

A-HYDROCORT®

Hydrocortisone Sodium Succinate for Injection, USP

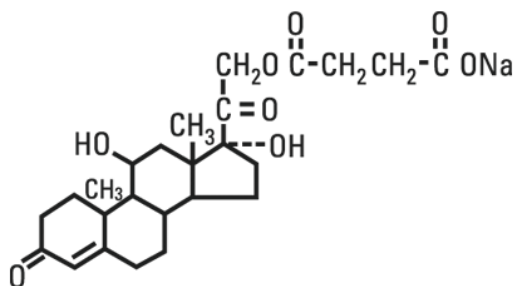
R_x only

For Intravenous or Intramuscular Administration

DESCRIPTION

A-Hydrocort sterile powder contains hydrocortisone sodium succinate as the active ingredient. Hydrocortisone sodium succinate, is a white, or nearly white, odorless, hygroscopic, amorphous solid. It is very soluble in water and in alcohol, very slightly soluble in acetone and insoluble in chloroform. The chemical name is pregn-4-ene-3,20-dione,21-(3-carboxy-1-oxopropoxy)-11,17-dihydroxy-, monosodium salt, (11β)- and its molecular weight is 484.52.

The structural formula is represented below:



Hydrocortisone sodium succinate is an anti-inflammatory adrenocortical steroid. This highly water-soluble sodium succinate ester of hydrocortisone permits the immediate intravenous administration of high doses of hydrocortisone in a small volume of diluent and is particularly useful where high blood levels of hydrocortisone are required rapidly.

A-Hydrocort sterile powder is available for intravenous or intramuscular administration.

100 mg – Vials containing hydrocortisone sodium succinate equivalent to 100 mg hydrocortisone, also 0.8 mg monobasic sodium phosphate anhydrous, 8.73 mg dibasic sodium phosphate anhydrous.

When necessary, the pH was adjusted with sodium hydroxide so that the pH of the reconstituted solution is within the USP specified range of 7 to 8.

For intravenous or intramuscular injection, vial should be reconstituted with Bacteriostatic Water for Injection or Bacteriostatic Sodium Chloride.

For intravenous infusion, vial should be reconstituted with Bacteriostatic Water for Injection.

CLINICAL PHARMACOLOGY

Hydrocortisone sodium succinate has the same metabolic and anti-inflammatory actions as hydrocortisone. When given parenterally and in equimolar quantities, the two compounds are equivalent in biologic activity. Following the intravenous injection of hydrocortisone sodium succinate, demonstrable effects are evident within one hour and persist for a variable period. Excretion of the administered dose is nearly complete within 12 hours. Thus, if constantly high blood levels are required, injections should be made every 4 to 6 hours. This preparation is also rapidly absorbed when administered intramuscularly and is excreted in a pattern similar to that observed after intravenous injection.

INDICATIONS AND USAGE

When oral therapy is not feasible, and the strength, dosage form and route of administration of the drug reasonably lend the preparation to the treatment of the condition, A-Hydrocort sterile powder is indicated for intravenous or intramuscular use in the following conditions:

1. Endocrine Disorders

- Primary or secondary adrenocortical insufficiency (hydrocortisone or cortisone is the drug of choice; synthetic analogs may be used in conjunction with mineralocorticoids where applicable; in infancy, mineralocorticoid supplementation is of particular importance)
- Acute adrenocortical insufficiency (hydrocortisone or cortisone is the drug of choice; mineralocorticoid supplementation may be necessary, particularly when synthetic analogs are used)
- Preoperatively and in the event of serious trauma or illness, in patients with known adrenal insufficiency or when adrenocortical reserve is doubtful
- Shock unresponsive to conventional therapy if adrenocortical insufficiency exists or is suspected
- 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:

- Post-traumatic osteoarthritis
- Synovitis of osteoarthritis
- Rheumatoid arthritis, including juvenile rheumatoid arthritis (selected cases may require low-dose maintenance therapy)
- Acute and subacute bursitis
- Epicondylitis
- Acute nonspecific tenosynovitis
- Acute gouty arthritis
- Psoriatic arthritis
- Ankylosing spondylitis

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
- Severe erythema multiforme (Stevens-Johnson syndrome)
- Exfoliative dermatitis
- Bullous dermatitis herpetiformis
- Severe seborrheic dermatitis
- Severe psoriasis
- Mycosis fungoides

5. Allergic States

Control of severe or incapacitating allergic conditions intractable to adequate trials of conventional treatment in:

- Bronchial asthma
- Contact dermatitis
- Atopic dermatitis
- Serum sickness
- Seasonal or perennial allergic rhinitis
- Drug hypersensitivity reactions
- Urticarial transfusion reactions
- Acute noninfectious laryngeal edema (epinephrine is the drug of first choice)

6. Ophthalmic Diseases

Severe acute and chronic allergic and inflammatory processes involving the eye, such as:

- Herpes zoster ophthalmicus
- Iritis, iridocyclitis
- Chorioretinitis
- Diffuse posterior uveitis and choroiditis
- Optic neuritis
- Sympathetic ophthalmia
- Anterior segment inflammation
- Allergic conjunctivitis
- Allergic corneal marginal ulcers
- Keratitis

7. Gastrointestinal Diseases

To tide the patient over a critical period of the disease in:

- Ulcerative colitis (systemic therapy)
- Regional enteritis (systemic therapy)

8. Respiratory Diseases

- Symptomatic sarcoidosis
- Berylliosis
- Fulminating or disseminated pulmonary tuberculosis when used concurrently with appropriate antituberculous chemotherapy
- Loeffler's syndrome not manageable by other means
- Aspiration pneumonitis

9. Hematologic Disorders

- Acquired (autoimmune) hemolytic anemia
- Idiopathic thrombocytopenic purpura in adults (IV only; IM administration is contraindicated)
- Secondary thrombocytopenia in adults
- Erythroblastopenia (RBC anemia)
- Congenital (erythroid) hypoplastic anemia

10. Neoplastic Diseases

For palliative management of:

- Leukemias and lymphomas in adults
- Acute leukemia of childhood

11. Edematous States

To induce diuresis or remission of proteinuria in the nephrotic syndrome, without uremia, of the idiopathic type or that due to lupus erythematosus

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

The use of A-Hydrocort sterile powder is contraindicated in premature infants because the 100 mg vial is reconstituted with Bacteriostatic Water for Injection or Bacteriostatic Sodium Chloride Injection containing benzyl alcohol. Benzyl alcohol has been reported to be associated with a fatal "Gasping Syndrome" in premature infants. A-Hydrocort sterile powder is also contraindicated in systemic fungal infections and patients with known hypersensitivity to the product and its constituents.

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. 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 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 A-Hydrocort sterile powder 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 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.

Because rare instances of anaphylactoid reactions (eg, bronchospasm) have occurred in patients receiving parenteral corticosteroid therapy, appropriate precautionary measures should be taken prior to administration, especially when the patient has a history of allergy to any drug.

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 reinstated. Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticoid should be administered concurrently.

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 for fear of 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 must 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, also in 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 followed.

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 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

Dermatologic

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

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 of insulin or oral hypoglycemic agents in diabetics

Ophthalmic

Posterior subcapsular cataracts, Increased intraocular pressure, Glaucoma, Exophthalmos

Metabolic

Negative nitrogen balance due to protein catabolism

The following additional reactions are related to parenteral corticosteroid therapy:

Allergic, anaphylactic or other hypersensitivity reactions, Hyperpigmentation or hypopigmentation, Subcutaneous and cutaneous atrophy, Sterile abscess

DOSAGE AND ADMINISTRATION

This preparation may be administered by intravenous injection, by intravenous infusion, or by intramuscular injection, the preferred method for initial emergency use being intravenous injection. Following the initial emergency period, consideration should be given to employing a longer acting injectable preparation or an oral preparation.

Therapy is initiated by administering A-Hydrocort sterile powder intravenously over a period of 30 seconds (eg, 100 mg) to 10 minutes (eg, 500 mg or more). In general, high-dose corticosteroid therapy should be continued only until the patient's condition has stabilized – usually not beyond 48 to 72 hours. Although adverse effects associated with high-dose, short-term corticoid therapy are uncommon, peptic ulceration may occur. Prophylactic antacid therapy may be indicated.

When high-dose hydrocortisone therapy must be continued beyond 48-72 hours, hypernatremia may occur. Under such circumstances it may be desirable to replace hydrocortisone sodium succinate with a corticoid such as methylprednisolone sodium succinate which causes little or no sodium retention.

The initial dose of A-Hydrocort sterile powder is 100 mg to 500 mg, depending on the severity of the condition. This dose may be repeated at intervals of 2, 4 or 6 hours as indicated by the patient's response and clinical condition. While the dose may be reduced for infants and children, it is governed more by the severity of the condition and response of the patient than by age or body weight but should not be less than 25 mg daily.

Patients subjected to severe stress following corticosteroid therapy should be observed closely for signs and symptoms of adrenocortical insufficiency.

Corticoid therapy is an adjunct to, and not a replacement for, conventional therapy.

Preparation of Solutions

100 mg – For intravenous or intramuscular injection, prepare solution by aseptically adding **not more than 2 mL** of Bacteriostatic Water for Injection or Bacteriostatic Sodium Chloride Injection to the contents of one vial. **Further dilution is not necessary for intravenous or intramuscular injection. For intravenous infusion**, first prepare solution by adding **not more than 2 mL** of Bacteriostatic Water for Injection to the vial; this solution may then be added to 100 to 1000 mL of the following: 5% dextrose in water (or isotonic saline solution or 5% dextrose in isotonic saline

solution if patient is not on sodium restriction). In cases where administration of a small volume of fluid is desirable, 100 mg of hydrocortisone sodium succinate may be added to 50 mL of the above diluents. The resulting solutions are stable for at least 4 hours and may be administered either directly or by IV piggyback.

When reconstituted as directed, pH's of the solutions range from 7 to 8 and the tonicities are: 100 mg vial, .36 osmolar. (Isotonic saline = .28 osmolar.)

HOW SUPPLIED

A-Hydrocort sterile powder is available in the following package:

NDC	Container	Concentration
0409-4856-15	Single-Dose Vial	100 mg

STORAGE CONDITIONS

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

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

Use solution only if it is clear. Unused solution should be discarded after 3 days.

Lyophilized in container.

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