

For Injection  
**Solomed**  
(Methylprednisolone Sodium Succinate)

سولوميد فار انجكشن  
(متن سداسي هيدروكورتيزون سولوميد)

#### COMPOSITION

##### Solomed For Injection 40mg

Each vial contains:

Methylprednisolone (as sodium succinate).....40mg

##### (USP Specifications)

##### Solomed For Injection 125mg

Each vial contains:

Methylprednisolone (as sodium succinate).....125mg

##### (USP Specifications)

##### Solomed For Injection 500mg

Each vial contains:

Methylprednisolone (as sodium succinate).....500mg

##### (USP Specifications)

##### Solomed For Injection 1g

Each vial contains:

Methylprednisolone (as sodium succinate).....1g

##### (USP Specifications)

#### DESCRIPTION

SOLOMED Sterile Powder is an anti-inflammatory glucocorticoid which contains methylprednisolone sodium succinate as an active ingredient. It is a synthetic glucocorticoid corticosteroid and a corticosteroid ester.

#### INDICATIONS

SOLOMED 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 lide 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:

Typhoid fever 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 lide 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 salt-retaining 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.

Methylprednisolone is a potent anti-inflammatory steroid with greater anti-inflammatory potency than prednisolone and even less tendency than prednisolone to induce sodium and water retention. Methylprednisolone sodium succinate has the same metabolic and anti-inflammatory actions as methylprednisolone. When given parenterally and in equimolar quantities, the two compounds are equivalent in biologic activity. Following 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.

#### DOSEAGE & ADMINISTRATION

Because of possible physical incompatibilities, SOLOMED should not be diluted or mixed with other solutions. Use only Bacteriostatic Water for Injection with Benzyl Alcohol when reconstituting SOLOMED. Use within 48 hours after mixing.

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. There are reports of cardiac arrhythmias and/or cardiac arrest following the rapid administration of large IV doses of SOLOMED (greater than 0.5 gram 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. When high dose therapy is desired, the recommended dose of SOLOMED Sterile Powder 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.

In other indications, initial dosage will vary from 10 to 40 mg of methylprednisolone depending on the specific disease entity being treated. However, in certain overwhelming, acute, life-threatening situations, administrations in dosages exceeding the usual dosages may be justified and may be in multiples of the oral dosages. In treatment of acute exacerbations of multiple sclerosis, daily doses of 160 mg of methylprednisolone for a week followed by 64 mg every other day for 1 month have been shown to be effective. In pediatric patients, the initial dose of methylprednisolone may vary depending on the specific disease entity being treated. The range of initial doses is 0.11 to 1.6 mg/kg/day in three or four divided doses (3.2 to 48 mg/m<sup>2</sup> bsa/day). The National Heart, Lung, and Blood Institute (NHLBI) recommended dosing for systemic prednisone, prednisolone, or methylprednisolone in pediatric patients whose asthma is uncontrolled by inhaled corticosteroids and long-acting bronchodilators is 1-2 mg/kg/day in single or divided doses. It is further recommended that short course, or "burst" therapy, be continued until the patient achieves a peak expiratory flow rate of 80% of his or her personal best or until symptoms resolve. This usually requires 3 to 10 days of treatment, although it can take longer. There is no evidence that tapering the dose after improvement will prevent a relapse. 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 per kg every 24 hours.

#### PREPARATION OF SOLUTIONS:

**FOR RECONSTITUTION. USE ONLY BACTERIOSTATIC WATER FOR INJECTION WITH BENZYL ALCOHOL.**

**USE WITHIN 48 HOURS AFTER MIXING.**

#### For 40mg & 125mg:

**For intravenous or intramuscular injection:** Prepare solution by adding 2 ml of Bacteriostatic water for Injection to the contents of the vial.

#### For 500mg:

**For intravenous or intramuscular injection:** Prepare solution by adding 7.8ml of Bacteriostatic water for Injection to the contents of the vial.

**For 1g:** **For intravenous or intramuscular injection:** Prepare solution by adding 15.6ml of Bacteriostatic water for Injection to the contents of the vial.

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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

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. 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. Kaposi's sarcoma has been reported to occur in patients receiving corticosteroid therapy, most often for chronic conditions. Discontinuation of corticosteroids may result in clinical improvement.

#### Cardio-renal:

As sodium retention with resultant edema and potassium loss may occur in patients receiving corticosteroids, these agents should be used with care in patients with congestive heart failure, hypertension, or renal insufficiency.

#### 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 reinstated. 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., 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 perforation. Signs of peritoneal irritation following gastrointestinal perforation in patients receiving corticosteroids may be minimal or absent. There is an enhanced effect due to decreased 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 avoid 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 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 sub-capsular cataracts, and rare instances of blindness associated with periorcular 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**

**SOLEMED 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. Solomed 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.

**Note: Small-volume injection** (also referred to as Small-volume parenteral). An injectable dosage form that is packaged in Containers labeled as containing 100 ml or less. The formulation containing benzyl alcohol should not be used in neonates.

#### **STORAGE & INSTRUCTIONS:**

Store between 20-25°C.

Protect from heat, sunlight and moisture. Do not freeze.

Keep away from the reach of children.

Use within 48 hours (2 days) after mixing.

**To be sold on the prescription of a registered medical practitioner only.**

#### **HOW SUPPLIED**

**Solomed For Injection 40mg**

1 vial, 25 vials

**Solomed For Injection 125mg**

1 vial, 25 vials

**Solomed For Injection 500mg**

1 vial, 25 vials

**Solomed For Injection 1g**

1 vial, 25 vials

خودک و مطریقتی استمال:  
و آئوکی بدایت کے مطابق استمال کریں۔

بہایت:

دوا کو ۲۵-۲۵۰ ڈگری سینٹی گریڈ درجہ حرارت کے درمیان رکھیں۔  
دھوپ، گرمی، نمی اور ٹھنڈ ہونے سے بچائیں۔ بچوں کی تکفیت سے  
دور رکھیں۔ تیار کردہ مکمل ۲۸ گھنٹوں میں استمال کریں۔  
صرف مشورہ آئوکر کے نسخہ پر فروخت کریں۔

Manufactured by:

**PHARMASOL  
PRIVATE LIMITED**

Plot # 549, Sundar Industrial Estate,  
Lahore, Pakistan.