Cortef®

brand of hydrocortisone tablets, USP

Upjohn

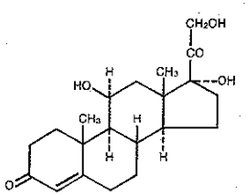
Cortef
hydrocortisone
tablets, USP

0810681407

DESCRIPTION

CORTEF Tablets contain hydrocortisone which is a glucocorticoid. Glucocorticoids are adrenocortical steroids, both naturally occurring and synthetic, which are readily absorbed from the gastrointestinal tract. Hydrocortisone USP is white to practically white, odorless, crystalline powder with a melting point of about 215° C. It is very slightly soluble in water and in ether; sparingly soluble in acetone and in alcohol; slightly soluble in chloroform.

The chemical name for hydrocortisone is pregn-4-ene-3,20-dione,11,17,21-trihydroxy-, (11β)-. Its molecular weight is 362.46 and the structural formula is as outlined below.



CORTEF Tablets are available for oral administration in three strengths: each tablet contains either 5 mg, 10 mg, or 20 mg of hydrocortisone. Inactive ingredients: calcium stearate, corn starch, lactose, mineral oil, sorbic acid, sucrose.

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ACTIONS

Naturally occurring glucocorticoids (hydrocortisone and cortisone), which also have salt-retaining properties, are used as replacement therapy in adrenocortical deficiency states. Their synthetic analogs are primarily 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

CORTEF Tablets are indicated in the following conditions.

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
   - Non suppurative 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 of osteoarthritis
   - Epicondylitis
3. **Collagen Diseases**
   - During an exacerbation or as maintenance therapy in selected cases of:
   - Systemic lupus erythematosus
   - Systemic dermatomyositis (polymyositis)
   - Acute rheumatic carditis
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
   - Serum sickness
   - Bronchial asthma
   - Contact dermatitis

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   - Atopic dermatitis
   - 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 Diseases**
   - Symptomatic sarcoidosis
   - Loeffler's syndrome not manageable by other means
   - Berylliosis
   - Fulminating or disseminated pulmonary tuberculosis when used concurrently with appropriate antituberculous chemotherapy
   - Aspiration pneumonitis
8. **Hematologic Disorders**
   - Idiopathic thrombocytopenic purpura in adults
   - Secondary thrombocytopenia in adults
   - Acquired (autoimmune) hemolytic anemia
   - Erythroblastopenia (RBC anemia)
   - Congenital (erythroid) hypoplastic anemia
9. **Neoplastic Diseases**
   - 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. **Nervous System**
    - Acute exacerbations of multiple sclerosis
13. **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 and known hypersensitivity to components

WARNINGS

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

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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.

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, the use of these drugs in pregnancy, nursing mothers or women of childbearing potential requires that the possible benefits of the drug be weighed against the potential 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.

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 the synthetic derivatives except when used in large doses. Dietary salt restriction and potassium supplementation may be necessary. All corticosteroids increase calcium excretion.

While on corticosteroid therapy patients should not be vaccinated against smallpox. Other immunization procedures should not be undertaken in patients who are on corticosteroids, especially on high dose, because of possible hazards of neurological complications and a lack of antibody response.

The use of CORTEF 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.

Persons who are on drugs which suppress the immune system are more susceptible to infections than healthy individuals. Chicken pox 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 chicken pox, 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 chicken pox develops, treatment with antiviral agents may be considered.

PRECAUTIONS

General Precautions

Drug-induced secondary adrenocortical insufficiency 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. Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticoid should be administered concurrently.

There is an enhanced effect of corticosteroids on 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.

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.

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

Although controlled clinical trials have shown corticosteroids to be effective in speeding the resolution of acute exacerbations of multiple sclerosis, they do not show that corticosteroids affect the ultimate outcome or natural history of the disease. The studies do show that relatively high doses of corticosteroids are necessary to demonstrate a significant effect. (See DOSAGE AND ADMINISTRATION.)

Since complications of treatment with glucocorticoids are dependent on the size of the dose and the duration of treatment, a risk/benefit decision must be made in each individual case as to dose and duration of treatment and as to whether daily or intermittent therapy should be used.

Drug Interactions

The pharmacokinetic interactions listed below are potentially clinically important. Drugs that induce hepatic enzymes such as phenobarbital, phenytoin and rifampin may increase the clearance of corticosteroids and may require increases in corticosteroid dose to achieve the desired response. Drugs such as troleandomycin and ketoconazole may inhibit the metabolism of corticosteroids and thus decrease their clearance. Therefore, the dose of corticosteroid should be titrated to avoid steroid toxicity. Corticosteroids may increase the clearance of chronic high dose aspirin. This could lead to decreased salicylate serum levels or increase the risk of salicylate toxicity when corticosteroid is withdrawn. Aspirin should be used cautiously in conjunction with corticosteroids in patients suffering from hypoprothrombinemia. The effect of corticosteroids on oral anticoagulants is variable. There are reports of enhanced as well as diminished effects of anticoagulants when given concurrently with corticosteroids. Therefore, coagulation indices should be monitored to maintain the desired anticoagulant effect.

Information for the Patient

Persons who are on immunosuppressant doses of corticosteroids should be warned to avoid exposure to chicken pox 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

Gastrointestinal
- Peptic ulcer with possible perforation and hemorrhage
- Pancreatitis
- Abdominal distention
- Ulcerative esophagitis
- Increases in alanine transaminase (ALT, SGPT), aspartate transaminase (AST, SGOT) and alkaline phosphatase have been observed following corticosteroid treatment. These changes are usually small, not associated with any clinical syndrome and are reversible upon discontinuation.

Dermatologic
- Impaired wound healing
- Thin fragile skin
- Petechiae and ecchymoses
- Facial erythema
- Increased sweating
- May suppress reactions to skin tests

Neurological
- Increased intracranial pressure with papilledema (pseudotumor cerebri) usually after treatment
- Convulsions
- Vertigo
- Headache

Endocrine
- 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
- Menstrual irregularities
- Decreased carbohydrate tolerance
- Manifestations of latent diabetes mellitus
- Increased requirements for insulin or oral hypoglycemic agents in diabetics

Ophthalmic
- Posterior subcapsular cataracts
- Increased intraocular pressure
- Glaucoma
- Exophthalmos

Metabolic
- Negative nitrogen balance due to protein catabolism

DOSAGE AND ADMINISTRATION

The initial dosage of CORTEF Tablets may vary from 20 mg to 240 mg of hydrocortisone per day depending on the specific disease entity being treated. In situations of less severity lower doses will generally suffice while in selected patients higher initial doses may be required. The initial dosage should be maintained or adjusted until a satisfactory response is noted. If after a reasonable period of time there is a lack of satisfactory clinical response, CORTEF should be discontinued and the patient transferred to other appropriate therapy. IT SHOULD BE EMPHASIZED THAT DOSAGE REQUIREMENTS ARE VARIABLE AND MUST BE INDIVIDUALIZED ON THE BASIS OF THE DISEASE UNDER TREATMENT AND THE RESPONSE OF THE PATIENT. After a favorable response is noted, the proper maintenance dosage should be determined by decreasing the initial drug dosage in small decrements at appropriate time intervals until the lowest dosage which will maintain an adequate clinical response is reached. It should be kept in mind that constant monitoring is needed in regard to drug dosage. Included in the situations which may make dosage adjustments necessary are changes in clinical status secondary to remissions or exacerbations in the disease process, the patient's individual drug responsiveness, and the effect of patient exposure to stressful situations not directly related to the disease entity under treatment; in this latter situation it may be necessary to increase the dosage of CORTEF for a period of time consistent with the patient's condition. If after long-term therapy the drug is to be stopped, it is recommended that it be withdrawn gradually, rather than abruptly.

(continued below)

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Multiple Sclerosis

In treatment of acute exacerbations of multiple sclerosis, daily doses of 200 mg of prednisolone for a week followed by 80 mg every other day for 1 month have been shown to be effective (20 mg of hydrocortisone is equivalent to 5 mg of prednisolone).

HOW SUPPLIED

CORTEF Tablets are available in the following strengths and package sizes:

5 mg (white, round, scored, imprinted CORTEF 5)
Bottles of 50 NDC 0009-0012-01

10 mg (white, round, scored, imprinted CORTEF 10)
Bottles of 100 NDC 0009-0031-01

20 mg (white, round, scored, imprinted CORTEF 20)
Bottles of 100 NDC 0009-0044-01

Store at controlled room temperature 15° to 30° C (59° to 86° F).

Caution: Federal law prohibits dispensing without prescription.

The Upjohn Company
Kalamazoo, Michigan 49001, USA

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