

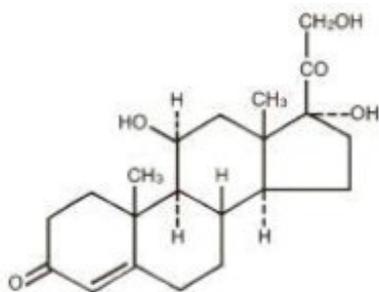
HYDROCORTISONE- hydrocortisone tablet
Vensun Pharmaceuticals, Inc.

Hydrocortisone Tablets, USP
5 mg, 10 mg and 20 mg

DESCRIPTION

Hydrocortisone tablets, USP 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.



Hydrocortisone tablets, USP are available for oral administration in three strengths: each tablet contains either 5 mg, 10 mg, or 20 mg of hydrocortisone. Inactive ingredients: colloidal silicon dioxide, lactose monohydrate, magnesium stearate and microcrystalline cellulose.

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

Hydrocortisone 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

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.

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.

Corticosteroids have been shown to impair fertility in male rats.

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 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.

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, corticosteroid-induced 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 reinstated.

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.

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.

Pheochromocytoma crisis, which can be fatal, has been reported after administration of systemic corticosteroids. In patients with suspected pheochromocytoma, consider the risk of pheochromocytoma crisis prior to administering corticosteroids.

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

Tendon rupture, particularly of the Achilles tendon

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

Epidural lipomatosis

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

Central serous chorioretinopathy

Posterior subcapsular cataracts

Increased intraocular pressure

Glaucoma

Exophthalmos

Metabolic

Negative nitrogen balance due to protein catabolism

Blood and lymphatic system disorders

Leukocytosis

DOSAGE AND ADMINISTRATION

The initial dosage of hydrocortisone 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, hydrocortisone tablets 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 hydrocortisone tablets 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.

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

Hydrocortisone tablets, USP are available in the following strengths and package sizes:

5 mg

White to off-white oval tablets debossed on one side with a bisect and other side with "P5".

NDC 42543-140-50: Bottles of 50 tablets

10 mg

White to off-white oval tablets debossed on one side with a bisect and other side with "P10".

NDC 42543-141-01: Bottles of 100 tablets

20 mg

White to off-white oval tablets debossed on one side with a bisect and other side with "P20".

NDC 42543-142-01: Bottles of 100 tablets

Store at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature].

REFERENCES

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

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

Rx only

Manufactured for:

Vensun Pharmaceuticals, Inc.

Yardley, PA 19067

Manufactured by
Pharmaceutics International, Inc.
Hunt Valley, MD 21031

Rev. 02, August 2017

Principal Display Panel - 5 mg Bottle Label

NDC 42543-140-50 50 Tablets

**Hydrocortisone
Tablets, USP**

5 mg

Rx Only

**VEN SUN
PHARMACEUTICALS, INC.**

The image shows a rectangular label for Hydrocortisone Tablets, USP, 5 mg. The label is divided into several sections. On the left, there is a text block containing: 'Each tablet contains: Hydrocortisone.....5 mg', 'DOSAGE AND USE: See accompanying prescribing information.', 'Warning - This potent drug must be used only under the direct supervision of a physician.', 'Dispense in tight containers (USP).', 'Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature].', and 'Rev. 01, 10-17'. In the center, there is a blue-bordered box containing the text 'Hydrocortisone Tablets, USP' and a green pill-shaped graphic with '5 mg' written on it. Below this box is the text 'Rx Only' and the VENSUN PHARMACEUTICALS, INC. logo. On the right, there is a text block containing: 'NDC 42543-140-50 50 Tablets', 'Manufactured for: Vensun Pharmaceuticals, Inc. Yardley, PA 19067', and 'Manufactured by: Pharmaceutics International, Inc. Hunt Valley, MD 21031'. Below this text is a barcode with the numbers 'N 3 42543 14050 9' printed below it. To the right of the main label area, there is a vertical rectangular area with diagonal pink hatching and the text 'Non-Varnish Area' written vertically.

Principal Display Panel - 10 mg Bottle Label

NDC 42543-141-01 100 Tablets

**Hydrocortisone
Tablets, USP**

10 mg

Rx Only

**VEN SUN
PHARMACEUTICALS, INC.**

<p>Each tablet contains: Hydrocortisone.....10 mg DOSAGE AND USE: See accompanying prescribing information. Warning - This potent drug must be used only under the direct supervision of a physician. Dispense in tight containers (USP). Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature].</p> <p>Rev. 01, 10-17</p>	<p>NDC 42543-141-01 100 Tablets</p>	<p>Manufactured for: Vensun Pharmaceuticals, Inc. Yardley, PA 19067 Manufactured by: Pharmaceutics International, Inc. Hunt Valley, MD 21031</p>	<p style="writing-mode: vertical-rl; transform: rotate(180deg);">Non-Varnish Area</p>
<p style="text-align: center;">Hydrocortisone Tablets, USP</p> <p style="text-align: center;">10 mg</p> <p>Rx Only </p>	<p>N 3  42543 14101 8</p>		

Principal Display Panel - 20 mg Bottle Label

NDC 42543-142-01 100 Tablets

**Hydrocortisone
Tablets, USP**

20 mg

Rx Only

**VENSUN
PHARMACEUTICALS, INC.**

<p>Each tablet contains: Hydrocortisone.....20 mg DOSAGE AND USE: See accompanying prescribing information. Warning - This potent drug must be used only under the direct supervision of a physician. Dispense in tight containers (USP). Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature].</p> <p>Rev. 01, 10-17</p>	<p>NDC 42543-142-01 100 Tablets</p>	<p>Manufactured for: Vensun Pharmaceuticals, Inc. Yardley, PA 19067 Manufactured by: Pharmaceutics International, Inc. Hunt Valley, MD 21031</p>	<p style="writing-mode: vertical-rl; transform: rotate(180deg);">Non-Varnish Area</p>
<p style="text-align: center;">Hydrocortisone Tablets, USP</p> <p style="text-align: center;">20 mg</p> <p>Rx Only </p>	<p>N 3  42543 14201 5</p>		

HYDROCORTISONE

hydrocortisone tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:42543-140
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
Hydrocortisone (UNII: W14X0 X7BPJ) (Hydrocortisone - UNII:W14X0 X7BPJ)	Hydrocortisone	5 mg

Inactive Ingredients

Ingredient Name	Strength
Lactose Monohydrate (UNII: EWQ57Q8I5X)	
Cellulose, Microcrystalline (UNII: OP1R32D61U)	
Silicon Dioxide (UNII: ETJ7Z6XBU4)	
Magnesium Stearate (UNII: 70097M6I30)	

Product Characteristics

Color	WHITE (to off White)	Score	2 pieces
Shape	OVAL (OVAL)	Size	8mm
Flavor		Imprint Code	P;5
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:42543-140-50	50 in 1 BOTTLE, PLASTIC; Type 0: Not a Combination Product	07/07/2017	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA207029	07/07/2017	

HYDROCORTISONE

hydrocortisone tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:42543-141
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name		Basis of Strength	Strength	
Hydrocortisone (UNII: W14X0X7BPJ) (Hydrocortisone - UNII:W14X0X7BPJ)		Hydrocortisone	10 mg	
Inactive Ingredients				
Ingredient Name		Strength		
Lactose Monohydrate (UNII: EWQ57Q8I5X)				
Cellulose, Microcrystalline (UNII: OP1R32D61U)				
Silicon Dioxide (UNII: ETJ7Z6XBU4)				
Magnesium Stearate (UNII: 70097M6I30)				
Product Characteristics				
Color	WHITE (to off White)	Score	2 pieces	
Shape	OVAL (OVAL)	Size	9mm	
Flavor		Imprint Code	P;10	
Contains				
Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:42543-141-01	100 in 1 BOTTLE, PLASTIC; Type 0: Not a Combination Product	07/07/2017	
Marketing Information				
Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date	
ANDA	ANDA207029	07/07/2017		

HYDROCORTISONE			
hydrocortisone tablet			
Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:42543-142
Route of Administration	ORAL		
Active Ingredient/Active Moiety			
Ingredient Name		Basis of Strength	Strength
Hydrocortisone (UNII: W14X0X7BPJ) (Hydrocortisone - UNII:W14X0X7BPJ)		Hydrocortisone	20 mg
Inactive Ingredients			
Ingredient Name		Strength	
Lactose Monohydrate (UNII: EWQ57Q8I5X)			

Cellulose, Microcrystalline (UNII: OP1R32D61U)	
Silicon Dioxide (UNII: ETJ7Z6XBU4)	
Magnesium Stearate (UNII: 70097M6I30)	

Product Characteristics

Color	WHITE (to off White)	Score	2 pieces
Shape	OVAL (OVAL)	Size	10mm
Flavor		Imprint Code	P;20
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:42543-142-01	100 in 1 BOTTLE, PLASTIC; Type 0: Not a Combination Product	07/07/2017	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA207029	07/07/2017	

Labeler - Vensun Pharmaceuticals, Inc. (078310501)

Registrant - Pharmaceutics International, Inc. (Pii) (878265586)

Establishment

Name	Address	ID/FEI	Business Operations
Pharmaceutics International, Inc. (Pii)		878265586	MANUFACTURE(42543-140, 42543-141, 42543-142) , ANALYSIS(42543-140, 42543-141, 42543-142)