Mepcort Injection
Methylprednisolone Sodium Succinate

Presentation
Mepcort 500 mg IM/IV Injection: Each vial contains 500 mg of Methylprednisolone as Methylprednisolone Sodium Succinate USP.
Mepcort 1 gm IM/IV Injection: Each vial contains 1 gm of Methylprednisolone as Methylprednisolone Sodium Succinate USP.

Description
Methylprednisolone, a naturally occurring glucocorticoid (hydrocortisone and cortisone), which has also salt-retaining properties, is used as replacement therapy in adrenocortical deficiency states. This synthetic analogs is primarily used for their potent anti-inflammatory effects in disorders of many organ systems.
The intravenous injection of Methylprednisolone 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.
Its anti-inflammatory potency is greater than prednisolone in the ratio of 5 to 4. It has only minimal mineralocorticoid properties and has less tendency than prednisolone to induce sodium and water retention. It influences carbohydrate, protein, fat and purine metabolism, electrolyte and water balance, and the functional capacities of the cardiovascular system, the kidney, the skeletal muscle, nervous system and other organs and tissues. It exerts a suppressive effect on the immune response.

Indications
Mepcort IM/IV is indicated in the following conditions:
• *Endocrine disorder*
Primary or secondary adrenocortical insufficiency, acute adrenocortical insufficiency, shock unresponsive to conventional, congenital adrenal hyperplasia, Nonsuppurative thyroiditis. Hypercalcemia associated with cancer.
• *Rheumatic disorder*
Rheumatoid arthritis, including juvenile rheumatoid arthritis, acute and subacute bursitis, epicondylitis, acute nonspecific tenosynovitis, acute gouty arthritis, psoriatic arthritis, ankylosing spondylitis.
• *Collagen disease*
During an exacerbation or as maintenance therapy in selected cases of : systemic lupus erythematosus; acute rheumatic carditis, systemic dermatomyositis (polymyositis).
• *Dermatological disease*
Pemphigus,severe erythema multiforme (Stevens-Johnson syndrome), exfoliative dermatitis, bullous dermatitis herpetiformis, severe seborrheic dermatitis, severe psoriasis, mucosis fungoides.
• *Allergic states*
Controls bronchial asthma, contact dermatitis, atopic dermatitis, serum sickness, seasonal or perennial allergic rhinitis, drug hypersensitivity reaction, urticarial transfusion reactions, acute noninfectious laryngeal edema (epinephrine is the drug of first choice), anaphylactic reactions.
• *Ophthalmic disease*
Severe acute and chronic allergic and inflammatory processes involving the eye, such as: herpes zoster ophthalmicus, iritis, iridocyclitis, chorioretinitis, diffuse posterior uveitis and chroiditis, optic neuritis, sympathetic ophthalmia, anterior segment inflammation, allergic conjunctivitis, allergic corneal marginal ulcers, keratitis.
• *Gastrointestinal disease*
To tide the patient over a critical period of the disease in: ulcerative colitis (systemic therapy), regional enteritis (systemic therapy), Crohn's disease.
• *Respiratory disease*
Symptomatic sarcoidosis, berylliosis, fulminating or disseminated pulmonary tuberculosis when used concurrently with appropriate antituberculosis chemotherapy, Loeffler syndrome not manageable by other means, aspiration pneumonitis.

• *Hematologic disorder*

Acquired (autoimmune) hemolytic anemia, idiopathic thrombocytopenic purpura in adults (IV only, IM administration is contraindicated), erythroblastopenia (RBC anemia), congenital (erythroid) hypoplastic anemia, secondary thrombocytopenia in adults.

• *Neoplastic disease*

For palliative management of: leukemias and lymphoma in adults, acute leukemia of childhood.

• *Edematous state*

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

• *Miscellaneous*

Tuberculous meningitis with subarachnoid block or impending block when used concurrently with appropriate antituberculosis chemotherapy. Trichinosis with neurologic or myocardial involvement .

Dosage & Administration

Mepcort may be administered by IM or IV or by IV infusion. To administer by IM or IV injection, prepare solution as direction for reconstitution. The desired dose may be administered intravenously over a period of several minutes.
When high dose therapy is desired, the recommended dose of Methylprednisolone Sodium Succinate for Injection, USP is 30 mg/kg administered intravenously over at least 30 minutes. This dose may be repeated every 4 to 6 hours for 48 hours. 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.
In other indications initial dosage will vary from 10 to 40 mg of Methylprednisolone depending on the clinical problem being treated. The larger doses may be required for short-term management of severe, acute conditions. The initial dose usually should be given intravenously over a period of several minutes. Subsequent doses may be given intravenously or intramuscularly at intervals dictated by the patient's response and clinical condition. Corticoid therapy is an adjunct to, and not replacement for conventional therapy.
Dosage must be decreased or discontinued gradually when the drug has been administered for more than a few days. If a period of spontaneous remission occurs in a chronic condition, treatment should be discontinued. Routine laboratory studies, such as urinalysis, two-hour postprandial blood sugar, determination of blood pressure and body weight, and a chest X-ray should be made at regular intervals during prolonged therapy. Upper GI X-rays are desirable in patients with an ulcer history or significant dyspepsia.
In pediatric patients, the initial dose of Methylprednisolone may vary depending on the specific disease being treated. The initial dose is 0.11-1.6 mg/day in three or four divided doses. Dosage may be reduced for infants and children but should be governed more by the severity of the condition and response of the patient than by age or size but it should not be less than 0.5 mg per kg every 24 hours.
In the treatment of acute exacerbations of multiple sclerosis daily doses is 160 mg daily for 3 days. Methylprednisolone powder for injection/infusion should be given as an intravenous infusion over at least 30 minutes.

Directions for Reconstitution

1. Remove protective plastic flip-off seal.
2. Cleanse stopper with suitable germicide.
3. Aseptically add 8 mL Water for Injection BP for the 500 mg vial or 16 ml for 1 gm vial by means of a syringe into the vial.
4. Agitate to effect solution to dissolve the powder content.
5. Invert vial. Insert needle through target area of stopper until tip is just visible. Withdraw dose.

Contraindication

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

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, severe arthralgia, vertebral compression fractures, aseptic necrosis of femoral and humeral heads, pathologic fracture of long bones, osteoporosis

Gastrointestinal

Peptic ulcer with possible perforation and hemorrhage, pancreatitis, abdominal distention, and ulcerative esophagitis

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 (pseudo-tumor cerebri) usually after treatment, convulsions, vertigo, headache

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

Posterior subcapsular cataracts, increased intraocular pressure, glaucoma, exophthalmos

Others

Negative nitrogen balance due to protein catabolism

The following additional adverse reactions are related to parenteral corticosteroid therapy: hyperpigmentation or hypopigmentation, subcutaneous and cutaneous atrophy, sterile abscess, anaphylactic reaction with or without circulatory collapse, cardiac arrest, bronchospasm, urticaria, nausea and vomiting, cardiac arrhythmias; hypotension or hypertension

Precaution

Methylprednisolone, 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. The lowest possible dose of corticosteroid should be used to control the condition under treatment. When reduction in dosage is possible, the reduction should be gradual. 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. For chronic conditions, discontinuation of corticosteroids may result in clinical improvement.

Use in Pregnancy & Lactation

Pregnancy: Corticosteroids have been shown to be teratogenic in many species when given in doses equivalent to the human dose. There are no adequate and well-controlled studies in pregnant women. Corticosteroids should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Infants born to mothers who have received corticosteroids during pregnancy should be carefully observed for signs of hypoadrenalism.

Lactation: 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.

Pediatric Use

The adverse effects of corticosteroids in pediatric patients are similar to those in adults. Like adults, pediatric patients should be carefully observed with frequent measurements of blood pressure, weight, height, intraocular pressure and clinical evaluation for the presence of infection, psychosocial disturbances, thromboembolism, peptic ulcers, cataracts and osteoporosis. Pediatric patients who are treated with corticosteroids by any route, including systemically administered corticosteroids, may experience a decrease in their growth velocity**.** In order to minimize the potential growth effects of corticosteroids, pediatric patients should be titrated to the lowest effective dose.

Geriatric Use
Clinical studies did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal or cardiac function and of concomitant disease or other drug therapy.

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.

Drug Interaction
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.
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.
Antidiabetics- Because corticosteroids may increase blood glucose concentrations, dosage adjustments of antidiabetic agents may be required.
Antitubercular drugs- Serum concentrations of isoniazid may be decreased.
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 Inhibitors - Drugs which inhibit cytochrome P450 3A4 have the potential to result in increased plasma concentrations of corticosteroids.
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 and corticosteroids increases the risk of gastrointestinal side effects.
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.

Storage
Protect from light. Store at controlled room temperature 20° to 25°C (68° to 77°F) . Store solution at controlled room temperature 20° to 25°C (68° to 77°F) .Use solution within 48 hours after mixing.

Commercial Pack
Mepcort 500 mg IM/IV Injection: Each vial contains sterile powder of Methylprednisolone Sodium Succinate USP equivalent to Methylprednisolone 500 mg and one ampoule of 10 ml water for injection BP.
Mepcort 1gm IM/IV Injection: Each vial contains sterile powder of Methylprednisolone Sodium Succinate USP equivalent to Methylprednisolone 1 gm and two ampoules of 10 ml water for injection BP.

Manufactured by
Globe Pharmaceuticals Ltd.
Bangladesh.