULOSE, MICROCRYSTALLINE (UNII: OP1R32D61U)	
SODIUM STARCH GLYCOLATE TYPE A POTATO (UNII: 5856J3G2A2)	
ANHYDROUS LACTOSE (UNII: 3SY5LH9PMK)	
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	

Product Characteristics			
Color	white (WHITE)	**Score**	2 pieces
Shape	ROUND (ROUND)	**Size**	9mm

Flavor		**Imprint Code**	WW;254
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:54868-1743-0	50 in 1 BOTTLE		
2	NDC:54868-1743-1	100 in 1 BOTTLE		
3	NDC:54868-1743-2	60 in 1 BOTTLE		
4	NDC:54868-1743-3	30 in 1 BOTTLE		
5	NDC:54868-1743-4	90 in 1 DOSE PACK		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA083365	07/05/2007	

Labeler - Physicians Total Care, Inc. (194123980)

Establishment

Name	Address	ID/FEI	Business Operations
Physicians Total Care, Inc.		194123980	repack, relabel

Revised: 12/2009 Physicians Total Care, Inc.