121.00 mm

Injection

Hicartif

(Hydrocortisone Sodium Succinate)

ہائی کارٹف انجیکشن

(ہائیڈروکارٹیسون سوڈیم سکسینیٹ)

COMPOSITION

Hicartif Injection 100mg
Each vial contains:
Hydrocortisone (as sodium succinate).....100mg
(USP specifications)

Hicartif Injection 250mg
Each vial contains:
Hydrocortisone (as sodium succinate).....250mg
(USP specifications)

Hicartif Injection 500mg
Each vial contains:
Hydrocortisone (as sodium succinate).....500mg
(USP specifications)

DESCRIPTION

HICARTIF Sterile Powder is an anti-inflammatory glucocorticoid which contains hydrocortisone sodium succinate as the active ingredient. It is the main glucocorticoid secreted by the adrenal cortex. Its synthetic counterpart is used, either as an injection or topically, in the treatment of inflammation, allergy, collagen diseases, asthma, adrenocortical deficiency, shock, and some neoplastic conditions.

INDICATIONS

HICARTIF Sterile Powder is indicated as follows:

Allergic states:
Control of severe or incapacitating allergic conditions intractable to adequate trials of conventional treatment in asthma, atopic dermatitis, contact dermatitis, drug hypersensitivity reactions, perennial or seasonal allergic rhinitis, serum sickness, transfusion reactions.

Dermatologic diseases:
Bullous dermatitis herpetiformis, exfoliative erythroderma, mycosis fungoides, pemphigus, severe erythema multiforme (Stevens-Johnson syndrome).

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), congenital adrenal hyperplasia, hypercalcemia associated with cancer, nonsuppurative thyroiditis.

Gastrointestinal diseases:
To tide the patient over a critical period of the disease in regional enteritis (systemic therapy) and ulcerative colitis.

Hematologic disorders:
Acquired (autoimmune) hemolytic anemia, congenital (erythroid) hypoplastic anemia (Diamond-Blackfan anemia), idiopathic thrombocytopenic purpura in adults (intravenous administration only; intramuscular administration is contraindicated), pure red cell aplasia, selected cases of secondary thrombocytopenia.

Miscellaneous:
Trichinosis with neurologic or myocardial involvement, tuberculous meningitis with subarachnoid block or impending block when used concurrently with appropriate antituberculous chemotherapy.

Neoplastic diseases:
For the palliative management of leukemias and lymphomas.

Nervous System:
Acute exacerbations of multiple sclerosis; cerebral edema associated with primary or metastatic brain tumor, or craniotomy.

Ophthalmic diseases:
Sympathetic ophthalmia, uveitis and ocular inflammatory conditions unresponsive to topical corticosteroids.

Renal diseases:
To induce diuresis or remission of proteinuria in idiopathic nephrotic syndrome or that due to lupus erythematosus.

Respiratory diseases:
Berylliosis, fulminating or disseminated pulmonary tuberculosis when used concurrently with appropriate anti-tuberculous chemotherapy, idiopathic eosinophilic pneumonias, symptomatic sarcoidosis.

Rheumatic disorders:
As adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in acute gouty arthritis; acute rheumatic carditis; ankylosing spondylitis; psoriatic arthritis; rheumatoid arthritis, including juvenile rheumatoid arthritis (selected cases may require low-dose maintenance therapy). For the treatment of dermatomyositis, temporal arteritis, polymyositis, and systemic lupus erythematosus.

CLINICAL PHARMACOLOGY

Glucocorticoids, naturally occurring and synthetic, are adrenocortical steroids that are readily absorbed from the gastrointestinal tract. Naturally occurring glucocorticoids (hydrocortisone and cortisone), which also have saltretaining properties, are used as replacement therapy in adrenocortical deficiency states. Their synthetic analogs are primarily used for their anti-inflammatory effects in disorders of many organ systems. 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. The 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. 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. Glucocorticoids cause profound and varied metabolic effects. In addition, they modify the body's immune response to diverse stimuli.

DOSAGE & ADMINISTRATION

For intravenous or intramuscular use.
Because of possible physical incompatibilities, HICARTIF should not be diluted or mixed with other solutions.
Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. 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 HICARTIF Sterile Powder intravenously over a period of 30 seconds (e.g., 100 mg) to 10 minutes (e.g., 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. When high dose hydrocortisone therapy must be continued beyond 48–72 hours, hypernatremia may occur. Under such circumstances it may be desirable to replace HICARTIF with a corticoid such as methylprednisolone sodium succinate which causes little or no sodium retention.
The initial dose of HICARTIF Sterile Powder is 100 mg to 500 mg, depending on the specific disease entity being treated. However, in certain overwhelming, acute, life threatening situations, administration in dosages exceeding the usual dosages may be justified and may be in multiples of the oral dosages. This dose may be repeated at intervals of 2, 4 or 6 hours as indicated by the patient's response and clinical condition.
In the treatment of acute exacerbations of multiple sclerosis, daily doses of 800 mg of hydrocortisone for a week followed by 320 mg every other day for one month are recommended.

PREPARATION OF SOLUTIONS:

For 100mg & 250mg:
For intravenous or intramuscular injection: Prepare solution by aseptically adding not more than 2 ml of water for Injection to the contents of one vial.
For intravenous infusion: First prepare solution by adding not more than 2ml of water for injection to the vial;this solution may then be added to 100 to 1000ml 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).

For 500mg:
For intravenous or intramuscular injection: Prepare solution by aseptically adding not more than 4ml of water for Injection to the contents of one vial.
For intravenous infusion: First prepare solution by adding not more than 4ml of water for injection to the vial;this solution may then be added to 100 to 1000ml 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).
This product, like many other steroid formulations, is sensitive to heat. Therefore, it should not be autoclaved when it is desirable to sterilize the exterior of the vial.

WARNINGS & PRECAUTIONS

General:
Injection of HICARTIF may result in dermal and/or subdermal changes forming depressions in the skin at the injection site. In order to minimize the incidence of dermal and subdermal atrophy, care must be exercised not to exceed recommended doses in injections.
Injection into the deltoid muscle should be avoided because of a high incidence of subcutaneous atrophy. Rare instances of anaphylactoid reactions have occurred in patients receiving corticosteroid therapy. Increased dosage of rapidly acting corticosteroids is indicated in patients on corticosteroid therapy subjected to any unusual stress before, during, and after the stressful situation.
High doses of systemic corticosteroids, including HICARTIF, should not be used for the treatment of traumatic brain injury.

Cardio-renal:
Average and large doses of corticosteroids 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.

Endocrine:
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. Metabolic clearance of corticosteroids is decreased in hypothyroid patients and increased in hyperthyroid patients. Changes in thyroid status of the patient may necessitate adjustment in dosage.

Fungal infections:
Corticosteroids may exacerbate systemic fungal infections and therefore should not be used in the presence of such infections unless they are needed to control drug reactions.

Tuberculosis:
The use of corticosteroids 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 anti-tuberculous 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.

Vaccination:
Administration of live or live, attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of corticosteroids. Killed or inactivated vaccines may be administered. However, the response to such vaccines cannot be predicted. Immunization procedures may be undertaken in patients who are receiving corticosteroids as replacement therapy, e.g., for Addison's disease.

Viral infections:
Chicken pox and measles can have a more serious or even fatal course in pediatric and adult patients on corticosteroids. In pediatric and adult patients who have not had these diseases, particular care should be taken to avoid exposure.

Musculoskeletal:
Corticosteroids decrease bone formation and increase bone resorption both through their effect on calcium regulation (i.e.,

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decreasing absorption and increasing excretion) and inhibition of osteoblast function. This, together with a decrease in the protein matrix of the bone secondary to an increase in protein catabolism, and reduced sex hormone production, may lead to inhibition of bone growth in pediatric patients and the development of osteoporosis at any age. Special consideration should be given to patients at increased risk of osteoporosis (i.e., postmenopausal women) before initiating corticosteroid therapy. Local injection of a steroid into a previously infected site is not usually recommended.

Gastrointestinal:
Steroids should be used with caution in active or latent peptic ulcers, diverticulitis, fresh intestinal anastomoses, and nonspecific ulcerative colitis, since they may increase the risk of a perforation. Signs of peritoneal irritation following gastrointestinal perforation in patients receiving corticosteroids may be minimal or absent. There is an enhanced effect due to increased metabolism of corticosteroids in patients with cirrhosis.

Ophthalmic:
Intraocular pressure may become elevated in some individuals. If steroid therapy is continued for more than 6 weeks, intraocular pressure should be monitored.

Information for Patients:
Patients should be warned not to discontinue the use of corticosteroids abruptly or without medical supervision, to advise any medical attendants that they are taking corticosteroids and to seek medical advice at once should they develop fever or other signs of infection. Persons who are on 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.

DRUG INTERACTIONS

Aminoglutethimide: Aminoglutethimide may lead to a loss of corticosteroid-induced adrenal suppression.
Amphotericin B injection and potassium-depleting agents: When corticosteroids are administered concomitantly with potassium-depleting agents (i.e., amphotericin-B, diuretics), patients should be observed closely for development of hypokalemia. There have been cases reported in which concomitant use of amphotericin B and hydrocortisone 8 was followed by cardiac enlargement and congestive heart failure.
Antibiotics: Macrolide antibiotics have been reported to cause a significant decrease in corticosteroid clearance.
Anticholinesterases: Concomitant use of anticholinesterase agents and corticosteroids may produce severe weakness in patients with myasthenia gravis. If possible, anticholinesterase agents should be withdrawn at least 24 hours before initiating corticosteroid therapy.
Anticoagulants, oral: Coadministration of corticosteroids and warfarin usually results in inhibition of response to warfarin, although there have been some conflicting reports. Therefore, coagulation indices should be monitored frequently to maintain the desired anticoagulant effect.
Antidiabetics: Because corticosteroids may increase blood glucose concentrations, dosage adjustments of antidiabetic agents may be required.
Anti-tubercular drugs: Serum concentrations of isoniazid may be decreased.
Cholestyramine: Cholestyramine may increase the clearance of corticosteroids.
Cyclosporine: Increased activity of both cyclosporine and corticosteroids may occur when the two are used concurrently. Convulsions have been reported with this concurrent use.
Digitalis glycosides: Patients on digitalis glycosides may be at increased risk of arrhythmias due to hypokalemia. **Estrogens, including oral contraceptives:** Estrogens may decrease the hepatic metabolism of certain corticosteroids, thereby increasing their effect.
Hepatic Enzyme Inducers (e.g., barbiturates, phenytoin, carbamazepine, and rifampin): Drugs which induce cytochrome P450 3A4 enzyme activity may enhance the metabolism of corticosteroids and require that the dosage of the corticosteroid be increased.
Hepatic Enzyme Inhibitors (e.g., ketoconazole, macrolide antibiotics such as erythromycin and troleandomycin): Drugs which inhibit cytochrome P450 3A4 have the potential to result in increased plasma concentrations of corticosteroids.
Ketoconazole: Ketoconazole has been reported to significantly decrease the metabolism of certain corticosteroids by up to 60%, leading to an increased risk of corticosteroid side effects.
Nonsteroidal anti-inflammatory agents (NSAIDS): Concomitant use of aspirin (or other nonsteroidal anti-inflammatory agents) and corticosteroids increases the risk of gastrointestinal side effects. Aspirin should be used cautiously in conjunction with corticosteroids in hypoprothrombinemia. The clearance of salicylates may be increased with concurrent use of corticosteroids.
Skin tests: Corticosteroids may suppress reactions to skin tests.
Vaccines: Patients on prolonged corticosteroid therapy may exhibit a diminished response to toxoids and live or inactivated vaccines due to inhibition of antibody response. Corticosteroids may also potentiate the replication of some organisms contained in live attenuated vaccines. Routine administration of vaccines or toxoids should be deferred until corticosteroid therapy is discontinued if possible
Carcinogenesis, Mutagenesis, Impairment of Fertility: No adequate studies have been conducted in animals to determine whether corticosteroids have a potential for carcinogenesis or mutagenesis. Steroids may increase or decrease motility and number of spermatozoa in some patients.
Pregnancy:
Teratogenic effects: Pregnancy Category C. Corticosteroids have been shown to be teratogenic in many species when given in doses equivalent to the human dose.
Nursing Mothers:
Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. Because of the potential for serious adverse reactions in nursing infants from corticosteroids, a decision should be made whether to continue nursing, or discontinue the drug, taking into account the importance of the drug to the mother.

SIDE EFFECTS:

Allergic reactions: Allergic or hypersensitivity reactions, anaphylactoid reaction, anaphylaxis, angioedema.
Cardiovascular: Bradycardia, cardiac arrest, cardiac arrhythmias, cardiac enlargement, circulatory collapse, congestive heart failure, fat embolism, hypertension, hypertrophic cardiomyopathy in premature infants, myocardial rupture following recent myocardial infarction, pulmonary edema, syncope, tachycardia, thromboembolism, thrombophlebitis, vasculitis. Dermatologic: Acne, allergic dermatitis, burning or tingling (especially in the perineal area, after intravenous injection), cutaneous and subcutaneous atrophy, dry scaly skin, ecchymoses and petechiae, edema, erythema, hyperpigmentation, hypopigmentation, impaired wound healing, increased sweating, rash, sterile abscess, striae, suppressed reactions to skin tests, thin fragile skin, thinning scalp hair, urticaria.
Endocrine: Decreased carbohydrate and glucose tolerance, development of cushingoid state, glycosuria, hirsutism, hypertrichosis, increased requirements for insulin or oral hypoglycemic agents in diabetes, manifestations of latent diabetes mellitus, menstrual irregularities, secondary adrenocortical and pituitary unresponsiveness (particularly in times of stress, as in trauma, surgery, or illness), suppression of growth in pediatric patients.
Fluid and electrolyte disturbances: Congestive heart failure in susceptible patients, fluid retention, hypokalemic alkalosis, potassium loss, sodium retention.
Gastrointestinal: Abdominal distention, bowel/bladder dysfunction (after intrathecal administration), elevation in serum liver enzyme levels (usually reversible upon discontinuation), hepatomegaly, increased appetite, nausea, pancreatitis, peptic ulcer with possible perforation and hemorrhage, perforation of the small and large intestine (particularly in patients with inflammatory bowel disease), ulcerative esophagitis.
Metabolic: Negative nitrogen balance due to protein catabolism.
Musculoskeletal: Aseptic necrosis of femoral and humeral heads, Charcot-like arthropathy, loss of muscle mass, muscle weakness, osteoporosis, pathologic fracture of long bones, postinjection flare (following intra-articular use), steroid myopathy, tendon rupture, vertebral compression fractures.
Neurologic/Psychiatric: Convulsions, depression, emotional instability, euphoria, headache, increased intracranial pressure with papilledema (pseudotumor cerebri) usually following discontinuation of treatment, insomnia, mood swings, neuritis, neuropathy, paresthesia, personality changes, psychic disorders, vertigo. Arachnoiditis, meningitis, paraparesis/paraplegia, and sensory disturbances have occurred after intrathecal administration.
Ophthalmic: Exophthalmoses, glaucoma, increased intraocular pressure, posterior subcapsular cataracts, and rare instances of blindness associated with periocular injections.
Other: Abnormal fat deposits, decreased resistance to infection, hiccups, increased or decreased motility and number of spermatozoa, injection site infections following nonsterile administration, malaise, moon face, and weight gain.

CONTRAINDICATIONS

HICARTIF Sterile Powder is contraindicated in systemic fungal infections and patients with known hypersensitivity to the product and its constituents. Intramuscular corticosteroid preparations are contraindicated for idiopathic thrombocytopenic purpura. HICARTIF Sterile Powder is contraindicated for intrathecal administration. Reports of severe medical events have been associated with this route of administration.

OVERDOSE

Treatment of acute over dosage is by supportive and symptomatic therapy. For chronic over dosage in the face of severe disease requiring continuous steroid therapy, the dosage of the corticosteroid may be reduced only temporarily, or alternate day treatment may be introduced.

STORAGE & INSTRUCTIONS:

Store between 20-25°C. Protect from heat, sunlight and moisture. Do not freeze. Keep away from the reach of children.
Constituted solution prepared from Hydrocortisone Sodium Succinate for Injection is suitable for use only if it is clear, and that the solution is to be discarded after 3 days.
To be sold on the prescription of a registered medical practitioner only.

HOW SUPPLIED

Hicartif Injection 100mg
1 vial,25 vials
Hicartif Injection 250mg
1 vial,25 vials
Hicartif Injection 500mg
1 vial,25 vials

خوراک وطریقہ استعمال:

ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

ہدایت:

دوا کو ۲۰-۲۵ ڈگری سینٹی گریڈ درجہ حرارت کے درمیان رکھیں۔ دھوپ، گرمی، نمی اور منجمد ہونے سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔ تیار کردہ محلول ۳ دن تک قابل استعمال رہتا ہے۔ صرف مستند ڈاکٹر کے نسخہ پر فروخت کریں۔

Manufactured by:
PHARMASOL
PRIVATE LIMITED
Plot # 549,Sundar Industrial Estate,
Lahore, Pakistan.