Methsolon™

Methylprednisolone tablets & injections

1318

Presentation

Methsolon™ 4 tablet: Each tablet contains Methylprednisolone USP 4 mg.
Methsolon™ 16 tablet: Each tablet contains Methylprednisolone USP 16 mg.
Methsolon™ 40 IV/IM injection: Each vial contains sterile powder of Methylprednisolone Sodium Succinate USP equivalent to Methylprednisolone 40 mg.
Methsolon™ 500 IV/IM injection: Each vial contains sterile powder of Methylprednisolone Sodium Succinate USP equivalent to Methylprednisolone 500 mg.
Methsolon™ 1 gm IV/IM injection: Each vial contains sterile powder of Methylprednisolone Sodium Succinate USP equivalent to Methylprednisolone 1 gm.

Description

Methsolon™ contain methylprednisolone which is a glucocorticoid. Glucocorticoids are adrenocortical steroids, both naturally occurring and synthetic, which are readily absorbed from the gastrointestinal tract. It has greater anti-inflammatory potency and less mineralocorticoid potency than Prednisolone. The relative potency of Methylprednisolone is to Hydrocortisone is at least 4 to 1. The bio-availability of methylprednisolone is 82-89% following oral administration. Maximum plasma concentration in blood is achieved in around 1.5 to 2.3 hours in healthy adults.The volume of distribution is 41-61.5 L. It crosses the blood-brain barrier, placenta and is excreted in the breast milk. The plasma protein binding in human is linear and approximately 77%. No dosage adjustment is required in renal failure.

Indications And Usage

1. Endocrine Disorders: Primary or secondary adrenocortical insufficiency, Congenital adrenal hyperplasia, Nonsuppurative thyroiditis, Hypercalcemia associated with cancer **2. Rheumatic Disorders:** Rheumatoid arthritis, including juvenile rheumatoid arthritis, Ankylosing spondylitis, Acute and subacute bursitis, Synovitis of osteoarthritis, Acute nonspecific tenosynovitis, Post-traumatic osteoarthritis, Psoriatic arthritis, Epicondylitis, Acute gouty arthritis. **3. Collagen Diseases:** Systemic lupus erythematosus, Systemic dermatomyositis (polymyositis), Acute rheumatic carditis. **4. Dermatologic Diseases:** Bullous dermatitis herpetiformis, Severe erythema multiforme (Stevens-Johnson syndrome), Severe seborrheic dermatitis, Exfoliative dermatitis, Mycosis fungoides, Pemphigus Severe psoriasis. **5. Allergic States:** Seasonal or perennial allergic rhinitis, Drug hypersensitivity reactions, Serum sickness, Contact dermatitis, Bronchial asthma, Atopic dermatitis. **6. Ophthalmic Diseases:** Allergic corneal marginal ulcers, Herpes zoster ophthalmicus, Anterior segment inflammation, Diffuse posterior uveitis and choroiditis, Sympathetic ophthalmia, Keratitis, Optic neuritis, Allergic conjunctivitis Chorioretinitis, Iritis and iridocyclitis. **7. Respiratory Diseases:** Symptomatic sarcoidosis, Berylliosis Loeffler's syndrome not manageable by other means, Fulminating or disseminated pulmonary tuberculosis when used concurrently with appropriate antituberculous chemotherapy, Aspiration pneumonitis. **8. Hematologic Disorders:** Idiopathic thrombocytopenic purpura in adults, Secondary thrombocytopenia in adults, Acquired (autoimmune) hemolytic anemia, Erythroblastopenia (RBC anemia), Congenital (erythroid) hypoplastic anemia. **9. Neoplastic Diseases:** Leukemias and lymphomas in adults, Acute leukemia of childhood. **10. Edematous States:** To induce a diuresis or remission of proteinuria in the nephrotic syndrome, without uremia, of the idiopathic type or that due to lupus erythematosus. **11. Gastrointestinal Diseases:** Ulcerative colitis, Regional enteritis. **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.

Dosage and administration

The initial dosage of Methsolon™ tablet

The initial dosage of Methsolon™ tablet may vary from 4 to 48 mg as methylprednisolone per day depending on the specific disease entity being treated. In situations of less severity, lower doses will generally suffice while in selected patients higher initial doses may be required. If after a reasonable period of time there is lack of satisfactory clinical response, Methsolon™ tablet should be discontinued and the patient transferred to other appropriate therapy. If after long-term therapy the drug is to be stopped, it is recommended that it be withdrawn gradually rather than abruptly. After a favourable response is noted, the proper maintenance dosage should be determined by decreasing the initial drug dosage in small decrements at appropriate time intervals until the lowest dosage which will maintain an adequate clinical response is reached. It should be kept in mind that constant monitoring is needed in regard to drug dosage. Included in the situations which may make dosage adjustments necessary are changes in clinical status secondary to remissions or exacerbations in the disease process, the patient's individual drug responsiveness, and the effect of patient exposure to stressful situations not directly related to the disease entity under treatment; in this latter situation it may be necessary to increase the dosage of Methsolon tablets for a period of time consistent with the patient's condition. It should be emphasized that dosage requirements are variable and must be individualized on the basis of the disease under treatment and the response of the patient. ADT Alternate Day Therapy: Alternate day therapy is a corticosteroid dosing regimen in which twice the usual daily dose of corticosteroid is administered every other morning. The purpose of this mode of therapy is to provide a patient requiring long-term, pharmacologic dose treatment with the beneficial effects of corticoids while minimizing certain undesirable effects, including pituitary-adrenal suppression, the cushingoid state, corticoid withdrawal symptoms, and growth suppression in children.

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The initial dosage of Methsolon™ Injection

Indications	Dosage
Adjunctive therapy in life threatening conditions	30 mg/kg IV over a period of at least 30 minutes. Dose may be repeated every 4 to 6 hours for up to 48 hours.
Acute respiratory distress syndrome (ARDS)	Initially 2 to 3 mg/kg/day IV, decreasing after 7 days
Rheumatic disorders Unresponsive to standard therapy (or during exacerbation episodes)	1gm/day for 1 to 4 days, or 1gm/month for 6 months. Administer either regimen as pulse dosing over at least 30 minutes. The regimen may be repeated if improvement has not occurred within a week after therapy.
Systemic Lupus Erythromatosus (SLE) – (Unresponsive to standard therapy or during exacerbation episodes)	Administer 1 g/day for 3 days as IV pulse dosing over at least 30 minutes. The regimen may be repeated if improvement has not occurred within a week after therapy or as the patient's condition dictates.
Multiple sclerosis Unresponsive to standard therapy (or during exacerbation episodes)	Administer 1 g/day for 3 to 5 days days as IV pulse dosing over at least 30 minutes. The regimen may be repeated if improvement has not occurred within a week after therapy or as the patient's condition dictates.
Acute spinal chord injury	Treatment should begin within 8 hours of injury. • Within 3 hours of injury: Bolus 30 mg/kg in 50 ml IV fluid over 15 minutes, wait 45 minutes, then continuous infusion of 5.4 mg/kg/hour for 23 hours. • 3 to 8 hours after injury: Bolus 30 mg/kg in 50 ml IV fluid over 15 minutes, wait 45 minutes, then continuous infusion oof 5.4 mg/kg/hour for 47 hours. There should be a separate intravenous site for the infusion pump.
Edamatous states such as glomerulonephritis or lupus nephritis, unresponsive to standard therapy (or during exacerbation episodes)	30 mg/kg every other day for 4 days or 1 gm day for 3, 5 or 7 days Administer either regimen as IV pulse dosing over over at least 30 minutes. The regimen may be repeated if improvement has not occurred within 1 week after therapy or as the patient's condition dictates.
Terminal cancer (to improve quality of life)	Administer 125 mg/day IV for up to 8 weeks.
Chronic obstructive pulmonary disease (COPD)	125 mg IV every 6 hours for 3 days, switch to an oral corticosteroid and taper dose. Total treatment period should be at least 2 weeks.
Pemphigus and Bullous pemphigoid	20-30 mg/kg IV as pulse therapy depending on patient's condition.
Other indications	Initial dosage will vary from 10 to 500 mg depending on the clinical problem being treated. The larger dosage may be required for short-term management severe acute conditions. The initial dose should be given IV over a period of at least 5 minutes (e.g. up to 250 mg) to at least 30 minutes (dose exceeding 250 mg). Subsequent doses may be given intravenously or intramuscularly at intervals dictated by the patient's response and clinical conditions.

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. It should not be less than 0.5 mg/kg every 24 hours. 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.

Direction for reconstitution

- Remove protective plastic flip-off seal
- Clean stopper with suitable germicide
- Aseptically add 1 ml water for injection for the 40 mg vial, 8 ml water for injection for the 500 mg vial and 16 ml water for injection for the 1 gm vial by means of syringe.
- Shake the vial gently to dissolve the powder content.
- Withdraw the dose in usual manner with the syringe provided.
- Unused portion should be discarded.

Preparation of solutions for IV infusion

First prepare the solution for injection as directed. Therapy may be initiated by administering Methylprednisolone sodium succinate solution intravenously over a period of at least 5 minutes (e.g. doses up to and including 250 mg) to at least 30 minutes (e.g. doses exceeding 250 mg). Subsequent doses may be withdrawn and administered similarly. If desired, the medication may be administered in diluted solutions by admixing the reconstituted dextrose 5% in water, normal saline, dextrose 5% in 0.45% sodium chloride.

Incompatibilities

To avoid compatibility and stability problems, whenever possible, it is recommended that solutions of methylprednisolone sodium succinate be administered separately as IV.

Use in pregnancy and lactation

USFDA pregnancy category C. Adequate well-controlled studies in pregnant women have not been done with corticosteroids. Since there is inadequate evidence of safety in human pregnancy, this drug should be used in pregnancy or by women of child bearing potential only if clearly needed and the potential benefit justifies the potential risk to the mother and embryo or fetus.

Side effects

Short courses of methylprednisolone is usually well tolerated with a few, mild side effects. However, long term and high dose corticosteroids may cause potential side effects. These include- Fluid and Electrolyte Disturbances: Sodium retention, Congestive heart failure in susceptible patients, Hypertension, Fluid retention, Potassium loss, Hypokalemic alkalosis. Musculoskeletal: Muscle weakness, Loss of muscle mass, Steroid myopathy, 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, Petechiae and ecchymoses, May suppress reactions to skin tests, Thin fragile skin, Facial erythema, Increased sweating. 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, Metabolic, Negative nitrogen balance due to protein catabolism. The following additional reactions have been reported following oral as well as parenteral therapy: Urticaria and other allergic, anaphylactic or hypersensitivity reactions.

Contraindication

Methsolon™ is contraindicated in patients with known hypersensitivity to any components of the product; in patients with systemic fungal infections; in patients administered with live or live, attenuated vaccines while receiving, immunosuppressive doses of corticosteroids; in herpes simplex of the eye, except when used for short-term or emergency therapy as in acute sensitivity reactions; in patients with vaccinia and varicella, except when used for short-term or emergency therapy as in acute sensitivity reactions. Methylprednisolone sodium succinate is contraindicated in systemic fungal infections and patients with known hypersensitivity to the product and its constituents.

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 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. The lowest possible dose of corticosteroid should be used to control the condition under treatment, and when reduction in dosage is possible, the reduction should 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; 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 observed. 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. Convulsions have been reported with concurrent use of methylprednisolone and cyclosporine.

Drug interactions

Drug Class	Drug Interaction
Antibacterial -ISONIAZID	CYP3A4 INHIBITOR. In addition, there is a potential effect of methylprednisolone to increase the acetylation rate and clearance of isoniazid.
Antibiotic - RIFAMPIN	CYP3A4 INDUCER. Drugs which induce cytochrome P450 3A4 enzyme activity may enhance the metabolism of corticosteroids and require that the dosage of the corticosteroid be increased.
Anticoagulants (oral)	There are reports of enhanced as well as diminished effects of anticoagulants when given concurrently with corticosteroids. Co-administration 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 effects.
Anticonvulsants - CARBAMAZEPINE	CYP3A4 INDUCER (and SUBSTRATE). Drugs which induce cytochrome P450 3A4 enzyme activity may enhance the metabolism of corticosteroids and require that the dosage of the corticosteroid be increased.
Anticonvulsants - PHENOBARBITAL & PHENYTOIN	CYP3A4 INDUCERS. Drugs which induce cytochrome P450 3A4 enzyme activity may enhance the metabolism of corticosteroids and require that the dosage of the corticosteroid be increased.
Anticholinergics - NEUROMUSCULAR BLOCKERS	1) An acute myopathy has been reported with the concomitant use of high doses of corticosteroids and anticholinergics, such as neuromuscular blocking drugs. 2) Antagonism of the neuromuscular blocking effects of pancuronium and vecuronium has been reported in patients taking corticosteroids. This interaction may be expected with all competitive neuromuscular blockers.
Anticholinesterases	Steroids may reduce the effects of anticholinesterases in myasthenia gravis. 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.
Antidiabetics	Because corticosteroids may increase blood glucose concentrations, dosage adjustments of antidiabetic agents may be required.
Antiemetic - APREPITANT & FOSAPREPITANT	CYP3A4 INHIBITORS (and SUBSTRATES). Drugs which inhibit cytochrome P450 3A4 have the potential to result in increased plasma concentrations of corticosteroids. Therefore the dose of methylprednisolone should be titrated to avoid steroid toxicity.
Antitubercular Drugs • ISONIAZID	CYP3A4 INDUCER. Serum concentrations of isoniazid may be decreased. Drugs which induce cytochrome P450 3A4 enzyme activity may enhance the metabolism of corticosteroids and require that the dosage of the corticosteroid be increased.
Aromatase inhibitors - AMINOGLUTETHIMIDE	Aminoglutethimide-induced adrenal suppression may exacerbate endocrine changes caused by prolonged glucocorticoid treatment. Aminoglutethimide may lead to a loss of corticosteroid-induced adrenal suppression.
Calcium Channel Blocker - DILTIAZEM	CYP3A4 INHIBITOR (and SUBSTRATE)
Contraceptives (oral) - ETHINYLESTRADIOL/ NORETHINDRONE	CYP3A4 INHIBITOR (and SUBSTRATE). Estrogens may decrease the hepatic metabolism of certain corticosteroids, thereby increasing their effect.
Digitalis glycosides	Patients on digitalis glycosides may be at increased risk of arrhythmias due to hypokalemia.
Immunosuppressant - CYCLOSPORINE	CYP3A4 INHIBITOR (and SUBSTRATE). 1) Mutual inhibition of metabolism occurs with concurrent use of cyclosporine and methylprednisolone, which may increase the plasma concentrations of either or both drugs. Therefore, it is possible that adverse events associated with the use of either drug alone may be more likely to occur upon coadministration. 2) Convulsions have been reported with concurrent use of methylprednisolone and cyclosporine. 3) Increased activity of both cyclosporine and corticosteroids may occur when the two are used concurrently.
Immunosuppressant - CYCLOPHOSPHAMIDE & TACROLIMUS	CYP3A4 SUBSTRATES
Macrolide Antibacterial - CLARITHROMYCIN & ERYTHROMYCIN	CYP3A4 INHIBITORS (and SUBSTRATES). Macrolide antibiotics have been reported to cause a significant decrease in corticosteroid clearance. Drugs which inhibit cytochrome P450 3A4 have the potential to result in increased plasma concentrations of corticosteroids. Therefore the dose of methylprednisolone should be titrated to avoid steroid toxicity.
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.
NSAIDs (nonsteroidal antiinflammatory drugs)- high-dose ASA (acetylsalicylic acid)	1) There may be increased incidence of gastrointestinal bleeding and ulceration when corticosteroids are given with NSAIDs. 2) Methylprednisolone may increase the clearance of high-dose ASA. This decrease in salicylate serum levels could lead to an increased risk of salicylate toxicity when methylprednisolone is withdrawn. ASA should be used cautiously in conjunction with corticosteroids in patients suffering from hypoprothromboinemia.
Potassium-depleting agents	When corticosteroids are administered concomitantly with potassium-depleting agents (i.e., diuretics), patients should be observed closely for development of hypokalemia. There is also an increased risk of hypokalemia with concurrent use of corticosteroids with amphotericin B, xanthenes, or beta2 agonists. There have been cases reported in which concomitant use of amphotericin B and hydrocortisone was followed by cardiac enlargement and congestive heart failure.
Antivirals - HIV-PROTEASE INHIBITORS	CYP3A4 INHIBITORS (and SUBSTRATES). 1) Protease inhibitors, such as indinavir and ritonavir, may increase plasma concentrations of corticosteroids. 2) Corticosteroids may induce the metabolism of HIV-protease inhibitors resulting in reduced plasma concentrations.
Cholestyramine	Cholestyramine may increase the clearance of oral corticosteroids.
Vaccines	Patients on prolonged corticosteroid therapy may exhibit a diminished response to toxoids and live or attenuated 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.

Overdose

Treatment of acute overdosage is by supportive and symptomatic therapy. For chronic overdosage in the face of severe disease requiring continuous steroid therapy, the dosage of corticosteroid may be reduced only temporarily. Methylprednisolone is dialyzable.

Storage

Do not store above 30^0 C. Keep away from light and out of the reach of children.

Commercial Pack

Methsolon™ 4 Tablet: Each box contains 50 tablets in 5×10's strips.
Methsolon™ 16 Tablet: Each box contains 20 tablets in 2×10's strips.
Methsolon™ 40 IV/IM injection: Each box contains one combipack and one 3 ml disposable syringe. The combipack contains one vial of Methylprednisolone 40 mg and one ampoule of water for injection BP 1 ml.
Methsolon™ 500 IV/IM injection: Each box contains one combipack and one 10 ml disposable syringe. The combipack contains one vial of Methylprednisolone 500 mg and one ampoule of water for injection BP 10 ml.
Methsolon™ 1 gm IV/IM injection: Each box contains one combipack and one 20 ml disposable syringe. The combipack contains one vial of Methylprednisolone 1 gm and two ampoules of water for injection BP 10 ml.

Manufactured by
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