METHYLPREDNISOLONE SODIUM SUCCINATE

MEDRONE

500 mg Lyophilized Powder for Injection (IM/IV)

Corticosteroid

FORMULATION
Each vial contains:
Methylprednisolone (as Sodium Succinate), USP ..... 500 mg

PRODUCT DESCRIPTION
Freeze dried white powder in a vial / colorless and transparent solution in a colorless ampoule.

PHARMACOKINETICS
Methylprednisolone is fairly rapidly distributed following oral administration, with a plasma half-life of 3.5 hours or more. The tissue half-life is reported to range from 18 to 36 hours. Methylprednisolone acetate is absorbed from joints over a week but is more slowly absorbed following deep intramuscular injection. The sodium succinate ester is rapidly absorbed following intramuscular administration, with peak plasma concentrations obtained in 2 hours.

INDICATIONS
Methylprednisolone Sodium Succinate for Injection is indicated for intramuscular or intravenous use in the following conditions:

1. **Endocrine Disorders**
   - Primary or secondary adrenocortical insufficiency, acute adrenocortical insufficiency, 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: rheumatoid arthritis including juvenile rheumatoid arthritis (selected cases may require low-dose maintenance therapy), acute gouty arthritis, psoriatic arthritis, ankylosing spondylitis, acute and subacute bursitis. For the treatment of dermatomyositis, temporal arteritis, polymyositis and systemic lupus erythematosus.
3. **Collagen Diseases**
   - During 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 erythroderma, bullous dermatitis herpetiformis, mycosis fungoides.
5. **Allergic States**
   - Control of severe or incapacitating allergic conditions intractable to adequate trials of conventional treatment in asthma, contact dermatitis, atopic dermatitis, serum sickness, seasonal or perennial allergic rhinitis, drug hypersensitivity reactions, transfusion reactions.
6. **Gastrointestinal Diseases**
   - Ulcerative colitis (systemic therapy), regional enteritis (systemic therapy).
7. **Respiratory Diseases**
   - Symptomatic sarcoidosis, berylliosis, fulminating or disseminated pulmonary tuberculosis when used concurrently with appropriate anti-tuberculous chemotherapy, loeffler's syndrome not manageable by other means.
8. **Hematologic Disorders**
   - Acquired (autoimmune) hemolytic anemia, selective cases of secondary thrombocytopenia in adults, erythroblastopenia (red blood cell anemia), congenital (erythroid) hypoplastic anemia, idiopathic thrompocytopenic purpura in adults (intravenous administration only) intramuscular administration is contraindicated.
9. **Neoplastic Disorders**
   - For palliative management of leukemias and lymphomas.
10. **Renal Diseases**
    - To induce or remission of proteinuria in idiopathic nephrotic syndrome or that due to lupus erythematosus.
11. **Nervous System**
    - Acute exacerbations of multiple sclerosis; cerebral edema associated with primary or metastatic brain tumor, or craniotomy.

DOSAGE AND ADMINISTRATION
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 patients condition has stabilized; usually not beyond 48 to 72 hours.
In other indications, initial dosage will vary from 10 to 40 mg of methylprednisolone depending on the specific disease entity being treated. Dosage may be reduced for infants and children but should be governed more by the severity of the condition and response of the patients than by age or size. It should not less than 0.5 mg per kg every 24 hours.
Parenteral doses in children have varied considerably, depending on the condition: a range of 1 to 30 mg/kg of methylprednisolone daily has been given by the intravenous or intramuscular routes. A total dose of 1 g daily should not normally be exceeded.

CONTRAINDICATIONS
The use of Methylprednisolone Sodium Succinate for Injection, USP is contraindicated in premature infants because the 40 mg single dose vial and the 125 mg single dose vial when reconstituted will contain benzyl alcohol. Benzyl alcohol has been reported to be associated with a fatal "Gasping Syndrome" in premature infants. Methylprednisolone Sodium Succinate for Injection, USP is also contraindicated in systemic fungal infections and patients with known hypersensitivity to the product and its constituents.

ADVERSE 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, hypertropic 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 atropy, dry scaly skin, ecchymoses and petechiae, edema, 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 cushinggoid 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, post injection 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, insomia, mood swings, neuritis, neuropathy, paresthesia, personality changes, psychic disorders, vertigo. Arachnoiditis, meningitis, paraparesis/paraplegia and sensory disturbances have occured after intrathecal administration.
- **Ophthalmic**: Exophthalmos, glaucoma, increased intraocular pressure, posterior subcapsular cataracts and rare instances of blindness associated with periocular injections.

WARNINGS
In patients on corticosteroid therapy subjected to any unusual stress, increased dosage of rapidly acting corticosteroids before, during, and after the stressful situation is induced.
Corticosteroids may mask some signs of injection and new infections 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.
Average and large doses of cortisone or 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 small pox. 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 methylprednisolone 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.
Because rare instances of anaphylactic (e.g., bronchospasm) reactions have occurred in patients receiving parenteral corticosteroids therapy, appropriate precautionary measures should be taken prior to administration, especially when the patient has a history of allergy to the drug.
There are reports of cardiac arrhythmias and/or circulatory collapse and/or cardiac arrest following the rapid administration of large intravenous doses of methylprednisolone (greater than 500 mg administered over a period of less than 10 minutes). Bradycardia has been reported during or after the administration of large doses of methylprednisolone sodium succinate, and may be unrelated to the speed or duration of infusion.
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 who have not had these diseases, particular care should be taken to avoid exposure. How the dose, route and duration of corticosteroid administration affect the risk of developing a disseminated infection is not known. The contribution of the underlying disease and/or prior 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. 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 occuring 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.
Psychic derangements may appear when corticosteroids are used, ranging from euphoria, insomia, mood swings, personality changes, and severe depression, to frank psychotic manifestations. Also, existing emotional instability or psychotic tendencies may be aggravated by corticosteroids. 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 infant and children on prolonged corticosteroid therapy should be carefully observed.
Since complications of treatment with glucocorticoids are dependent on the size of the dose and the duration of treatment and as to whether daily or intermittent therapy should be used.
Convulsions have been reported with concurrent use of methylprednisolone and cyclosporine. Since concurrent use of these agents results in a mutual inhibition of metabolism, it is possible that adverse events associated with the individual use of either drug may be more apt to occur.
Aspirin should be used cautiously in conjunction with corticosteroids in patients suffering from hypoprothrombinemia.

DRUG INTERACTIONS
The pharmacokinetic interactions listed below are potentially clinically important. Mutual inhibition of metabolism occurs with concurrent use of ciclosporin and methylprednisolone; therefore, it is possible that adverse events associated with the individual use of either drug may be more apt to occur. Convulsions have been reported with concurrent use of methylprednisolone and ciclosporin. Drugs that induce hepatic enzymes such as phenobarbital, phenytoin and rifampicin may increase the clearance of methylprednisolone and may require increases in methylprednisolone dose to achieve the desired response. Drugs such as troleandomycin and ketoconazole may inhibit the metabolism of methylprednisolone and thus decrease its clearance. Therefore, the dose of methylprednisolone should be titrated to avoid steroid toxicity. Methylprednisolone 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 methylprednisolone is withdrawn. Aspirin should be used cautiously in conjunction with corticosteroids in patients suffering from hypoprothrombinemia. The effect of methylprednisolone on oral anticoagulants is variable. There are reports of enhanced as well as diminished effects of anticoagulant when given concurrently with corticosteroids. Therefore, coagulation indices should be monitored to maintain the desired anticoagulant effect.

Pregnancy and Nursing Mothers - Pregnancy Category C
Since adequate human reproduction studies have not been done with corticosteroids, the use of these drugs in pregnancy, nursing mothers or women of child-bearing 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.

STORAGE CONDITION
Store at temperatures not exceeding 30°C.

AVAILABILITY
15 mL-capacity USP Type I clear and colorless glass vial with grey rubber stopper and green colored flip-off seal + 8 mL in 10 mL-capacity clear and colorless glass ampoule (bacteriostatic water for injection as diluent) [Box of 1's].

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

"For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph. Seek medical attention immediately at the first sign of any adverse drug reaction."

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