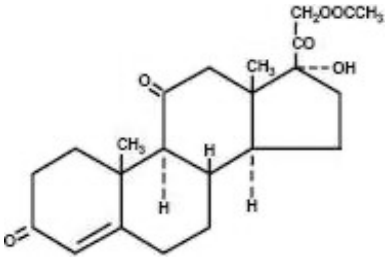
CORTISONE ACETATE- cortisone acetate tablet
Pharmacia and Upjohn Company

Cortisone Acetate Tablets, USP

DESCRIPTION

Cortisone acetate is a glucocorticoid. Glucocorticoids are adrenocortical steroids, both naturally occurring and synthetic, which are readily absorbed from the gastrointestinal tract. Cortisone acetate is a white to practically white, odorless, crystalline powder. It is insoluble in water; freely soluble in chloroform; soluble in dioxane; sparingly soluble in acetone; slightly soluble in alcohol.

The chemical name for cortisone acetate is pregn-4-ene-3,11,20-trione, 21-(acetyloxy)-17-hydroxy and the molecular weight is 402.49. The structural formula is represented below:



Cortisone Acetate Tablets are available in 2 strengths: 5 mg or 10 mg. Inactive ingredients: calcium stearate, corn starch, lactose, mineral oil, sorbic acid, sucrose.

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

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
- Hypercalcemia associated with cancer
- Nonsuppurative thyroiditis

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
- Post-traumatic osteoarthritis
- Acute and subacute bursitis
- Synovitis of osteoarthritis
- Acute nonspecific tenosynovitis
- Epicondylitis
- Acute gouty arthritis

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
- Exfoliative dermatitis
- Bullous dermatitis herpetiformis
- Mycosis fungoides
- Severe erythema multiforme (Stevens-Johnson syndrome)
- 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
- Contact dermatitis
- Atopic dermatitis
- Serum sickness
- Drug hypersensitivity reactions
- Bronchial asthma

6. Ophthalmic Diseases

Severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa such as:
- Allergic conjunctivitis
- Anterior segment inflammation
- Keratitis
- Allergic corneal marginal ulcers
- Diffuse posterior uveitis and choroiditis
- Herpes zoster ophthalmicus
- Iritis and iridocyclitis
- Optic neuritis
- Chorioretinitis
- Sympathetic ophthalmia

7. Respiratory Diseases
- Symptomatic sarcoidosis
- Loeffler's syndrome not manageable by other means

- Fulminating or disseminated pulmonary tuberculosis when used concurrently with appropriate antituberculous chemotherapy
- Berylliosis
- Aspiration pneumonitis

8. Hematologic Disorders
- Idiopathic thrombocytopenic purpura in adults
- Acquired (autoimmune) hemolytic anemia
- Secondary thrombocytopenia in adults
- 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. 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.

Corticosteroids may mask some signs of infection, and new infections may appear during their use. Infections with any pathogen including viral, bacterial, fungal, protozoan or helminthic infections, in any location of the body, may be associated with the use of corticosteroids alone or in combination with other immunosuppressive agents that affect cellular immunity, humoral immunity, or neutrophil function.[1]

These infections may be mild, but can be severe and at times fatal. With increasing doses of corticosteroids, the rate of occurrence of infectious complications increases.[2] 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.

Administration of live or live, attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of corticosteroids. Killed or inactivated vaccines may be administered to patients receiving immunosuppressive doses of corticosteroids; however, the response to such vaccines may be diminished. Indicated immunization procedures may be undertaken in patients receiving nonimmunosuppressive doses of corticosteroids.

The use of cortisone acetate 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. Similarly, corticosteroids should be used with great care in patients with known or suspected Strongyloides (threadworm) infestation. In such patients, corticosteroidinduced immunosuppression may lead to Strongyloides hyperinfection and dissemination with widespread larval migration, often accompanied by severe enterocolitis and potentially fatal gram-negative septicemia.

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.

Kaposi's sarcoma has been reported to occur in patients receiving corticosteroid therapy. Discontinuation of corticosteroids may result in clinical remission.

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

Musculoskeletal

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

Gastrointestinal

- Peptic ulcer with possible perforation and hemorrhage
- Abdominal distention
- Ulcerative esophagitis
- Pancreatitis
- 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
- Facial erythema
- Thin fragile skin
- Increased sweating
- Petechiae and ecchymoses
- May suppress reactions to skin tests

Neurological

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

Endocrine

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

Ophthalmic

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

Metabolic

- Negative nitrogen balance due to protein catabolism

DOSAGE AND ADMINISTRATION

The initial dosage of cortisone acetate may vary from 25 to 300 mg 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, cortisone acetate 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 cortisone acetate 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.

HOW SUPPLIED

Cortisone Acetate Tablets, USP are available in the following strengths and package sizes:

5 mg

(white, round, scored, imprinted UPJOHN 15)

Bottles of 50 NDC 0009-0015-01

10 mg

(white, round, scored, imprinted UPJOHN 23)

Bottles of 100 NDC 0009-0023-01

Store at controlled room temperature 20° to 25°C (68° to 77°F) [see USP].

REFERENCES

[1] Fekety R. Infections associated with corticosteroids and immunosuppressive therapy. In: Gorbach SL, Bartlett JG, Blacklow NR, eds.*Infectious Diseases*. Philadelphia: WBSaunders Company 1992:1050–1.

[2] Stuck AE, Minder CE, Frey FJ. Risk of infectious complications in patients taking glucocorticoids.*Rev Infect Dis* 1989:11(6):954–63.

Rx only

Distributed by

Pharmacia & Upjohn Company

Division of Pfizer Inc, NY, NY 10017

810 931 813

692851

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CORTISONE ACETATE

cortisone acetate tablet

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0009-0015

Route of Administration	ORAL

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
Cortisone Acetate (UNII: 883WKN7W8X) (Cortisone - UNII:V27W9254FZ)		5 mg

Inactive Ingredients	
Ingredient Name	**Strength**
calcium stearate (UNII: 776XM7047L)	
corn starch ()	
lactose ()	
mineral oil ()	
sorbic acid (UNII: X045WJ989B)	
sucrose (UNII: C151H8M554)	

Product Characteristics			
Color	WHITE (WHITE)	**Score**	2 pieces
Shape	DIAMOND (ROUND)	**Size**	7mm
Flavor		**Imprint Code**	UPJOHN;15
Contains			
Coating	false	**Symbol**	false

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:0009-0015-01	50 in 1 BOTTLE		

CORTISONE ACETATE

cortisone acetate tablet

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0009-0023
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
Cortisone Acetate (UNII: 883WKN7W8X) (Cortisone - UNII:V27W9254FZ)		10 mg

Inactive Ingredients	
Ingredient Name	**Strength**

calcium stearate (UNII: 776XM7047L)	
corn starch ()	
lactose ()	
mineral oil ()	
sorbic acid (UNII: X045WJ989B)	
sucrose (UNII: C151H8M554)	

Product Characteristics			
Color	WHITE (WHITE)	**Score**	2 pieces
Shape	DIAMOND (ROUND)	**Size**	8mm
Flavor		**Imprint Code**	UPJOHN;23
Contains			
Coating	false	**Symbol**	false

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0009-0023-01	100 in 1 BOTTLE		

Labeler - Pharmacia and Upjohn Company

Revised: 1/2006 Pharmacia and Upjohn Company