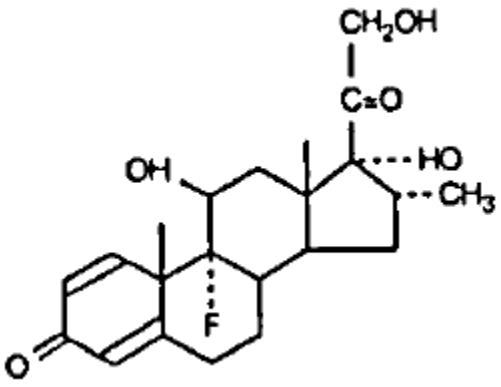
HEXADROL®

(dexamethasone elixir, USP)

DESCRIPTION

Hexadrol® (dexamethasone USP) is an analog of prednisolone. Its spectrum of anti-inflammatory activity is similar to other corticosteroids but it is clinically effective in much lower doses. Unlike earlier corticosteroids it has the added advantage of lacking significant mineralocorticoid activity so that salt and water retention are rarely observed. Dexamethasone, $C_{22}H_{29}FO_5$, has a molecular weight of 392.47, its chemical name is *9-Fluoro-11β,17,21-trihydroxy-16α-methylpregna-1,4-diene-3, 20-dione*. It is a white to practically white crystalline powder which is practically insoluble in water and melts at about 250°C (with decomposition).

It has the following structural formula:



Hexadrol® Elixir 0.5mg/5mL also contains: absolute alcohol, glycerine, methylparaben, natural & artificial cherry flavor, sorbitol solution, and D&C Red #33, as inactive ingredients.

CLINICAL PHARMACOLOGY

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 response to diverse stimuli.

INDICATIONS -

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 of osteoarthritis.

   Epicondylitis.

3. ***Collagen diseases:***

   During an exacerbation or as maintenance therapy in selected cases of:

   Systemic lupus erythematosus.

   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 anti-tuberculous 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. Miscellaneous:

Tuberculous meningitis with subarachnoid block or impending block when used concurrently with appropriate antituberculous chemotherapy.

Trichinosis with neurologic or myocardial involvement.

Diagnostic testing of adrenocortical hyperfunction.

CONTRAINDICATIONS

Systemic fungal infections.

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.

Ophthalmic Effects - 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.

Vaccination - 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.

Immunosuppression and Increased Risk of Infection - Corticosteroids, including HEXADROL, suppress the immune system and increase the risk of infection with any pathogen, including viral, bacterial, fungal, protozoan, or helminthic pathogens. Corticosteroids can:

- Reduce resistance to new infections
- Exacerbate existing infections
- Increase the risk of disseminated infections
- Increase the risk of reactivation or exacerbation of latent infections
- Mask some signs of infection

Corticosteroid-associated infections can be mild but can be severe and at times fatal. The rate of infectious complications increases with increasing corticosteroid dosages. Monitor for the development of infection and consider HEXADROL withdrawal or dosage reduction as needed.

Tuberculosis

If HEXADROL is used to treat a condition in patients with latent tuberculosis or tuberculin reactivity, reactivation of the disease may occur. Closely monitor such patients for reactivation. During prolonged HEXADROL therapy, patients with latent tuberculosis or tuberculin reactivity should receive chemoprophylaxis.

Varicella Zoster and Measles Viral Infections

Varicella and measles can have a serious or even fatal course in non-immune patients taking corticosteroids, including HEXADROL. In corticosteroid-treated patients who have not had these diseases or are non-immune, particular care should be taken to avoid exposure to varicella and measles:

- If a HEXADROL-treated patient is exposed to varicella, prophylaxis with varicella zoster immune globulin (VZIG) may be indicated. If varicella develops, treatment with antiviral agents may be considered.
- If a HEXADROL-treated patient is exposed to measles, prophylaxis with immunoglobulin (IG) may be indicated.

Hepatitis B Virus Reactivation

Hepatitis B virus reactivation can occur in patients who are hepatitis B carriers treated with immunosuppressive dosages of corticosteroids, including HEXADROL. Reactivation can also occur infrequently in corticosteroid-treated patients who appear to have resolved hepatitis B infection.

Screen patients for hepatitis B infection before initiating immunosuppressive (e.g., prolonged) treatment with HEXADROL. For patients who show evidence of hepatitis B infection, recommend consultation with physicians with expertise in managing hepatitis B regarding monitoring and consideration for hepatitis B antiviral therapy.

Fungal Infections

Corticosteroids, including HEXADROL, may exacerbate systemic fungal infections; therefore, avoid HEXADROL use in the presence of such infections unless HEXADROL is needed to control drug reactions. For patients on chronic HEXADROL therapy who

develop systemic fungal infections, HEXADROL withdrawal or dosage reduction is recommended.

Amebiasis

Corticosteroids, including HEXADROL, may activate latent amebiasis. Therefore, it is recommended that latent amebiasis or active amebiasis be ruled out before initiating HEXADROL in patients who have spent time in the tropics or patients with unexplained diarrhea.

Strongyloides Infestation

Corticosteroids, including HEXADROL, 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.

Cerebral Malaria

Avoid corticosteroids, including HEXADROL, in patients with cerebral malaria.

Kaposi's Sarcoma - Kaposi's sarcoma has been reported to occur in patients receiving corticosteroid therapy, most often for chronic conditions. Discontinuation of corticosteroids may result in clinical improvement of Kaposi's sarcoma.

Use 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.

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.

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.

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

Information tor Patients: Patients who are on immunosuppressant doses of corticosteroids should be warned to avoid exposure to chickenpox or measles and, if exposed, to obtain medical advice.

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.

Dermatologic.

Impaired wound healing.

Thin fragile skin.

Petechiae and ecchymoses.

Facial erythema.

Increased sweating.

Neurological.

Convulsions.

Increased intracranial pressure with papilledema (pseudotumor cerebri) usually after

treatment.

Vertigo.

Headache.

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

Posterior subcapsular cataracts.

Increased intraocular pressure.

Glaucoma.

Exophthalmos.

Metabolic.

Negative nitrogen balance due to protein catabolism.

DOSAGE AND ADMINISTRATION

The initial dosage of Hexadrol® (dexamethasone elixir, USP) may vary from 0.75 mg to 9.0 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, Hexadrol® (dexamethasone elixir, USP) 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 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 Hexadrol® (dexamethasone elixir, USP) 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.

Patients currently being treated with other corticosteroids may be transferred conveniently to this agent using the following dosage equivalents:

0.75 mg dexamethasone equivalent to	25 mg cortisone
	20 mg hydrocortisone
	5 mg prednisone or prednisolone
	4 mg methylprednisolone
	4 mg triamcinolone

HOW SUPPLIED

Hexadrol® (dexamethasone elixir, USP)

0.5mg/5mL elixir (alcohol 5%), bottles of 120 mL NDC XXXXX-XXX-XX

STORAGE:

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

CAUTION:

Federal law prohibits dispensing without prescription.

Manufactured for:

Aspen Global, Inc.
Grand Bay, Mauritius

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