SCHEDULING STATUS: S4

PROPRIETARY NAME AND DOSAGE FORM:

SOLU-MEDROL™ 40 mg (Injection)

SOLU-MEDROL™ 125 mg (Injection)

SOLU-MEDROL™ 500 mg (Injection)

SOLU-MEDROL™ 1000 mg (Injection)

COMPOSITION:

SOLU-MEDROL 40 mg: Each 1 ml (when mixed) contains methylprednisolone sodium succinate equivalent to 40 mg methylprednisolone.

SOLU-MEDROL 125 mg: Each 2 ml (when mixed) contains methylprednisolone succinate equivalent to 125 mg methylprednisolone.

SOLU-MEDROL 500 mg: Each 8 ml (when mixed) contains methylprednisolone sodium succinate equivalent to 500 mg methylprednisolone.

SOLU-MEDROL 1000 mg: Each 16 ml (when mixed) contains methylprednisolone sodium succinate equivalent to 1 000 mg methylprednisolone.

Preservative: 0,9 % m/v benzyl alcohol.

PHARMACOLOGICAL CLASSIFICATION:

A 21.5.1 Corticosteroids and analogues

PHARMACOLOGICAL ACTION:

Methylprednisolone is a potent anti-inflammatory corticosteroid. The relative potency of methylprednisolone sodium succinate and hydrocortisone sodium succinate as indicated by the depression of eosinophil count, following intravenous administration, is at least four to one. This is in good agreement with the relative oral potency of methylprednisolone and hydrocortisone.

INDICATIONS:

SOLU-MEDROL is indicated for use in the following:

1. **Endocrine Disorders**

   Primary and secondary adrenocortical insufficiency. (Hydrocortisone or cortisone is the medicine of choice; synthetic analogues must be used in conjunction with mineralocorticoids where applicable; in infancy, mineralocorticoid supplementation is of particular importance).

2. **Rheumatic Disorders**

   Acute rheumatic carditis.

3. **Collagen Disease (Immune Complex Disease)**

   During exacerbation in selected cases of:

   Systemic lupus erythematosus and lupus nephritis

   Systemic dermatomyositis (polymyositis)

   Polyarteritis nodosa

4. **Dermatological Disorders**

   In steroid responsive cases of severe dermatological disorders.

5. **Allergic States**

   Control of severe or incapacitating allergic states necessitating intravenous therapy.

6. **Gastrointestinal Diseases**

   Control of severe or incapacitating ulcerative colitis necessitating intravenous therapy.

7. **Haematological Disorders**

   Secondary thrombocytopenia of immunological origin in adults in whom IV therapy is indicated.

   Idiopathic thrombocytopenic purpura in adults (IV administration only; IM administration is contraindicated).

8. **Nervous System**

   Cerebral oedema due to tumour, either primary or metastatic and/or associated with surgical procedures, radiation therapy or head trauma. Acute exacerbations of multiple sclerosis.

9. **Acute Spinal Cord Injury**

   As adjunctive therapy in the treatment of the symptoms of acute spinal cord injury. The treatment should begin within eight hours of injury.

10. **Cardiovascular Conditions**

Shock secondary to adrenocortical insufficiency or shock unresponsive to conventional therapy when adrenal cortical insufficiency may be present. (Hydrocortisone is generally the medication of choice.)

11. Organ Transplantation

To prevent or treat rejection of organ transplantation.

12. Neoplastic Diseases

For the palliative management of leukaemias and lymphomas in adults.

13. As adjunctive therapy for nausea and vomiting associated with cancer therapy.

CONTRAINDICATIONS:

SOLU-MEDROL is contraindicated in patients with known hypersensitivity to methylprednisolone or other components of the product and in patients with systemic fungal infections.

Unless considered life-saving it should not be given to patients with acute psychosis, peptic ulcer or osteoporosis.

WARNINGS AND SPECIAL PRECAUTIONS:

1. The efficacy of SOLU-MEDROL in septic shock has not been established. Increased mortality may occur in some subgroups at higher risk, i.e. elevated creatinine greater than 2,0 mg % (170 µmol/l) or secondary infections.
2. Some animal studies have shown that corticosteroids, when administered to the mother at high doses, may cause foetal malformations. Adequate human reproductive studies have not been done with corticosteroids. Safety in pregnancy and lactation has not been established.
3. This product contains benzyl alcohol. Benzyl alcohol has been reported to be associated with a "gasping syndrome" in premature infants.
4. In patients on corticosteroid therapy subjected to unusual stress, increased dosages of rapidly acting corticosteroids, before, during and after the stressful situation is indicated.
5. Corticosteroids may mask some signs of infection, and new infections may appear during their use. There may be decreased resistance and inability to localise infection when corticosteroids are used.

6. Corticosteroids readily cross the placental barrier. Infants born of mothers who have received substantial doses of corticosteroids during pregnancy must be carefully observed for signs of adrenal insufficiency. There are no known effects of corticosteroids on labour and delivery. Corticosteroids are excreted in breast milk.
7. Immunization procedures should not be undertaken in patients who are on corticosteroids, especially on high doses, because of possible hazards of neurological complications and lack of antibody response.
8. The use of SOLU-MEDROL 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-tuberculosis regimen. If corticosteroids are indicated in patients with latent or tuberculin reactivity, close observation is necessary as reactivation of the disease may occur. During prolonged corticosteroid therapy these patients should receive chemoprophylaxis.
9. Because instances of anaphylactoid (e.g. bronchospasms) reactions have occurred in patient receiving parenteral corticosteroids therapy, appropriate precautionary measures should be taken prior to administration, especially when the patient has a history of allergy to any drug.
10. **There are reports of cardiac arrhythmias and/or circulatory collapse and/or cardiac arrest following the rapid administration of large IV doses of methylprednisolone sodium succinate (greater than 0,5 g administered over a period of less than 10 minutes). Bradycardia has been reported during or after the administration of methylprednisolone sodium succinate, and may be unrelated to the speed or duration of infusion.**
11. Corticosteroids should be used cautiously in patients with ocular herpes simplex because of possible corneal perforation.
12. 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 or psychotic tendencies may be aggravated by corticosteroids.
13. Corticosteroids should be used with caution in non-specific ulcerative colitis, if there is a probability of impending perforation, abscess or other pyogenic infection, also in diverticulitis, fresh intestinal

anastomoses, active or latent ulcer, renal insufficiency, hypertension, osteoporosis, or myasthenia gravis.

14. Convulsions have been reported with concurrent use of methylprednisolone and cyclosporin. Since concurrent administration of these agents results in a mutual inhibition of metabolism, it is possible that convulsions and other adverse events associated with the individual use of either agent may be more apt to occur.

DOSAGE AND DIRECTIONS FOR USE:

Corticosteroid therapy is an adjunct to, and not a replacement for, conventional therapy.

As adjunctive therapy in life-threatening conditions the recommended dose of SOLU-MEDROL is 30 mg per kg, given IV over a period of at least 30 minutes. This dose may be repeated every 4 – 6 hours for up to 48 hours.

For corticosteroid responsive diseases in exacerbation, and unresponsive to standard therapy, pulse dosing may be used.

Suggested dosing schedules are:

Systemic Lupus Erythematosus:	1 g/day for 3 days IV
Multiple Sclerosis:	1 g/day for 3 days IV or 1 g/day for 5 days IV.
Oedematous states (e.g. lupus nephritis):	30 mg/kg every other day for 4 days IV or 1 g/day for 3, 5 or 7 days IV.

The regimen should be administered over at least 30 minutes, and may be repeated if improvement has not occurred within a week after therapy or as the patient's condition dictates.

Acute Spinal Cord Injury:

As adjunctive therapy in the treatment of acute spinal cord injury, administer intravenously, 30 mg methylprednisolone per kilogram of body weight in a bolus dose over a 15 minute period, followed by a 45 minute pause, and then a continuous infusion of 5,4 mg/kg per hour for 23 hours and then stopped abruptly. There should be a separate intravenous site for the infusion pump. The treatment should begin within eight hours of injury.

As adjunctive therapy for the prevention of nausea and vomiting associated with cancer chemotherapy the suggested dosage schedules are:

Mild to moderate emetogenic chemotherapy: Administer 250 mg of SOLU-MEDROL IV over at least 5 minutes, one hour before chemotherapy, at the initiation of chemotherapy, and at the time of discharge.

Severely emetogenic chemotherapy: Administer 250 mg of SOLU-MEDROL IV over at least 5 minutes with appropriate doses of metoclopramide or butyrophenone one hour before chemotherapy, then 250 mg SOLU-MEDROL IV at the initiation of chemotherapy and at time of discharge.

In other indications, the initial dose will vary from 10 to 500 mg IV depending on the severity of the disorder being treated. Larger doses may be required for short term management of severe acute conditions. The initial dose, up to 250 mg, should be given intravenously over a period of at least 5 minutes, and if greater than 250 mg, should be given over at least 30 minutes. Subsequent doses may be given intravenously or intramuscularly at intervals dictated by the patient's response and clinical condition.

Dosage must be reduced for infants and children but should be governed by the severity of the condition and response of the patient rather than by the age or size. It should, however, not be less than 0,5 mg per kg every 24 hours.

Dosage must be decreased or discontinued gradually when the medicine has been administered for more than a few days. Routine laboratory studies must be performed such as urinalysis, 2 hour postprandial blood sugar, determination of blood pressure and body mass, and a chest X-ray should be taken at regular intervals during prolonged therapy. Upper gastrointestinal X-rays are desirable in patients with an ulcer history or significant dyspepsia.

To avoid compatibility and stability problems, it is recommended that SOLU-MEDROL be administered separately from other drugs and as either an IV push, through an IV medication chamber, or as an IV "piggy-back" solution.

Preparation of Solutions:

To prepare solutions for intravenous infusion, first reconstitute SOLU-MEDROL as directed. Therapy may be initiated by administering SOLU-MEDROL intravenously over a period of at least 5 minutes (for doses up to 250 mg) to at least 30 minutes (for doses of 250 mg or more). Subsequent doses may be withdrawn and administered similarly.

If desired, the medication may be administered in dilute solutions by admixing the reconstituted product with Dextrose 5 % in Water; Normal Saline; Dextrose 5 % in 0,45 % or 0,9 % m/v Sodium Chloride. The resulting solutions are physically and chemically stable for 48 hours.

Parenteral medicinal products should be inspected visually for particulate matter and discolouration prior to administration whenever solution and container permit.

Directions for using the Act-O-Vial:

1. Press down on plastic activator to force diluent into the lower compartment.
2. Gently agitate to effect solution. Use solution within 48 hours.
3. Remove plastic tab covering centre of stopper.
4. Sterilize top of stopper with a suitable germicide.
5. Insert needle through centre of plunger-stopper until tip is just visible. Invert vial and withdraw dose.

Dosage must be decreased or discontinued gradually when the medicine has been administered for more than a few days.

SIDE EFFECTS:

Since complications of treatment with glucocorticoids are dependent on the size of the dose (oral or parenteral) 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.

Fluid and electrolyte disturbances

Sodium retention, fluid retention, potassium loss, electrolyte imbalance. Congestive heart failure may occur in susceptible patients, as well as hypertension.

Musculoskeletal

Steroid myopathy, muscle weakness, osteoporosis, pathological fractures, vertebral compression fractures, aseptic necrosis, spontaneous fractures.

Gastrointestinal

Peptic ulceration with possible perforation and haemorrhage, pancreatitis, oesophagitis, perforation of the bowel.

Dermatologic

Impaired wound healing, petechiae and ecchymosis, thin, fragile skin, purpura, allergic reactions involving the skin, facial erythema, thinning of hair and scalp. Subcutaneous and cutaneous atrophy, post-injection flare, sterile abscess at injection site, hyperpigmentation, hypopigmentation, striae and acne.

Metabolic

Negative nitrogen balance due to protein catabolism, hypokalemic alkalosis.

Thromboembolic complications due to increased coagulability.

Neurological

Increased intracranial pressure, pseudotumour cerebri, psychic derangements, seizures, insomnia, nervousness, vertigo, sweating.

Endocrine

Menstrual irregularities, development of cushingoid state (moon face and supra clavicular fat pads), suppression of pituitary-adrenal axis, decreased carbohydrate tolerance resulting in manifestation of latent diabetes mellitus or increased requirements for insulin or oral hypoglycaemic agents in diabetes, suppression of growth in children. Relative adrenocortical insufficiency, particularly in time of stress due to trauma, severe illness or surgery.

Ophthalmic

Posterior subcapsular cataracts, increased intraocular pressure, exophthalmos.

Immune system

Masking of infections, latent infections becoming active, opportunistic infections, hypersensitivity reactions including anaphylaxis, reactions to skin test may be suppressed.

Interactions:

Methylprednisolone has a wide spectrum of clinical use and is therefore used with numerous concurrent medicines. Below is a list of the classes of medicine which may result in interactions of known or likely clinical significance. The need for dosage adjustment of either medication will depend on the clinical situation, the dose regimen prescribed and the observed clinical response. The interactions have either a pharmacokinetic or pharmacodynamic basis.

Classes of medicines which may result in interactions:

Antibiotics, antifungals, anticholinesterases, anticoagulants, anticonvulsants, antidiabetic medicines, antihypertensive agents, cardiovascular medicines, diuretics, immunizing agents,

immunosuppressants, neuromuscular blocking agents, psychotherapeutic agents, salicylates and sympathomimetic agents, analgesics and antacids.

The following additional reactions are related to parenteral corticosteroids therapy:

Anaphylactic reactions with or without circulatory collapse, cardiac arrest, brochospasms, cardiac arrhythmias, hypotension or hypertension.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Treatment should be symptomatic and supportive. Methylprednisolone is dialysable.

IDENTIFICATION:

White freeze-dried cake or powder.

PRESENTATION:

Sterile SOLU-MEDROL is available in the following strengths:

40 mg Act-O-Vial

125 mg Act-O-Vial

500 mg Vial with Bacteriostatic Water for Injection

1000 mg Vial with Bacteriostatic Water for Injection

STORAGE DIRECTIONS:

Unreconstituted product:

Do not store above 25°C.

Reconstituted product:

Store reconstituted solution below 25°C and use within 12 hours.

Keep out of reach of children.

REGISTRATION NUMBERS:

SOLU-MEDROL 40 mg: D/21.5.1/135

SOLU-MEDROL 125 mg: D/21.5.1/136

SOLU-MEDROL 500 mg: L/21.5.1/25

SOLU-MEDROL 1000 mg: L/21.5.1/26

Bacteriostatic Water for Injection: H/34/60

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

Pfizer Laboratories (Pty) Ltd

85 Bute Lane

Sandton 2196

South Africa

DATE OF PUBLICATION OF THIS PACKAGE INSERT:

15 December 1992

BOTSWANA: S2

SOLU-MEDROL 40 mg: Reg. No.: B9312160

SOLU-MEDROL 125 mg: Reg. No.: B9312165

SOLU-MEDROL 500 mg: Reg. No.: B9312170

SOLU-MEDROL 1000 mg: Reg. No.: B9312175

NAMIBIA: S2

SOLU-MEDROL 40 mg: Reg. No.: 90/21.5.1/001362

SOLU-MEDROL 125 mg: Reg. No.: 90/21.5.1/001360

SOLU-MEDROL 500 mg: Reg. No.: 90/21.5.1/001363

SOLU-MEDROL 1000 mg: Reg. No.: 90/21.5.1/001359