HYDROCORTISONE

Rx HYZONATE

100 mg, 250 mg, 500 mg

Powder for Injection

(I.M / I.V)

CORTICOSTEROID

INTRODUCTION:
Hydrocortisone Sodium Succinate (Hyzonate) is mono Sodium salt of Hydroxy Cortisone 21-(Hydrogen Succinate). Its Empirical formula is $C_{25}H_{33}NaO_8$.

PRODUCT DESCRIPTION:
Sterile white powder filled in clear glass vial.

FORMULATIONS:
Each vial of 100 mg contains :
Hydrocortisone, USP (as Sodium Succinate) ..... 100 mg

Each vial of 250 mg contains :
Hydrocortisone, USP (as Sodium Succinate) ..... 250 mg

Each vial of 500 mg contains :
Hydrocortisone, USP (as Sodium Succinate) ..... 500 mg

PHARMACOLOGY:
1. Pharmacodynamics:
The therapeutic activity of Hydrocortisone Sodium Succinate (Hyzonate) sterile powder is qualitatively identical to that of Hydrocortisone. Glucocorticoids diffuse across cell membrane and complex with specific cytoplasmic receptors. These complexes then enter the cell nucleus, bind to DNA (chromatin) stimulate transcription of mRNA and subsequent protein synthesis of various enzymes thought to be ultimately responsible for the effects of systemic use of glucocorticoids. Maximum pharmacologic activity of corticosteroids lays behind peak blood levels, suggesting that most effects of the drug results from modification of enzyme activity rather than from direct action by the drug.

2. Pharmacokinetics:
Peak plasma levels are obtained approximately 30 to 60 minutes. Approximately 40 to 90% of Hydrocortisone is bound to plasma proteins. The largest amount is bound to a globulin (transcortin) and only a small amount is bound to albumin.

Free, unbound fraction of the hormone determines biological activity while the bound fraction serves as reserve. Hydrocortisone is mainly metabolized in the liver. 22 to 30% of the I.V or I.M. administered doses are excreted through the urine in 24 hours. Elimination of the administered dose is nearly completed within 12 hours. Thus if constantly high blood levels are required I.V or I.M injections should be made every 4 to 6 hours.

INDICATIONS:
Treatment of adrenocortical insufficiency; shock, hypersensitivity reactions; inflammatory bowel disease, ulcerative colitis, proctitis, proctosigmoiditis and rheumatic disease.

CONTRA-INDICATIONS:
Hydrocortisone (as Sodium Succinate) is contraindicated where there is known hypersensivity to the active subtance or any of the excipients and in systemic fungal infection unless specific anti-infective therapy is employed. Administration of live or live attenuated vaccine is contraindicated in patients receiving immunosuppressive doses of corticosteriods.

REPORTING OF SUSPECTED ADVERSE REACTIONS:
To allow continued monitoring of benefit/risk balance of the medicinal product, reporting of suspected adverse reaction is necessary. Healthcare professionals are encouraged to report any suspected adverse reactions directly to the importer/distributor and/or to FDA: www.fda.gov.ph. Patients are advised to seek immediate medical attention at the first sign/s of adverse reaction.

ADVERSE EFFECTS:
FLUID AND ELECTROLYTE DISTURBANCE
Salt and water retention, congestive heart failure in susceptible patients, Potassium loss, Hypokalemic alkalosis.

MUSCULOSKELETAL
Steroid myopathy, Muscle weakness, Osteoporosis, Pathological fractures, Vertebral Compression fractures Aseptic necrosis.

GASTROINTESTINAL
Peptic ulceration with possible perforation and hemorrhage, Gastric hemorrhage , Pancreatitis Esophagitis, Perforation of the bowel

DERMATOLOGIC
Impaired wound healing , Petechiae and ecchymosis, Thin fragile skin,

METABOLIC
Negative nitrogen balance due to protein catabolism

NEUROLOGICAL
Increased intracranial pressure, Pseudotumor cerebri, Psychic derangements, Seizures

ENDOCRINE
Menstrual irregularities, Development of Cushingoid state, Suppression of pituitary adrenal axis,
Decreased carbohydrate tolerance, Manifestation of latent diabetes mellitus,
Increased requirements for insulin or oral hypoglycemic agents in diabetics, Suppression of growth in children

OPHTHALMIC
Posterior subcapsular cataracts, Increased intraocular pressure,

IMMUNE SYSTEM
Masking of infections, Latent infections becoming active , Opportunistic infections. Hypersensitivity reactions including anaphylaxis, may suppress reactions to skin tests

PREPARATION OF SOLUTIONS:
Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration.

100 mg Vial / 250 mg Vial :
For intravenous or intramuscular injection, prepare solution by aseptically adding not more than 2 ml of water for injection or Sodium Chloride solution to the contents of one 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).

500 mg Vial :
For intravenous or intramuscular injection, prepare solution by aseptically adding not more than 5 ml of water for injection or Sodium Chloride solution to the contents of one vial.

For intravenous infusion, first prepare solution by adding not more than 5 ml of water for injection to the vial. This solution may than be added to 500 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).

DOSAGE AND ADMINISTRATION:
Hydrocortisone Sodium Succinate (Hyzonate) may be administered by intravenous injection, by intravenous infusion or by intramuscular injection, the preferred method for initial emergency use is intravenous injection. Therapy is initiated by administering Hydrocortisone Sodium Succinate (Hyzonate) Sterile Powder intravenously over a period of 30 seconds (e.g. Hydrocortisone sodium succinate equivalent to 100 mg of Hydrocortisone) to 10 minutes (e.g. 500 mg or more). In general, high-dose corticosteroid therapy should be continued 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 (Hyzonate) sterile powder with corticoid product such as one containing methylprednisolone sodium succinate which causes little or no sodium retention.

The initial dose of Hydrocortisone Sodium Succinate (Hyzonate) Sterile Powder is 100 mg to 500 mg or more (hydrocortisone equivalent to hydrocortisone sodium Succinate) 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 responses 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. The maximum dose being 15 mg/kg. Patients subjected to severe stress following corticosteroid therapy should be observed closely for signs and symptoms of adrenocortical insufficiency.
Corticosteroid therapy is an adjunct to, and not a replacement for conventional therapy

SPECIAL PRECAUTIONS:
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.

Average and large doses of Hydrocortisone can cause elevation of blood pressure, salt and water retention and increased excretion of potassium. 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
The use of Hydrocortisone Sodium Succinate (Hyzonate) 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 antituberculosis regimen.

If corticosteroid are indicated in patients with latent tuberculosis or tuberculin reactivity, close observation is necessary because reactivation of the disease may occur. During prolonged corticosteroid therapy these patients should receive chemoprophylaxis. Because rare instances of anaphylactoid reactions (e.g. bronchospasm) have occurred in patients receiving parenteral corticosteroid therapy.

The product contains benzyl alcohol which has been reported to be associated with "Gasping Syndrome" in premature infants.

Corticosteroid should be used cautiously in patients with ocular herpes simplex

Psychiatric derangements may appear when corticosteroids are used,. Also existing psychotic tendencies may be aggravated.

Steroids should be used with caution in nonspecific ulcerative colitis, if there is a probability of impending perforation abscess or other pyogenic infections,

There is no evidence that corticosteroids are carcinogenic, mutagenic or impair fertility. Growth may be suppressed in children receiving long-term, daily-divided dose glucocorticoid therapy. The use of such a regimen should be restricted to the most serious indications.

DRUG INTERACTIONS:
1. Convulsions have been reported with concurrent use of corticosteriods and ciclosporin. Since concurrent administration of these agents results in a mutual inhibition of metabolism, it is possible thtat convulsions and other effects associated with the individual use of either drug may be more apt to occur.

2. Drugs that induce hepatic enzymes, such as rifampicin, rifabutin, carbamazepine, phenobarbitone, phenytoin, primidone and aminoglutethimide enhance the metabolism of corticosteroids and its therapeutic effects may be reduced.

3. Drugs which inhibit the CYP3A4 enzyme such as cimetidine, erythromycin, ketoconazole, itraconazole, diltiazen and mibefradil may decrease the rate of metablism of corticosteriods and hence increase the serum concentration.

4. Steriod may reduce the effects of anticholiesterases in myasthenia gravis. The desired effects of hypoglycaemic agents (including insulin), anti-hypertensive and diuretics are antagonised by corticosteroid and the hypokalaemic effects of acetazolamide loop diuretics thiazide diuretics and carbenxolone are enchanced.

5. The efficacy of coumarin anticoagulants may be enhanced by concurrent corticosteriod therapy and close monitoring of the INR or prothrombin time is required to avoid spontaneous bleeding.

6. The renal clearance of salicylates is increased by corticosteroid and steroid withdrawal may result in salicylate intoxication. Salicylate and non steroidal anti-inflammatory agents should be used cautiously in conjunction with corticosteroid in hypothrombinaemia.

7. Steroids have been reported to interact with neuromuscular blocking agents such as pancuronium with partial reversal of the neuromuscular block.

PREGNANCY AND LACTATION:
Adequate human reproductive studies have not been done with corticosteroids. Therefore the use of this drug in pregnancy, nursing mothers, or women of child bearing potential requires that the benefits of the drug be carefully weighed against the potential risk to the mother, embryo or fetus. Corticosteroids readily cross the placenta. Infants born of mother who have received substantial doses of corticosteroids during pregnancy must be carefully observed and evaluated for signs of adrenal insufficiency. There are no known effects of corticosteroids on labor and delivery. Corticosteroids are excreted in breast milk,

OVER DOSAGE:
There is no clinical syndrome of acute over dosage with Hydrocortisone Sodium Succinate (Hyzonate), Hydrocortisone is dialyzable.

STORAGE:
- Store at temperatures not exceeding 30°C.
- Reconstituted solution may kept in refrigerator for 48 hours
- Discard the unused reconstituted solution after 48 hours.

CAUTION:
Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

AVAILABILITY:
100 mg vial: USP Type II Glass Vial with Aluminium Seal, Rubber Stopper and Red Protective Cap x 1's.
FDA Registration Number : DRP-5107
Date of First Authorization: 28 May 2021

250 mg vial: USP Type I Glass Vial with Aluminium Seal, Rubber Stopper and Red Protective Cap.

FDA Registration Number: DRP-4413
Date of Renewal of Authorization: 03 August 2020

500 mg vial: USP Type I Glass Vial with Aluminium Seal, Rubber Stopper and Red Protective Cap.
FDA Registration Number: DRP-4414
Date of Renewal of Authorization: 19 June 2020
Date of Revision of Package Insert: 27 August 2022

AMSON

Manufactured by:
AMSON VACCINES & PHARMA (PVT) LTD.
154, Industrial Triangle, Kahuta Road, Islamabad - Pakistan.

SAHAR

Imported & Distributed by:
SAHAR INTERNATIONAL TRADING INC.
354 Aguirre Ave. Phase III BF Homes Parañaque City

02-18-0081E