AUSTRALIAN PRODUCT INFORMATION – SOLU-MEDROL® and SOLU-MEDROL® ACT-O-VIAL (METHYLPREDNISOLONE SODIUM SUCCINATE)

1. NAME OF THE MEDICINE

Methylprednisolone sodium succinate

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

SOLU-MEDROL is available in several strengths for intravenous (IV) or intramuscular (IM) administration.

40 mg ACT-O-VIAL® System - Each mL (when mixed) contains methylprednisolone sodium succinate equivalent to 40 mg methylprednisolone;
125 mg ACT-O-VIAL System - Each 2 mL (when mixed) contains methylprednisolone sodium succinate equivalent to 125 mg methylprednisolone;

500 mg Vial with Diluent - Each 8 mL (when mixed as directed) contains methylprednisolone sodium succinate equivalent to 500 mg methylprednisolone;

1 gram Vial with Diluent - Each 15.6 mL (when mixed as directed) contains methylprednisolone sodium succinate equivalent to 1 gram methylprednisolone;

2 gram Vial with Diluent - Each 31.2 mL (when mixed as directed) contains methylprednisolone sodium succinate equivalent to 2 grams methylprednisolone;

500 mg Plain Vial - Each vial contains methylprednisolone sodium succinate equivalent to 500 mg methylprednisolone;

1 gram Plain Vial - Each vial contains methylprednisolone sodium succinate equivalent to 1 gram methylprednisolone;

For the full list of excipients, see Section 6.1 List of excipients.

3. PHARMACEUTICAL FORM

SOLU MEDROL 40 mg and 125 mg ACT-O-VIAL System

- Powder for injection: White freeze dried cake

- Diluent: Clear colourless liquid

SOLU-MEDROL 500 mg, 1 gram and 2 grams Vials with Diluent

- Powder for injection: White freeze dried cake

- Diluent: Clear colourless liquid

SOLU-MEDROL 500 mg and 1 gram Plain Vials

- Powder for injection: White freeze dried cake

When necessary, the pH of each formula was adjusted with sodium hydroxide so that the pH of the reconstituted solution is within the USP specified range of 7 to 8 and the tonicities are, for the 40 mg per mL solution, 0.50 osmolar; for the 125 mg per 2 mL, 500 mg per 8 mL and 1 gram per 16 mL solutions, 0.40 osmolar; for the 2 gram per 31.2 mL solutions, 0.42 osmolar (Isotonic saline = 0.28 osmolar).

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

When oral therapy is not feasible and the strength, dosage form and route of administration of the drug reasonably lend the preparation to the treatment of the condition, SOLU-MEDROL Powder for Injection is indicated only for intravenous or intramuscular use in the following conditions:

Endocrine Disorders

- Primary or secondary adrenocortical insufficiency (hydrocortisone or cortisone is the drug of choice; synthetic analogues may be used in conjunction with mineralocorticoids where applicable; in infancy, mineralocorticoid supplementation is of particular importance).

- Acute adrenocortical insufficiency (hydrocortisone or cortisone is the drug of choice; mineralocorticoid supplementation may be necessary, particularly when synthetic analogues are used).

- Preoperatively and in the event of serious trauma or illness, in patients with known adrenal insufficiency or when adrenocortical reserve is doubtful.

- Shock unresponsive to conventional therapy if adrenocortical insufficiency exists or is suspected.

- Congenital adrenal hyperplasia

- Nonsuppurative thyroiditis

- Hypercalcaemia associated with cancer.

Rheumatic Disorders

As adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in:

- Ankylosing spondylitis

- Psoriatic arthritis

- Acute and subacute bursitis
- Epicondylitis
- Synovitis of osteoarthritis
- Acute gouty arthritis
- Acute nonspecific tenosynovitis
- Post-traumatic osteoarthritis
- Rheumatoid arthritis, including juvenile rheumatoid arthritis (selected cases may require low-dose maintenance therapy).

Collagen Disease

During an exacerbation or as maintenance therapy in selected cases of:

- Systemic lupus erythematosus
- Systemic dermatomyositis (polymyositis)
- Acute rheumatic carditis.

Dermatological Diseases

- Bullous dermatitis herpetiformis
- Pemphigus
- Severe psoriasis
- Severe seborrhoeic dermatitis
- Exfoliative dermatitis
- Mycosis fungoides
- Severe erythema multiforme (Stevens-Johnson Syndrome).

Allergic States

Control of severe or incapacitating allergic conditions intractable to adequate trials of conventional treatment in:

- Bronchial asthma
- Drug hypersensitivity reactions
- Contact dermatitis

- Urticarial transfusion reactions
- Atopic dermatitis
- Serum sickness
- Acute noninfectious laryngeal oedema (adrenaline is the drug of first choice).

Ophthalmic Diseases

Severe acute and chronic allergic and inflammatory processes involving the eye, such as:

- Allergic corneal marginal ulcers
- Allergic conjunctivitis
- Chorioretinitis
- Anterior segment inflammation
- Herpes zoster ophthalmicus
- Iritis, iridocyclitis
- Diffuse posterior uveitis and choroiditis
- Keratitis
- Optic neuritis
- Sympathetic ophthalmia.

Gastrointestinal Diseases

To tide the patient over a critical period of the disease in:

- Ulcerative colitis (systemic therapy)
- Regional enteritis (systemic therapy).

Respiratory Diseases

- Symptomatic sarcoidosis
- Berylliosis
- Aspiration pneumonitis
- Loeffler's syndrome not manageable by other means
- Fulminating or disseminated pulmonary tuberculosis when used concurrently with appropriate antituberculous chemotherapy.

Haematologic Disorders

- Idiopathic thrombocytopenic purpura in adults (IV only; IM administration is contraindicated)
- Secondary thrombocytopenia in adults
- Acquired (autoimmune) haemolytic anaemia
- Erythroblastopenia (RBC anaemia)
- Congenital (erythroid) hypoplastic anaemia.

Neoplastic Diseases

For palliative management of:

- Leukaemias and lymphomas in adults
- Acute leukaemia of childhood.

Oedematous States

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

Nervous System

- Acute exacerbations of multiple sclerosis.

Miscellaneous

- Tuberculous meningitis with subarachnoid block or impending block when used concurrently with appropriate antituberculous chemotherapy.
- Trichinosis with neurologic or myocardial involvement.
- SOLU-MEDROL is beneficial as adjunctive therapy in the treatment of acquired immunodeficiency syndrome (AIDS) patients with moderate to severe *Pneumocystis jiroveci* pneumonia (PCP) when given within the first 72 hours of initial anti-pneumocystis treatment.

4.2 Dose and method of administration

Dosage

SOLU-MEDROL may be administered by intravenous or intramuscular injection or by intravenous infusion, the preferred method for initial emergency use being intravenous injection. To administer by intravenous (or intramuscular) injection, prepare solution as directed. The desired dose, if 250 mg or less, may be administered intravenously over at least 5 minutes. Intramuscular injections (250 mg or less) should be injected slowly into a large

muscle. If desired, the medication may be administered in diluted solutions by adding Water for Injections or other suitable diluent (see below) to the ACT-O-VIAL and withdrawing the indicated dose.

Methylprednisolone sodium succinate is so extremely soluble in water that it may be administered in a small volume of diluent and is especially well suited for intravenous use in situations in which high blood levels of methylprednisolone are required rapidly.

When high dose therapy is desired (i.e. greater than 250 mg), the recommended dose of SOLU-MEDROL Sterile Powder is 30 mg/kg administered intravenously over at least 30 minutes (see Sections 4.4 Special warnings and precautions for use and 4.9 Overdose). This dose may be repeated every 4 to 6 hours for up to 48 hours.

In general, high dose corticosteroid therapy should be continued only until the patient's condition has stabilised; usually not beyond 48 to 72 hours.

Although the 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 500 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, up to 250 mg, should be given intravenously over a period of at least 5 minutes, and if greater than 250 mg then over at least 30 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 may be reduced for infants 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.

Warning - Benzyl alcohol (as contained in the accompanying diluent for the 500 mg, 1 gram and 2 gram vials) has been reported to be associated with a fatal "Gasping Syndrome" in premature infants (see Section 4.4 Special warnings and precautions for use, Paediatric Use).

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 glucose, determination of blood pressure and body weight, and a chest X-ray should be made at regular intervals during prolonged therapy. The state of the upper GI tract should be monitored in patients with a history of ulceration or significant dyspepsia.

Pneumocystis Jiroveci Pneumonia

For patients diagnosed with *Pneumocystis jiroveci* pneumonia (PCP), presenting with a P_aO_2 (arterial oxygen pressure) under 55 mm Hg on room air, or where respiratory failure is considered likely, the following regimen should be administered:

Administer 40 mg of SOLU-MEDROL Powder for Injection intravenously every six (6) hours for 5 to 7 days. Upon improvement, oral prednisolone should be instituted with the following tapering regimen:

60 mg (divided four times daily) for 2 days

50 mg (divided twice daily) for 2 days

40 mg (divided twice daily) for 2 days

30 mg (divided twice daily) for 2 days

20 mg (divided twice daily) for 2 days

15 mg (divided twice daily) for 2 days

10 mg (divided twice daily) for 2 days

5 mg (divided twice daily) for 2 days then cease.

Treatment with prednisolone should last a maximum of 21 days or until the end of antipneumocystis therapy.

The following four (4) clinical points should be considered when using adjunctive corticosteroid therapy for AIDS related PCP:

1. Adjunctive corticosteroid therapy should be initiated early (within 72 hours of starting antipneumocystis therapy).

2. The diagnosis of PCP must be confirmed and other pulmonary pathogens ruled out because of the potential for masking symptoms of untreated infections.

3. Antimycobacterial therapy should be initiated along with antipneumocystis therapy in patients with a current positive PPD test or in other high risk patients.

4. Adjunctive corticosteroid therapy should be commenced with the maximum recommended dose. The duration of treatment at this dose should be dependent upon both the severity of the disease and the clinical response to therapy. Following a satisfactory clinical response a tapering regimen should be instituted. The use of a tapering regimen decreases the potential for relapse upon the discontinuation of corticosteroid therapy.

Multiple Sclerosis

Administer 500 mg/day or 1 g/day for 3 or 5 days as IV pulse dosing over at least 30 minutes. (4 mg of methylprednisolone is equivalent to 5 mg of prednisolone)

Summary of Dosage and Administration Recommendations

1. For Intravenous Use

DOSE	ADMINISTRATION TIME
≥ 2 g	at least 30 minutes
1 g	at least 30 minutes
500 mg	at least 30 minutes
250 mg	at least 5 minutes
125 mg	at least 5 minutes
≤ 40 mg	at least 5 minutes

2. For Intramuscular Use

   Intramuscular injections (250 mg or less) should be injected slowly into a large muscle.

Method of Administration

Directions for Using the ACT-O-VIAL System

1. Tap to ensure that the powder is at base of vial and away from the central stopper.
2. Place the Act-O-Vial on a flat, stable surface and hold with one hand.
3. Press down firmly on the plastic activator with the palm of the other hand to force diluent into the lower compartment.
4. Gently mix the solution by turning the vial upside down a number of times. **DO NOT SHAKE THE VIAL.**
5. Remove plastic tab covering centre of stopper.
6. Sterilise top of stopper with an alcohol swab.

Note: Steps 1-6 must be completed before proceeding.

7. Whilst on a flat surface, insert needle **squarely through centre** of stopper until tip is just visible.
8. Invert vial to allow the solution to flow into the top compartment and withdraw the dose.

Reconstitution of SOLU-MEDROL

SOLU-MEDROL should be reconstituted with the diluent where this is provided. Where no diluent is provided, the sterile powder should be reconstituted using Bacteriostatic Water for Injections with benzyl alcohol or Sterile Water for Injections. Parenteral drug products

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

It is recommended that the reconstituted solution of SOLU-MEDROL be used immediately upon preparation.

The volume of diluent recommended and the resulting concentration is as follows:

Product Strength	Diluent Volume Recommended	Resulting Concentration
500 mg	4 or 8 mL	125 or 62.5 mg/mL
1 g	8 or 16 mL	125 or 62.5 mg/mL

IMPORTANT - Use only the accompanying diluent to reconstitute SOLU-MEDROL Vial with Diluent (which is Bacteriostatic Water for Injections with benzyl alcohol) and SOLU-MEDROL ACT-O-VIALS (which is sterile Water for Injections). Bacteriostatic Water for Injections with benzyl alcohol or sterile Water for Injections may be used when reconstituting SOLU-MEDROL Plain Vials.

Preparation of Solutions for Intravenous Infusion

To prepare solutions for intravenous infusion, first prepare the solution for injection as directed above. This solution may then be added to Glucose Intravenous Infusion 5%, Sodium Chloride Intravenous Infusion 0.9% or Sodium Chloride 0.9% and Glucose 5% Intravenous Infusion; the resulting admixtures should be used immediately. This solution is for SINGLE USE ONLY.

4.3 Contraindications

Methylprednisolone sodium succinate is contraindicated:

- in patients who have systemic fungal infections
- in patients with known hypersensitivity to methylprednisolone or any component of the formulation. The 40 mg ACT-O-VIAL presentation includes lactose produced from cow's milk. This presentation may contain trace amounts of milk ingredients and is therefore contraindicated in patients with a known or suspected hypersensitivity to cow's milk or its components, or to other dairy products.

SOLU-MEDROL (METHYLPREDNISOLONE SODIUM SUCCINATE) IS CONTRAINDICATED FOR INTRATHECAL, EPIDURAL OR LOCAL INJECTION, OR ANY OTHER UNSPECIFIED ROUTE OF ADMINISTRATION.

Administration of live or live attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of corticosteroids (see Section 4.4 Special warnings and precautions for use, Immunosuppressant Effects/Increased Susceptibility to Infections).

4.4 Special warnings and precautions for use

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. 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.

Immunosuppressant Effects/Increased Susceptibility to Infections

Corticosteroids increase susceptibility to infection, 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. Infections with any pathogen including viral, bacterial, fungal, protozoan or helminthic infections, in any location in the body, may be associated with the use of corticosteroids alone or in combination with other immunosuppressive agents that affect cellular immunity, humoral immunity, or neutrophil function. These infections may be mild, but can be severe and at times fatal. With increasing doses of corticosteroids, the rate of occurrence of infectious complications increases.

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 on corticosteroids.

Similarly, corticosteroids should be used with great care in patients with known or suspected parasitic infections such as Strongyloides (threadworm) infestation, which may lead to Strongyloides hyperinfection and dissemination with widespread larval migration, often accompanied by severe enterocolitis and potentially fatal gram-negative septicaemia.

Administration of live or live attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of corticosteroids. Killed or inactivated vaccines may be administered to patients receiving immunosuppressive doses of corticosteroids; however, the response to such vaccines may be diminished. Indicated immunisation procedures may be undertaken in patients receiving non-immunosuppressive doses of corticosteroids.

The use of SOLU-MEDROL Powder for Injection 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 anti-tuberculosis 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.

The use of SOLU-MEDROL in patients with AIDS (as in the adjunctive treatment of *Pneumocystis jiroveci* pneumonia) may be associated with an increased rate of reactivation of tuberculosis. Consideration should therefore be given to the administration of antimycobacterial therapy if corticosteroids are used in this high risk group. Such patients should also be observed for the activation of other latent infections, and judicious examinations of sputum/bronchoalveolar fluid should be made for the presence of other infectious agents.

Kaposi's sarcoma has been reported to occur in patients receiving corticosteroid therapy. Discontinuation of corticosteroids may result in clinical remission.

A study has failed to establish the efficacy of SOLU-MEDROL in the treatment of sepsis syndrome and septic shock. Thus, routine use in septic shock is not recommended. The study also suggests that treatment of these conditions with SOLU-MEDROL may increase the risk of mortality in certain patients (i.e. patients with elevated serum creatinine levels or patients who develop secondary infections after SOLU-MEDROL).

Immune System Effects

Allergic reactions may occur. Because rare instances of skin reactions and anaphylactic/anaphylactoid reactions (e.g. bronchospasm) have occurred in patients receiving parenteral corticosteroid therapy, appropriate precautionary measures should be taken prior to administration, especially when the patient has a history of allergy to any drug.

In patients receiving the 40 mg presentation of methylprednisolone sodium succinate during the treatment for acute allergic conditions and where these symptoms worsen or any new allergic symptoms occur, consideration should be given to the potential for hypersensitivity reactions to cow's milk ingredients (see Section 4.3 Contraindications). If appropriate, administration of methylprednisolone sodium succinate should be stopped, and the patient's condition should be treated accordingly. Alternative treatments, including the use of corticosteroid formulations that do not contain ingredients produced from cow's milk, should be considered for acute allergy management, where appropriate.

Cardiac Effects

There are reports of cardiac arrhythmias and/or circulatory collapse and/or cardiac arrest following the rapid administration of large IV doses of SOLU-MEDROL (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 (see Sections 4.2 Dose and method of administration, 4.8 Adverse effects (undesirable effects) and 4.9 Overdose).

Adverse effects of glucocorticoids on the cardiovascular system, such as dyslipidemia and hypertension, may predispose treated patients with existing cardiovascular risk factors to additional cardiovascular effects if high doses and prolonged courses are used. Accordingly, corticosteroids should be employed judiciously in such patients and risk modification and additional cardiac monitoring may need to be considered. Low dose and alternate day therapy may reduce the incidence of complications in corticosteroid therapy.

Use of systemic corticosteroid is not recommended in patients with congestive heart failure.

Vascular Effects

Thrombosis including venous thromboembolism has been reported to occur with corticosteroids. As a result corticosteroids should be used with caution in patients who have or may be predisposed to thromboembolic disorders.

Corticosteroids should be used with caution in patients with hypertension.

Endocrine Effects

In patients on corticosteroid therapy subjected to unusual stress, increased dosage of rapidly acting corticosteroids before, during and after the stressful situation is indicated.

Pharmacologic doses of corticosteroids administered for prolonged periods may result in hypothalamic-pituitary-adrenal (HPA) suppression (secondary adrenocortical insufficiency). The degree and duration of adrenocortical insufficiency produced is variable among patients and depends on the dose, frequency, time of administration, and duration of glucocorticoid therapy. This effect may be minimised by use of alternate-day therapy.

In addition, acute adrenal insufficiency leading to a fatal outcome may occur if glucocorticoids are withdrawn abruptly.

Drug-induced secondary adrenocortical insufficiency may be minimised 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.

A steroid "withdrawal syndrome", seemingly unrelated to adrenocortical insufficiency, may also occur following abrupt discontinuance of glucocorticoids. This syndrome includes symptoms such as anorexia, nausea, vomiting, lethargy, headache, fever, joint pain, desquamation, myalgia, weight loss, and/or hypotension. These effects are thought to be due to the sudden change in glucocorticoid concentration rather than to low corticosteroid levels.

Because glucocorticoids can produce or aggravate Cushing's syndrome, glucocorticoids should be avoided in patients with Cushing's disease.

There is an enhanced effect of corticosteroids in patients with hypothyroidism.

Pheochromocytoma crisis, which can be fatal, has been reported after administration of systemic corticosteroids. Corticosteroids should only be administered to patients with suspected or identified pheochromocytoma after an appropriate risk/benefit evaluation.

Ocular Effects

Corticosteroids should be used cautiously in patients with ocular herpes simplex because of possible corneal perforation.

Prolonged use of corticosteroids may produce posterior subcapsular cataracts and nuclear cataracts (particularly in children), exophthalmos or increased intraocular pressure which may result in glaucoma with possible damage to the optic nerves and may enhance the establishment of secondary ocular infections due to fungi or viruses.

Corticosteroid therapy has been associated with central serous chorioretinopathy, which may lead to retinal detachment.

If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes.

Psychiatric Effects

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.

Potentially severe psychiatric adverse reactions may occur with systemic steroids (see Section 4.8 Adverse effects (undesirable effects)). Symptoms typically emerge within a few days or weeks of starting treatment. Most reactions recover after either dose reduction or withdrawal, although specific treatment may be necessary.

Psychological effects have been reported upon withdrawal of corticosteroids; the frequency is unknown. Patients/caregivers should be encouraged to seek medical attention if psychological symptoms develop in the patient, especially if depressed mood or suicidal ideation is suspected. Patients/caregivers should be alert to possible psychiatric disturbances that may occur either during or immediately after dose tapering/withdrawal of systemic steroids.

Gastrointestinal Effects

High doses of corticosteroids may produce acute pancreatitis.

Corticosteroid therapy may mask the symptoms of peptic ulcer so that perforation or haemorrhage may occur without significant pain. Glucocorticoid therapy may mask peritonitis or other signs or symptoms associated with gastrointestinal disorders such as perforation, obstruction or pancreatitis. In combination with non-steroidal anti-inflammatory drugs (NSAIDs), the risk of developing gastrointestinal ulcers is increased.

Corticosteroids should be used with caution in non-specific ulcerative colitis if there is a probability of impending perforation, abscess, or other pyogenic infection, diverticulitis, fresh intestinal anastomoses, or active or latent peptic ulcer.

Nervous System Effects

Use of corticosteroids is not recommended in patients with seizure disorders.

Corticosteroids should be used with caution in patients with myasthenia gravis (see Section 4.4 Special warnings and precautions for use, Musculoskeletal Effects).

Although controlled clinical trials have shown corticosteroids to be effective in speeding the resolution of acute exacerbations of multiple sclerosis, they do not show that corticosteroids affect the ultimate outcome or natural history of the disease. The studies do show that relatively high doses of corticosteroids are necessary to demonstrate a significant effect (see Section 4.2 Dose and method of administration).

Severe medical events have been reported in association with the intrathecal/epidural routes of administration (see Section 4.8 Adverse effects (undesirable effects)).

There have been reports of epidural lipomatosis in patients taking corticosteroids, typically with long-term use at high doses.

Musculoskeletal Effects

An acute myopathy has been described with the use of high doses of corticosteroids, most often occurring in patients with disorders of neuromuscular transmission (e.g. myasthenia gravis) or in patients receiving concomitant therapy with anticholinergics, such as neuromuscular blocking drugs (e.g. pancuronium). This acute myopathy is generalised, may involve ocular and respiratory muscles, and may result in quadriparesis. Elevations of creatine kinase may

occur. Clinical improvement or recovery after stopping corticosteroids may require weeks to years.

Corticosteroids should be used with caution in osteoporosis. Osteoporosis is a common but infrequently recognised adverse effect associated with a long-term use of large doses of glucocorticoid.

Metabolism and Nutrition

Corticosteroids, including methylprednisolone, can increase blood glucose, worsen pre-existing diabetes, and predispose those on long-term corticosteroid therapy to diabetes mellitus.

Injury, Poisoning and Procedural Complications

Systemic corticosteroids are not indicated for, and should therefore not be used to treat traumatic brain injury. A large multicentre randomised study in patients administered corticosteroid therapy after significant head injury revealed an increased risk of mortality in the corticosteroid group compared to the placebo group.

Other

Aspirin and non-steroidal anti-inflammatory agents should be used cautiously in conjunction with corticosteroids (see Section 4.5 Interactions with other medicines and other forms of interactions, Table 2, NSAIDs).

Benzyl alcohol is contained in the accompanying diluent for the 500 mg, 1 gram and 2 gram vials. Benzyl alcohol has been reported to be associated with a fatal "Gasping Syndrome" in premature infants (see Section 4.4 Special warnings and precautions for use, Paediatric Use). The 40 mg ACT-O-VIALS and the 125 mg ACT-O-VIALS do not contain benzyl alcohol.

Use in Hepatic Impairment

Drug-induced liver injury such as acute hepatitis can result from cyclical pulsed IV methylprednisolone (usually at doses of 1 g/day). The time to onset of acute hepatitis can be several weeks or longer. Resolution of the adverse event has been observed after treatment was discontinued. Serious hepatotoxicity has been reported.

There is an enhanced effect of corticosteroids in patients with cirrhosis.

Use in Renal Impairment

Caution is required in patients with systemic sclerosis because an increased incidence of scleroderma renal crisis has been observed with corticosteroids, including methylprednisolone.

Corticosteroids should be used with caution in patients with renal insufficiency.

Use in the Elderly

Caution is recommended with prolonged corticosteroid treatment in the elderly due to a potential increased risk for osteoporosis, as well as increased risk for fluid retention with possible resultant hypertension.

Paediatric Use

Benzyl alcohol is contained in the accompanying diluent for the 500 mg, 1 gram and 2 gram vials. The 40 mg ACT-O-VIALS and the 125 mg ACT-O-VIALS do not contain benzyl alcohol. Benzyl alcohol is associated with severe adverse effects, including fatal "gasping syndrome", in paediatric patients. The minimum amount of benzyl alcohol at which toxicity may occur is unknown. The risk of benzyl alcohol toxicity depends on the quantity administered and the liver and kidneys' capacity to detoxify the chemical. Premature and low-birth-weight infants, as well as patients receiving high dosages, may be more likely to develop toxicity. Practitioners administering this and other medications containing benzyl alcohol should consider the combined daily metabolic load of benzyl alcohol from all sources.

Growth and development of infants and children on prolonged corticosteroid therapy should be carefully observed. Growth may be suppressed in children receiving long-term, daily, divided-dose glucocorticoid therapy and use of such a regimen should be restricted to the most urgent indications. Alternate-day glucocorticoid therapy usually avoids or minimises this side effect.

Infants and children on prolonged corticosteroid therapy are at special risk from raised intracranial pressure.

High doses of corticosteroids may produce pancreatitis in children.

Hypertrophic cardiomyopathy may develop after administration of methylprednisolone to prematurely born infants, therefore appropriate diagnostic evaluation and monitoring of cardiac function and structure should be performed.

Effects on Laboratory Tests

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.

4.5 Interactions with other medicines and other forms of interactions

Methylprednisolone has a wide spectrum of clinical use and is therefore used with numerous concurrent drugs. The interactions summarised in the following table are 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 listed have either pharmacokinetic or pharmacodynamic basis.

Methylprednisolone is a cytochrome P450 enzyme (CYP) substrate and is mainly metabolised by the CYP3A4 enzyme. CYP3A4 catalyses 6β-hydroxylation of steroids, the essential Phase I metabolic step for both endogenous and synthetic corticosteroids. Many other compounds are also substrates of CYP3A4, some of which (as well as other drugs) have been shown to alter glucocorticoid metabolism by induction (upregulation) or inhibition of the CYP3A4 enzyme.

CYP3A4 Inhibitors

Drugs that inhibit CYP3A4 activity generally decrease hepatic clearance, resulting in increased plasma concentrations of corticosteroids. Co-administration of these substances may require titration of corticosteroid dosage to reduce the risk of adverse effects and avoid steroid toxicity.

CYP3A4 Inducers

Drugs that induce CYP3A4 activity generally increase hepatic clearance, resulting in decreased plasma concentrations of corticosteroids. Co-administration of these substances may require an increase in corticosteroid dosage to achieve the desired result.

CYP3A4 Substrates

In the presence of another CYP3A4 substrate, the hepatic clearance of methylprednisolone may be affected, with corresponding dosage adjustments required. It is possible that adverse events associated with the use of either drug alone may be more likely to occur with co-administration.

The most common and/or clinically important drug interactions or effects resulting from co-administration of SOLU-MEDROL and examples of CYP3A4 inhibitors, inducers and substrates are provided in Table 1 and 2. Table 1 and 2 should be used in conjunction with the detailed information provided above.

Table 1 Examples of CYP3A4 inhibitors, inducers and substrates that interact with SOLU-MEDROL.

	CYP3A4 Inhibitor	**CYP3A4 Inducers**	**CYP3A4 Substrates**
Antibiotics/Antifungal Agents			
• Triacetyloleandomycin	✓		✓
• Erythromycin	✓		✓
• Ketoconazole	✓		✓
• Itraconazole	✓		✓
Antibiotics/Antitubular Agents			
• Rifampicin		✓	
• Rifabutin		✓	
• Isoniazid (also see Table 2)	✓		
Anticonvulsants			
• Carbamazepine		✓	✓

	CYP3A4 Inhibitor	CYP3A4 Inducers	CYP3A4 Substrates
• Phenobartital		✓	
• Phenytoin		✓	
Antiemetics			
• Aprepitant	✓		✓
• Fosaprepitant	✓		✓
Antivirals			
• HIV Protease Inhibitors e.g. indinavir and ritonavir	✓		✓
Calcium Channel Blocker			
• Diltiazem	✓		✓
Contraceptives (Oral)			
• Ethinylestradiol	✓		✓
• Norethindrone	✓		✓
Grapefruit Juice	✓		
Immunosuppressants			
Ciclosporin (also see Table 2)	✓		✓
Cyclophosphamide			✓
Tacrolimus			✓
Macrolide Antibacterial Agents			
• Clarithromycin	✓		✓
• Erthryomycin	✓		✓
• Troleandomycin	✓		

Table 2 Important drug or substance interactions/effects with methylprednisolone.

Class of Drug/Drug(s) Involved	Drug(s) Affected/Mechanism/Clinical Implication
Antibiotic/Antifungal Therapy - Triacetyloleandomycin - Erythromycin - Ketoconazole	CYP3A4 inhibitor Co-administration may result in reduced corticosteroid clearance, enhanced clinical effects and an increased risk of adverse effects of methylprednisolone.
Antibiotics/Antitubular Therapy - Rifampicin	CYP3A4 inducer Increased hepatic clearance which may reduce efficacy of corticosteroid. Dosage adjustment may be required.
Anticholinesterase - Neostigmine - Pyridostigmine	Corticosteroids may reduce the effects of anticholinesterases in myasthenia gravis which may result in precipitation of myasthenic crisis.
Anticoagulants - Oral anticoagulants or heparin	Effect on anticoagulant is variable. Enhanced as well as diminished effects of anticoagulants with co-administration with corticosteroids have been reported. Coagulation indices should be monitored. Adjust dose accordingly to maintain desired anticoagulant effects.
Anticonvulsants - Phenobarbitone - Phenytoin	CYP3A4 inducers Co-administration may increase clearance of methylprednisolone leading to reduced methylprednisolone efficacy. Monitor clinical response. Adjust dose if necessary.
Antidiabetic Drugs - Insulin - Glibenclamide - Metformin	Diabetogenic effects of corticosteroid may impair glucose control of the antidiabetic agents. Monitor glucose levels and adjust dose of antidiabetic therapy if used concurrently with corticosteroids.
All Antihypertensive Agents	Antihypertensive agents are affected with co-administration due to mineralocorticoid effect of corticoid leading to raised blood pressure. May result in partial loss of hypertensive control.

Class of Drug/Drug(s) Involved	Drug(s) Affected/Mechanism/Clinical Implication
Antitubular Agents - Isoniazid	CYP3A4 inhibitor. In addition there is a potential effect of methylprednisolone to increase the acetylation rate and clearance of isoniazid.
Aromatase Inhibitors - Aminoglutethimide	Aminoglutethimide induced adrenal suppression may exacerbate endocrine changes caused by prolonged glucocorticoid treatment.
Cardioactive Drugs - Digoxin and related glycosides	Corticosteroid induced potassium loss (mineralocorticoid effect). Potentiation of digoxin toxicity.
Diuretic - All potassium losing diuretics e.g. frusemide, thiazide - Carbonic anhydrase inhibitors e.g. acetazolamide.	Excessive potassium loss may be experienced with concurrent use of corticosteroids and potassium depleting diuretics or carbonic anhydrase inhibitors. There is enhanced toxicity with co-administration and an increased risk of hypokalaemia. Monitor K+ levels and supplement if necessary.
HIV Protease Inhibitors - e.g. indinavir, ritonavir	Co-administration may increase plasma concentrations of corticosteroids. Corticosteroids may reduce plasma concentrations of HIV-protease inhibitors, by inducing their metabolism.
Immunising Agents - Live vaccine e.g. poliomyelitis, BCG, mumps, measles, rubella, smallpox. - Killed Virulent Vaccines	Co-administration may result in corticosteroid induced immunosuppression. There may be an increased toxicity from vaccine. Disseminated viral disease may occur (see Sections 4.3 Contraindications and 4.4 Special warnings and precautions for use). Co-administration may result in impaired immune response and/or reduced response to vaccine (see Sections 4.3 Contraindications and 4.4 Special warnings and precautions for use).

Class of Drug/Drug(s) Involved	Drug(s) Affected/Mechanism/Clinical Implication
Immunosuppressants - Methotrexate - Ciclosporin	Synergistic effect on disease state. 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 drug may be more likely to occur. May allow reduced dose of corticosteroid. Increased activity of both ciclosporin and corticosteroids with co-administration. Convulsions have been reported with concurrent use of methylprednisolone and ciclosporin. Monitor ciclosporin A levels. Adjust dose as necessary.
Anticholinergics - Neuromuscular Blocking Agent e.g. Pancuronium, Vecuronium	Partial reversal of neuromuscular block. Acute myopathy has been reported with concurrent use of high doses of corticosteroids and anticholinergics, such as neuromuscular blocking agents (see Section 4.4 Special warnings and precautions for use). Antagonism of the neuromuscular blocking effects of pancuronium and vecuronium has been reported in patients taking corticosteroids. This reaction may be expected with all competitive neuromuscular blockers.
Potassium depleting agents - Diuretics - Amphotericin B, xanthines or beta 2 agonists	When administered with potassium depleting agents, patients should be observed closely for development of hypokalaemia as there is an increased risk with concurrent use.
Psychotherapeutic - CNS active drugs such as Anxiolytics and Antipsychotics	Co-administration may potentiate CNS effects of corticosteroid. As the CNS active drug is affected with co-administration, recurrence or poor control of CNS symptoms may result. May require dose adjustment to obtain desired effect.

Class of Drug/Drug(s) Involved	Drug(s) Affected/Mechanism/Clinical Implication
NSAIDs - Aspirin	There may be increased incidence of gastrointestinal bleeding and ulceration when corticosteroids are given with NSAIDs. Methylprednisolone may increase the clearance of high-dose aspirin, which can lead to decreased salicylate serum levels. Discontinuation of methylprednisolone treatment can lead to raised salicylate serum levels, which could lead to an increased risk of salicylate toxicity.
Sympathomimetic Agents - Salbutamol	Co-administration leading to increased response to sympathetic agents with resulting increased efficacy and potentially increased toxicity.

4.6 Fertility, pregnancy and lactation

Effects on Fertility

Animal studies on the effects of methylprednisolone did not show an adverse impact on fertility in male and female rats treated with methylprednisolone aceponate at subcutaneous doses up to 0.1 mg/kg/day, although there was an increase in the number of non-viable fetuses. Other corticosteroids have been shown to impair fertility and reduce embryonic viability in studies in mice and rats.

Use in Pregnancy – Pregnancy Category A

Corticosteroids have been shown to be teratogenic in many species when given in doses equivalent to the human dose. In animal reproduction studies, glucocorticoids such as methylprednisolone have been shown to increase the incidence of malformations (cleft palate, ventricular septal defect, skeletal malformations), embryo-fetal lethality (e.g. increase in resorptions), intra-uterine growth retardation and abortions.

There is limited data on the use of methylprednisolone sodium succinate in human pregnancies, and animal reproduction studies have not been done. Methylprednisolone sodium succinate should be used in pregnancy only after a careful assessment of the benefit-risk ratio to the mother and fetus.

Some corticosteroids readily cross the placenta. An increased incidence of low-birth weights in infants born of mothers receiving corticosteroids has been reported.

Infants exposed *in utero* to substantial doses of corticosteroids must be carefully observed and evaluated for signs of adrenal insufficiency.

Cataracts have been observed in infants born to mothers treated with long-term corticosteroids during pregnancy.

Benzyl alcohol can cross the placenta (see Section 4.4 Special warnings and precautions for use, Paediatric Use).

Use in Lactation

Corticosteroids are excreted in breast milk.

Corticosteroids distributed into breast milk may suppress growth and interfere with endogenous glucocorticoid production in nursing infants. This medicinal product should be used during breast feeding only after a careful assessment of the benefit-risk ratio to the mother and infant.

4.7 Effects on ability to drive and use machines

The effect of corticosteroids on the ability to drive or use machinery has not been systematically evaluated. Undesirable effects, such as dizziness, vertigo, visual disturbances, and fatigue are possible after treatment with corticosteroids (see section 4.8 Adverse effects (Undesirable effects)). If affected, patients should not drive or operate machinery.

4.8 Adverse effects (undesirable effects)

Serious undesirable adverse events are also mentioned under the Section 4.4 Special warnings and precautions for use.

The following adverse reactions have been reported with the following contraindicated routes of administration: Intrathecal/Epidural: Arachnoiditis, functional gastrointestinal disorder/bladder dysfunction, headache, meningitis, paraparesis/paraplegia, seizure, sensory disturbance.

The adverse effects are listed in the table below by system organ class.

Infections and Infestations

Opportunistic infection, infection[a], peritonitis[g].

Blood and Lymphatic System Disorders

Leucocytosis.

Immune System Disorders

Drug hypersensitivity[b], anaphylactic reaction, anaphylactoid reaction.

Endocrine Disorders

Cushingoid, hypopituitarism, steroid withdrawal syndrome, adrenal insufficiency, secondary adrenocortical and pituitary unresponsiveness[c].

Metabolism and Nutrition Disorders

Metabolic acidosis, sodium retention, fluid retention, alkalosis hypokalaemic, dyslipidaemia, glucose tolerance impaired[d], increased insulin requirement (or oral hypoglycaemic agents in diabetics), lipomatosis, increased appetite (which may result in weight increased).

Psychiatric Disorders

Affective disorder (including depressed mood, euphoric mood, affect lability, drug dependence, suicidal ideation), psychotic disorder (including mania, delusion, hallucination and schizophrenia), mental disorder, personality change, confusional state, anxiety, mood swings, abnormal behaviour, insomnia, irritability.

Nervous System Disorders

Epidural lipomatosis, intracranial pressure increased (with papilloedema [benign intracranial hypertension]), seizure, amnesia, cognitive disorder, dizziness, headache.

Eye Disorders

Chorioretinopathy, cataract, glaucoma, exophthalmos, vision blurred.

Ear and Labyrinth Disorders

Vertigo.

Cardiac Disorders

Cardiac failure congestive (in susceptible patients), myocardial rupture[e], arrhythmia.

Vascular Disorders

Thrombosis, hypertension, hypotension.

Respiratory, Thoracic and Mediastinal Disorders

Pulmonary embolism, hiccups.

Gastrointestinal Disorders

Peptic ulcer (with possible peptic ulcer perforation and peptic ulcer haemorrhage), intestinal perforation, gastric haemorrhage, pancreatitis, oesophagitis ulcerative, oesophagitis, vomiting, abdominal distension, abdominal pain, diarrhoea, dyspepsia, nausea.

Hepatobiliary Disorders

Hepatitis[f].

Skin and Subcutaneous Tissue Disorders

Angioedema, hirsutism, petechiae, ecchymosis, subcutaneous atrophy, skin atrophy, erythema, hyperhidrosis, skin striae, rash, pruritus, urticaria, acne, skin hyperpigmentation, skin hypopigmentation.

Musculoskeletal and Connective Tissue Disorders

Muscular weakness, myalgia, myopathy, muscle atrophy, osteoporosis, osteonecrosis, pathological fracture, neuropathic arthropathy, arthralgia, growth retardation.

Reproductive System and Breast Disorders

Menstruation irregular.

General Disorders and Administration Site Conditions

Abscess sterile, impaired healing, oedema peripheral, fatigue, malaise, injection site reaction.

Investigations

Intraocular pressure increased, carbohydrate tolerance decreased, blood potassium decreased, urine calcium increased, alanine aminotransferase increased, aspartate aminotransferase increased, blood alkaline phosphatase increased, blood urea increased, suppression of reactions to skin tests[h].

Injury, Poisoning and Procedural Complications

Spinal compression fracture, tendon rupture.

a Including masking of infections and latent infections becoming active.
b With or without circulatory collapse, cardiac arrest, bronchospasm, or hypertension.
c Particularly in times of stress, as in trauma, surgery or illness.
d Manifestations of latent diabetes mellitus.
e Following a myocardial infarction.
f Hepatitis has been reported with IV administration (see Section 4.4 Special warnings and precautions for use).
g Peritonitis may be the primary presenting sign or symptom of a gastrointestinal disorder such as perforation, obstruction or pancreatitis (see Section 4.4 Special warnings and precautions for use).
h Not a MedDRA preferred term.

Reporting Suspected Adverse Effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 Overdose

Reports of acute toxicity and metabolic disturbances with glucocorticoids are rare but do occur. There is no clinical syndrome of acute overdosage with SOLU-MEDROL Powder for Injection. Acute overdose may possibly aggravate pre-existing disease states such as ulceration of the gastrointestinal tract, electrolyte disturbances, infections, diabetes and oedema. Repeated high

doses of methylprednisolone have caused hepatic necrosis and an increase in amylase. Bradyarrhythmias, ventricular arrhythmias and cardiac arrest have been observed in cases of intravenous administration of high doses of methylprednisolone.

Repeated frequent doses (daily or several times per week) over a protracted period may result in a Cushingoid state. The possibility of adrenal suppression should be guarded against by gradual diminution of dose levels over a period of time.

In the event of an overdose, treatment is symptomatic and supportive, including respiratory and cardiovascular function. In chronic toxicity, fluids and electrolytes should be monitored closely. Serum levels are not clinically useful.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Mechanism of Action

Methylprednisolone is a potent anti-inflammatory steroid. It has a 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. The relative potency of SOLU-MEDROL Powder for Injection and hydrocortisone sodium succinate, as indicated by 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.

Clinical Trials

No data available.

5.2 Pharmacokinetic properties

Absorption

Peak methylprednisolone plasma levels of approximately 20 µg/mL are reached after IV infusions of 30 mg/kg body weight administered over 20 minutes, or 1 g over 30 to 60 minutes, whilst levels of 42-47 µg/mL are measured after an IV bolus injection of 40 mg. Peak methylprednisolone plasma levels of 34 µg/100 mL are measured after 120 minutes following a 40 mg intramuscular (IM) injection. Lower peak methylprednisolone plasma levels are achieved following IM injection than IV administration. However, the peak plasma value persists for a longer period following IM administration resulting in equivalent quantities of methylprednisolone reaching the plasma independent of the route of administration.

The plasma half-life of methylprednisolone is 2.3 to 4 hours and appears to be independent of the route/pattern of administration. The biological half-life is 12 to 36 hours. The intracellular

activity of glucocorticoids results in the marked variation in the plasma and pharmacological half-lives. Pharmacological activity persists after plasma levels are no longer measurable.

The duration of the anti-inflammatory action of glucocorticoids approximately equals the duration of the hypothalmic-pituitary-adrenal (HPA) axis suppression.

Metabolism

In vivo, cholinesterases rapidly hydrolyse methylprednisolone sodium succinate to free methylprednisolone. In man, methylprednisolone forms a weak dissociable bond with albumin and transcortin; approximately 40 to 90% of the drug is bound.

Metabolism of methylprednisolone occurs via the hepatic route and is qualitatively similar to metabolism of cortisol. The major metabolites are 20 beta-hydroxymethylprednisolone and 20-beta-hydroxy-6-alpha-methylprednisolone.

Excretion

The metabolites are mainly excreted in the urine as glucuronides, sulphates and unconjugated compounds. Following intravenous (IV) administration of ^{14}C labelled methylprednisolone, 75% of the total radioactivity was recovered in the urine in 96 hours, 9% in faeces after 5 days and 20% in the bile.

5.3 Preclinical safety data

Genotoxicity

Methylprednisolone has not been formally evaluated in rodent carcinogenicity studies. Negative results for carcinogenicity have been obtained with various other glucocorticoids, including budesonide, prednisolone and triamcinolone acetonide in mice. However, all three of these compounds were shown to increase the incidence of hepatocellular adenomas and carcinomas after oral administration in a 2-year study in male rats. These tumorigenic effects occurred at doses that are less than the typical clinical doses on a mg/m^2 basis. Hepatocarcinogenicity is likely to involve an interaction with the glucocorticoid receptor.

Carcinogenicity

Methylprednisolone sodium succinate has not been formally evaluated for genotoxicity. However, methylprednisolone sulfonate, which is structurally similar to methylprednisolone sodium succinate, was not mutagenic in bacteria (Ames test), or in a mammalian cell gene mutation assay using Chinese hamster ovary cells. Methylprednisolone suleptanate did not induce unscheduled DNA synthesis in primary rat hepatocytes. Prednisolone farnesylate, which is also structurally similar to methylprednisolone, was not mutagenic in bacteria but displayed weak clastogenic activity *in vitro* in Chinese hamster lung fibroblasts in the presence of metabolic activation.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

SOLU-MEDROL 40 mg ACT-O-VIAL System

Monobasic sodium phosphate
Dibasic sodium phosphate
Lactose monohydrate
Sodium hydroxide

Diluent:
water for injections

SOLU-MEDROL 125 mg ACT-O-VIAL System

Monobasic sodium phosphate
Dibasic sodium phosphate
Sodium hydroxide

SOLU-MEDROL 500 mg, 1 gram and 2 g Vials with Diluent

Monobasic sodium phosphate monohydrate
Dibasic sodium phosphate
Sodium hydroxide

Diluent supplied with Solu-Medrol 500 mg and 2g vials with diluent
Benzyl alcohol
Water for injections

SOLU-MEDROL 500 mg and 1 g Plain Vials

Monobasic sodium phosphate
Dibasic sodium phosphate heptahydrate
Sodium hydroxide

6.2 Incompatibilities

To avoid compatibility and stability problems, whenever possible it is recommended that SOLU-MEDROL (methylprednisolone sodium succinate) be administered separately from other drugs and as either IV injection, through an IV medication chamber, microburette, or as an IV "piggy-back" solution. The IV compatibility and stability of methylprednisolone sodium succinate, either alone in solution or in admixtures with other drugs, is dependent on pH, concentration, time, temperature, and the ability of methylprednisolone to solubilise itself.

Drugs that are physically incompatible in solution with methylprednisolone sodium succinate include, but are not limited to: allopurinol sodium, doxapram hydrochloride, tigecycline,

diltiazem hydrochloride, calcium gluconate, vecuronium bromide, rocuronium bromide, cisatracurium besylate, glycopyrrolate, propofol.

6.3 Shelf life

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 Special precautions for storage

Store unreconstituted product below 25°C.

When reconstituted using either the diluent provided, or Bacteriostatic Water for Injections with benzyl alcohol, or Sterile Water for Injections, the resulting solution should be used immediately. Discard any unused portion.

6.5 Nature and contents of container

SOLU-MEDROL Powder for Injection is available in the following packages:

1 x 40 mg ACT-O-VIAL and diluent 1 mL in separate chambers.

1 x 125 mg ACT-O-VIAL and diluent 2 mL in separate chambers.

1 x 500 mg Vial and 1 x Diluent 8 mL.

1 x 1 gram Vial and 1 x Diluent 15.6 mL.

1 x 2 grams Vial and 1 x Diluent 31.2 mL.

1 x 500 mg Plain Vials

5 x 500 mg Plain Vials.

1 x 1 gram Plain Vials.

5 x 1 gram Plain Vials.

Not all presentations and pack sizes are marketed.

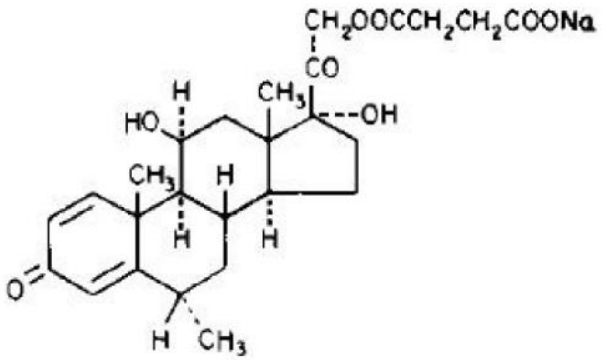
6.6 Special precautions for disposal

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 Physicochemical properties

Methylprednisolone sodium succinate, USP, occurs as a white, or nearly white, odourless, hygroscopic, amorphous solid. It is very soluble in water and in alcohol; it is insoluble in chloroform and is very slightly soluble in acetone.

Chemical Structure



Molecular formula: $C_{26}H_{33}NaO_8$

Molecular weight: 496.53

CAS Number

2375-03-3

7. MEDICINE SCHEDULE (POISONS STANDARD)

S4 - Prescription Only Medicine

8. SPONSOR

Pfizer Australia Pty Ltd

Level 17, 151 Clarence Street
Sydney NSW 2000
Toll Free Number: 1800 675 229
www.pfizer.com.au

9. DATE OF FIRST APPROVAL

SOLU-MEDROL Vial with Diluent: 2 August 1991

SOLU-MEDROL Plain Vial: 22 November 1994

SOLU-MEDROL ACT-O-VIAL: 23 September 2010

10. DATE OF REVISION

26 March 2021

® Registered trademark

Summary Table of Changes

Section changed	Summary of new information
All	• Minor editorial changes • Reformatting of the Australian PI to the European SPC format as requested by the Health Authority (TGA).
4.2	Revise dosing recommendation for acute exacerbations of multiple sclerosis according to company core data sheet.