PRODUCT INFORMATION
DEPO-MEDROL®
Suspension for Injection
For Intramuscular, Intra-articular, Soft Tissue or Intralesional Injection Only
Not for Intravenous or Intrathecal Use

NAME OF THE MEDICINE
Australian Approved Name (AAN): methylprednisolone acetate which is the 6-methyl derivative of prednisolone.

Chemical structure:

![Chemical Structure Image]

Chemical name: 11β, 17α, 21-trihydroxy-6α-methylpregna-1,4-diene-3,20-dione acetate

Molecular Formula: C₂₄H₃₂O₆
Molecular weight: 416.51
CAS registry number: 53-36-1

DESCRIPTION
Methylprednisolone acetate is a white or practically white, odourless, crystalline powder which melts at about 215°C with some decomposition. It is soluble in dioxane, sparingly soluble in acetone, in alcohol, in chloroform, and in methanol, and slightly soluble in ether. It is practically insoluble in water.

DEPO-MEDROL is an anti-inflammatory glucocorticoid, for intramuscular, intra-articular, soft tissue or intralesional injection.

It is available in a 40 mg/mL vial.
Each mL contains:

- Methylprednisolone acetate: 40 mg
- Macrogol 3350: 29 mg
- Sodium chloride: 8.7 mg
- Miripirium chloride: 0.195 mg

added as preservative.

When necessary, pH is adjusted with sodium hydroxide and/or hydrochloric acid. The pH of the finished product remains within the USP specified range, i.e. 3.0 to 7.0.

**PHARMACOLOGY**

Naturally occurring glucocorticoids (hydrocortisone), which also have salt-retaining properties, are used in replacement therapy in adrenocortical deficiency states. Their synthetic analogues are used primarily for their potent anti-inflammatory effects in disorders of many organ systems. Glucocorticoids cause profound and varied metabolic effects. In addition, they modify the body's immune response to diverse stimuli.

**INDICATIONS**

**A. For Intramuscular Administration**

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, the intramuscular use of DEPO-MEDROL is indicated as follows:

1. **Endocrine Disorders**
   - Primary or secondary adrenocortical insufficiency (hydrocortisone or cortisone acetate 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 acetate 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.
   - Congenital adrenal hyperplasia
   - Hypercalcaemia associated with cancer
   - Non-suppurative thyroiditis.
2. **Rheumatic Disorders**
As adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in:

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

3. **Collagen Diseases**
During an exacerbation or as maintenance therapy in selected cases of:

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

4. **Dermatological Diseases**

- Pemphigus
- Bullous dermatitis herpetiformis
- Severe erythema multiforme (Stevens-Johnson Syndrome)
- Severe seborrhoeic dermatitis
- Exfoliative dermatitis
- Severe psoriasis
- Mycosis fungoides.
5. **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
- Acute non-infectious laryngeal oedema (adrenaline is the drug of first choice)
- Serum sickness
- Seasonal or perennial allergic rhinitis.

6. **Ophthalmic Diseases**

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

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

7. **Gastrointestinal Diseases**

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

- Ulcerative colitis (systemic therapy)
- Regional enteritis (systemic therapy).
8. **Respiratory Diseases**
   - Symptomatic sarcoidosis
   - Berylliosis
   - Fulminating or disseminated pulmonary tuberculosis when used concurrently with appropriate anti-tuberculous chemotherapy.
   - Aspiration pneumonitis
   - Loeffler's Syndrome not manageable by other means.

9. **Haematological Disorders**
   - Acquired (autoimmune) haemolytic anaemia
   - Erythroblastopenia (RBC anaemia)
   - Secondary thrombocytopenia in adults
   - Congenital (erythroid) hypoplastic anaemia.

10. **Neoplastic Diseases**
    For palliative management of:
    - Leukaemias and lymphomas in adults
    - Acute leukaemia in childhood.

11. **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.

12. **Nervous System**
    - Acute exacerbations of multiple sclerosis.

13. **Miscellaneous**
    - Tuberculous meningitis with subarachnoid block or impending block when used concurrently with appropriate anti-tuberculous chemotherapy
    - Trichinosis with neurological or myocardial involvement.

B. **For Intra-Articular Or Soft Tissue Administration**
    DEPO-MEDROL is indicated as adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in:
• Synovitis of osteoarthritis
• Epicondylitis
• Rheumatoid arthritis
• Acute non-specific tenosynovitis
• Acute and subacute bursitis
• Post-traumatic osteoarthritis
• Acute gouty arthritis.

C. For Intralesional Administration
DEPO-MEDROL is indicated for intralesional use in the following conditions:
• Keloids
• Discoid lupus erythematosus
• Necrobiosis lipoidica diabeticorum
• Alopecia areata
• Localised hypertrophic, infiltrated inflammatory lesions of Lichen Planus, psoriatic plaques, Granuloma Annulare and Lichen Simplex Chronicus (neurodermatitis).

DEPO-MEDROL may also be useful in cystic tumours of an aponeurosis or tendon (ganglia).

*CONTRAINDICATIONS
• Intrathecal administration
• Systemic fungal infections
• Known hypersensitivity to methylprednisolone or any component of the formulation
• Intravenous administration
• Administration of live or live, attenuated vaccines in patients receiving immunosuppressive doses of corticosteroids (see PRECAUTIONS).

*PRECAUTIONS
While crystals of adrenal steroids in the dermis suppress inflammatory reactions, their presence may cause disintegration of the cellular elements and physiochemical changes in the ground substance of the connective tissue. The resultant infrequently occurring
dermal and/or subdermal changes may form depressions in the skin at the injection site. The degree to which this reaction occurs will vary with the amount of adrenal steroid injected. Regeneration is usually complete within a few months or after all crystals of the adrenal steroid have been absorbed.

In order to minimise the incidence of dermal and subdermal atrophy, care must be exercised not to exceed recommended doses in injections. Multiple small injections into the area of the lesion should be made whenever possible. The technique of intra-articular and intramuscular injection should include precautions against injection or leakage into the dermis. Injection into the deltoid muscle should be avoided because of a high incidence of subcutaneous atrophy.

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

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 of 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.

Do not use intra-articularly, intrabursally or for intratendinous administration for local effect in the presence of acute infection.

A clinical trial in patients with septic shock failed to establish the efficacy of DEPO_MEDROL for these conditions. Thus, routine use in septic shock is not recommended. The study also suggests that treatment of these conditions with DEPO-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 DEPO-MEDROL).

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.

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.

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 DEPO-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 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.

Allergic reactions may occur. Because rare instances of skin reactions and anaphylactic/anaphylactoid reactions 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.

Allergic skin reactions have been reported apparently related to the excipients in the formulation. Rarely has skin testing demonstrated a reaction to methylprednisolone acetate per se.

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. When using corticosteroids in these patients, attention should be paid to risk modification and additional cardiac monitoring should be considered.

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

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.

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. Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticoid should be administered concurrently.

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

High doses of corticosteroids may produce acute pancreatitis.

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

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

The lowest possible dose of corticosteroid should be used to control the condition under treatment, and when reduction in dosage is possible, the reduction must 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.

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. Symptoms typically emerge within a few days or weeks of starting treatment. 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.

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

Aspirin and non-steroidal anti-inflammatory agents should be used cautiously in conjunction with corticosteroids (see INTERACTIONS OF OTHER MEDICINES, Effect of Methylprednisolone on Other Medicines, NSAIDs).

Corticosteroid therapy may mask the symptoms of peptic ulcer so that perforation or haemorrhage may occur without significant pain.

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

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 DOSAGE AND ADMINISTRATION).
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 quadriplegia. Elevations of creatinine kinase may occur. Clinical improvement or recovery after stopping corticosteroids may require weeks to years.

Osteoporosis is a common but infrequently recognised adverse effect associated with a long-term use of large doses of glucocorticoid.

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

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

Additional Precautions Specific For Parenteral Corticosteroids

Intra-articular injection of a corticosteroid may produce systemic as well as local effects.

Appropriate examination of any joint fluid present is necessary to exclude a septic process.

A marked increase in pain accompanied by local swelling, further restriction of joint motions, fever, and malaise are suggestive of septic arthritis. If this complication occurs and the diagnosis of sepsis is confirmed, appropriate antimicrobial therapy should be instituted.

Local injection of a steroid into a previously infected joint is to be avoided.

Corticosteroids should not be injected into unstable joints.

Sterile technique is necessary to prevent infections or contamination.

The slower rate of absorption by intramuscular administration should be recognised.

Use in Pregnancy: Category C

In animal experiments, corticosteroids have been found to cause foetal malformations of various kinds (cleft palate, skeletal malformations) and abortions. Adequate human reproductive studies have not been done with corticosteroids. Therefore the use of this drug in pregnancy, nursing mothers, or women of child bearing potential requires that the benefits of the drug be carefully weighed against the potential risk to the mother and embryo or fetus. Since there is inadequate evidence of safety in human pregnancy, this drug should be used in pregnancy only if clearly needed.

Corticosteroids readily cross the placenta. Increased incidence of reduced placental and birth weight has been recorded in infants born of mothers receiving corticosteroids.
Infants exposed *in utero* to substantial doses of corticosteroids must be carefully observed and evaluated for signs of adrenal insufficiency. Since the possibility of suppression of the adrenal cortex in the newborn baby after long-term treatment must be considered, the needs of the mother must be carefully weighed against the risk to the foetus when prescribing corticosteroids.

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

The short-term use of corticosteroids antepartum for the prevention of respiratory distress syndrome does not seem to pose a risk to the foetus or the newborn infant. Maternal pulmonary oedema has been reported with tocolysis and fluid overload. No effect is known relating to use in labour and delivery.

**Use in Lactation**

Corticosteroids are excreted in milk.

Corticosteroids distributed into breast milk may suppress growth and interfere with endogenous glucocorticoid production in nursing infants. Since adequate reproductive studies have not been performed in humans with glucocorticoids, these drugs should be administered to nursing mothers only if the benefits of therapy are judged to outweigh the potential risks to the infant.

**Paediatric Use**

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 regimen should be restricted to the most urgent indications.

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

High doses of corticosteroids may produce pancreatitis in children.

**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.

**Use in Renal Impairment**

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

**Carcinogenicity**

No evidence exists showing that corticosteroids are carcinogenic or mutagenic.
Effects on Ability to Drive and Use of 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. If affected, patients should not drive or operate machinery.

*INTERACTIONS WITH OTHER MEDICINES

The pharmacokinetic interactions listed below are potentially clinically important.

Effects of Methylprednisolone and Other Medicines on Each Other

*Cyclosporin*

Mutual inhibition of metabolism occurs with concurrent use of cyclosporin and methylprednisolone. This may increase the plasma concentrations of either or both drugs. It is possible that adverse events associated with the individual use of either drug may be more apt to occur. Convulsions have been reported with concurrent use of methylprednisolone and cyclosporin.

*Cyclophosphamide and tacrolimus*

Cyclophosphamide and tacrolimus (immunosuppressants) compete for the same metabolic pathway as methylprednisolone. The concomitant use of either of these medicines with methylprednisolone may cause their hepatic clearance (or that of methylprednisolone) to be inhibited or induced, 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.

*Isoniazid*

Isoniazid decreases hepatic clearance of methylprednisolone, resulting in increased plasma concentration. In addition, there is a potential effect of methylprednisolone on the acetylation rate and clearance of isoniazid.

Effect of Methylprednisolone on Other Medicines

*NSAIDs*

There may be increased incidence of gastrointestinal bleeding and ulceration when corticosteroids are given with NSAIDs.

Methylprednisolone may increase the clearance of chronic high dose aspirin. This could lead to decreased salicylate serum levels or increase the risk of salicylate toxicity when methylprednisolone is withdrawn (see PRECAUTIONS).
Oral anticoagulants

The effect of corticosteroids on oral anticoagulants is variable. There are reports of enhanced as well as diminished effects of anticoagulant when given concurrently with corticosteroids. Therefore coagulation indices should be monitored to maintain the desired anticoagulant effect.

Potassium-depleting agents

When corticosteroids are administered concomitantly with potassium-depleting agents (i.e. diuretics), patients should be observed closely for development of hypokalaemia. There is also an increased risk of hypokalaemia with concurrent use of corticosteroids with amphotericin B, xanthenes, or beta2 agonists.

Anticholinergics (Neuromuscular blockers)

An acute myopathy has been reported with the concomitant use of high doses of corticosteroids and anticholinergics, such as neuromuscular blocking drugs (see PRECAUTIONS). Antagonism of the neuromuscular blocking effects of pancuronium and vecuronium has been reported in patients taking corticosteroids. This interaction may be expected with all competitive neuromuscular blockers.

Antidiabetics

Corticosteroids may increase blood glucose concentrations, therefore, dosage adjustments of antidiabetic agents may be required.

Effect of Other Medicines on Methylprednisolone

Inducers of Hepatic Enzymes

Drugs that induce hepatic enzymes such as phenobarbitone, phenytoin, carbamazepine (anticonvulsants) and rifampicin (antibiotic) may increase the clearance of corticosteroids and may require increases in methylprednisolone dose to achieve the desired response.

Inhibitors of Hepatic clearance

Drugs such as some macrolide antibiotics (e.g. triacylloleandomycin, erythromycin, clarithromycin), antifungals (e.g. ketoconazole, itraconazole), antiemetics (e.g. aprepitant, fosaprepitant), HIV-protease inhibitors (e.g. indinavir, ritonavir), diltiazem (a calcium channel blocker), oral contraceptives (e.g. ethinyloestradiol, norethisterone) may inhibit the metabolism of methylprednisolone and thus decrease their clearance. Therefore the dose of methylprednisolone should be titrated to avoid steroid toxicity.

Aromatase Inhibitors

Aminogluthethimide-induced adrenal suppression may impede endocrine changes caused by prolonged glucocorticoid treatment.
*ADVERSE EFFECTS*

**Fluid and electrolyte disturbances**

- Sodium retention
- Fluid retention
- Congestive heart failure in susceptible patients
- Potassium loss
- Hypokalaemic alkalosis
- Hypertension.

**Neurological**

- Convulsions
- Amnesia
- Cognitive disorder
- Dizziness
- Increased intracranial pressure with papilloedema (pseudotumour cerebri) usually after treatment
- Vertigo
- Headache
- Psychic derangements - affective disorder (including affect lability, depressed mood, euphoric mood, psychological dependence and suicidal ideation), psychotic disorder (including mania, delusion, hallucination, schizophrenia [aggravation of]), confusional state, mental disorder, anxiety, personality change, mood swings, abnormal behaviour, insomnia, irritability.

**Musculoskeletal**

- Muscle weakness
- Neuropathic arthropathy
- Myalgia
- Steroid myopathy
- Loss of muscle mass
- Osteoporosis
- Vertebral compression fractures
- Aseptic necrosis of femoral and humeral heads
- Osteonecrosis
- Arthralgia
- Pathological fracture of long bones
- Tendon rupture, particularly of the Achilles tendon.

**Endocrine**

- Menstrual irregularities
- Development of Cushingoid state
• Suppression of growth in children
• Secondary adrenocortical and pituitary unresponsiveness particularly in times of stress, as in trauma, surgery or illness.
• Suppression of pituitary – adrenal axis
• Manifestations of latent diabetes mellitus
• Decreased carbohydrate tolerance
• Increased requirements for insulin or oral hypoglycaemic agents in diabetes.

**Gastrointestinal**

• Peptic ulcer with possible subsequent perforation and haemorrhage
• Gastric haemorrhage
• Intestinal perforation
• Pancreatitis
• Abdominal distension
• Abdominal pain
• Peritonitis
• Diarrhoea
• Dyspepsia
• Oesophagitis
• Ulcerative oesophagitis
• Nausea.

**Investigations**

• Increases in alanine transaminase (ALT, SGPT), aspartate transaminase (AST, SGOT) and alkaline phosphatase have been observed following corticosteroid treatment. These changes are usually small, not associated with any clinical syndrome and are reversible upon discontinuation.
• Blood potassium decreased
• Urine calcium increased.

**Ophthalmic**

• Posterior subcapsular cataracts
• Increased intraocular pressure
• Glaucoma
• Exophthalmos.

**Metabolic**

• Negative nitrogen balance due to protein catabolism
• Glucose tolerance impaired
• Dyslipidaemia
• Increased appetite (which may result in increased weight)
• Lipomatosis
• Blood urea increased.

**Dermatological**
• Impaired wound healing
• Thin fragile skin
• Petechiae and ecchymosis
• Increased sweating
• Facial erythema
• May suppress reactions to skin tests
• Angioedema
• Oedema peripheral
• Skin striae
• Rash
• Pruritis
• Hirsutism
• Acne.

**Immune system**
• Masking of infections
• Latent infections becoming active
• Opportunistic infections
• Hypersensitivity reactions including anaphylaxis.

**Cardiovascular**
• Hypotension.

**Respiratory, Thoracic and Mediastinal**
• Persistent hiccups with high doses of corticosteroids.

**General Disorders and Administration Site Conditions**
• Injection site reaction
• Fatigue
• Malaise.

**Additional adverse reactions specifically related to parenteral corticosteroid therapy**
• Rare instances of blindness associated with intralesional therapy around the face and head
• Anaphylactic reaction
• Hyperpigmentation or hypopigmentation
• Allergic or hypersensitivity reactions
• Subcutaneous and cutaneous atrophy
• Urticaria
• Sterile abscess
• Injection site infections following non-sterile administration (see PRECAUTIONS)
• Post-injection flare following intra-articular use, Charcot-like arthropathy.

DEPO-MEDROL is not recommended for extradural, epidural, or any other route of administration that is not listed under INDICATIONS.

Administration by other than indicated routes has been associated with reports of serious medical events including arachnoiditis, meningitis, paraparesis/paraplegia, sensory disturbances, bowel/bladder dysfunction, seizures, visual impairment including blindness, ocular and periocular inflammation, and residue or slough at injection site.

DOSAGE AND ADMINISTRATION

Because of possible physical incompatibilities, DEPO-MEDROL should not be diluted or mixed with other solutions.

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

It is critical that, during administration of DEPO-MEDROL, appropriate technique be used and care taken to assure proper placement of drug.

A. Administration for Local Effect

Therapy with DEPO-MEDROL does not obviate the need for the conventional measures usually employed. Although this method of treatment will ameliorate symptoms, it is in no sense a cure and the hormone has no effect on the cause of the inflammation.

1. Rheumatoid and Osteoarthritis

The dose for intra-articular administration depends upon the size of the joint and varies with the severity of the condition in the individual patient. In chronic cases, injections may be repeated at intervals ranging from one to five or more weeks depending upon the degree of relief obtained from the initial injection. The doses in the following table are given as a general guide.

<table>
<thead>
<tr>
<th>Size of Joint</th>
<th>Examples</th>
<th>Range of Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Large</td>
<td>Knees, Ankles, Shoulders</td>
<td>20 to 80 mg</td>
</tr>
<tr>
<td>Medium</td>
<td>Elbows, Wrist</td>
<td>10 to 40 mg</td>
</tr>
<tr>
<td>Small</td>
<td>Metacarpophalangeal, Interphalangeal, Sternoclavicular, Acromioclavicular</td>
<td>4 to 10 mg</td>
</tr>
</tbody>
</table>
Procedure: It is recommended that the anatomy of the joint involved be reviewed before attempting intra-articular injection. In order to obtain the full anti-inflammatory effect it is important that the injection be made into the synovial space. Employing the same sterile technique as for a lumbar puncture, a sterile 20 to 24-gauge needle (on a dry syringe) is quickly inserted into the synovial cavity. Procaine infiltration is elective. The aspiration of only a few drops of joint fluid proves the needle has entered the joint space. **The injection site for each joint is determined by that location where the synovial cavity is most superficial and most free of large vessels and nerves.** With the needle in place, the aspirating syringe is removed and replaced by a second syringe containing the desired amount of DEPO-MEDROL. The plunger is then pulled outward slightly to aspirate synovial fluid and to make sure the needle is still in the synovial space. After injection, the joint is moved gently a few times to aid mixing of the synovial fluid and the suspension. The site is covered with a small sterile dressing. Suitable sites for intra-articular injection are the knee, ankle, wrist, elbow, shoulder, phalangeal and hip joints. Since difficulty is not infrequently encountered in entering the hip joint, precautions should be taken to avoid any large blood vessels in the area. Joints not suitable for injection are those that are anatomically inaccessible such as the spinal joints and those like the sacroiliac joints that are devoid of synovial space. Treatment failures are most frequently the result of failure to enter the joint space. Little or no benefit follows injection into surrounding tissue. If failures occur when injections into the synovial spaces are certain, as determined by aspiration of fluid, repeated injections are usually futile. Local therapy does not alter the underlying disease process and whenever possible, comprehensive therapy including physiotherapy and orthopaedic correction should be employed.

Following intra-articular steroid therapy, care should be taken to avoid overuse in joints in which symptomatic benefit has been obtained. Negligence in this matter may permit an increase in joint deterioration that will more than offset the beneficial effects of the steroid. Unstable joints should not be injected. Repeated intra-articular injection may in some cases result in instability of the joint. X-ray follow-up is suggested in selected cases to detect deterioration.

If a local anaesthetic is used prior to injection of DEPO-MEDROL, the anaesthetic package insert should be read carefully and all the precautions observed.

2. **Bursitis**

The area around the injection site is prepared in a sterile way and a wheal at the site made with 1% procaine hydrochloride solution. A 20 to 24-gauge needle attached to a dry syringe is inserted into the bursa and the fluid aspirated. The needle is left in place and the aspirating syringe changed for a small syringe containing the desired dose. After injection, the needle is withdrawn and a small dressing applied.

3. **Miscellaneous: Ganglion, Tendinitis, Epicondylitis**

In the treatment of conditions such as tendinitis or tenosynovitis, care should be taken, following application of a suitable antiseptic to the overlying skin, to inject the suspension into the tendon sheath rather than into the substance of the tendon. The tendon may be readily palpated when placed on a stretch. When treating conditions such as epicondylitis, the area of greatest tenderness should be outlined carefully and the suspension infiltrated into the area. For ganglia of the tendon sheaths, the suspension is injected directly into the cyst. In many
cases, a single injection causes a marked decrease in the size of the cystic tumour and may affect disappearance. The usual sterile precautions should be observed, of course, with each injection.

NOTE: Due to the absence of a true tendon sheath, the Achilles tendon should not be injected with DEPO-MEDROL.

The dose in the treatment of the various conditions of the tendinous or bursal structures listed above varies with the condition being treated and ranges from 4 mg to 30 mg. In recurrent or chronic conditions, repeated injections may be necessary.

4. Injections for local effect in dermatological conditions

Following cleansing with an appropriate antiseptic such as 70% alcohol, 20 mg to 60 mg of the suspension is injected into the lesion. It may be necessary to distribute doses ranging from 20 mg to 40 mg by repeated local injections in the case of large lesions. Care should be taken to avoid injection of sufficient material to cause blanching since this may be followed by a small slough. One to four injections are usually employed, the intervals between injections varying with the type of lesion being treated and the duration of improvement produced by the initial injection.

B. Administration for Systemic Effect

The intramuscular dosage will vary with the condition being treated. When a prolonged effect is desired, the weekly dose may be calculated by multiplying the daily oral dose by 7 and given as a single intramuscular injection.

Dosage must be individualised according to the severity of the disease and response of the patient. For infants and children, the recommended dosage will have to be reduced, but dosage should be governed by the severity of the condition rather than by strict adherence to the ratio indicated by age or bodyweight.

Hormone therapy is an adjunct to, and not a replacement for, conventional therapy. Dosage must be decreased or discontinued gradually when the drug has been administered for more than a few days. The severity, prognosis and expected duration of the disease and the reaction of the patient to medication are primary factors in determining dosage. 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 sugar, determination of blood pressure and body weight, and a chest X-ray should be made at regular intervals during prolonged therapy. Upper gastrointestinal X-rays are desirable in patients with an ulcer history or significant dyspepsia.

In patients with adrenogenital syndrome, a single intramuscular injection of 40 mg every two weeks may be adequate. For maintenance of patients with rheumatoid arthritis, the weekly intramuscular dose will vary from 40 mg to 120 mg. The usual dosage for patients with skin lesions benefited by systemic corticoid therapy is 40 mg to 120 mg of methylprednisolone acetate administered intramuscularly at weekly intervals for one to four weeks. In chronic contact dermatitis repeated injections at 5 to 10 day intervals may be necessary. In seborrhoeic dermatitis, a weekly dose of 80 mg may be adequate to control the condition.
Following intramuscular administration of 80 mg to 120 mg to **asthmatic patients**, relief may result within 6 to 48 hours and persist for several days to two weeks. Similarly in patients with **allergic rhinitis** (hay fever) an intramuscular dose of 80 mg to 120 mg may be followed by relief of coryzal symptoms within six hours persisting for several days to three weeks.

If signs of stress are associated with the condition being treated, the dosage of the suspension should be increased. If a rapid hormonal effect of maximum intensity is required, the intravenous administration of highly soluble methylprednisolone sodium succinate (SOLU-MEDROL®) is indicated.

**Multiple Sclerosis**

In the treatment of acute exacerbations of multiple sclerosis daily doses of 200 mg of prednisolone for a week followed by 80 mg every other day for 1 month have been shown to be effective (4 mg of methylprednisolone is equivalent to 5 mg of prednisolone).

**OVERDOSE**

Reports of acute toxicity and metabolic disturbances with glucocorticoids are rare but do occur. There is no clinical syndrome of acute overdosage with DEPO-MEDROL (methylprednisolone acetate). 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.

DEPO-MEDROL contains Macrogol (polyethylene glycol) as an excipient. Hypokalaemia has been reported following an unintentional large intravenous administration of Macrogol. In case of overdose, monitor acid-balance; renal, cardiac and pulmonary function in symptomatic patients and treat accordingly. Onset of acute lung injury may be delayed.

For information on the management of overdose, contact the Poison Information Centre on 131126 (Australia).

**PRESENTATION AND STORAGE CONDITIONS**

DEPO-MEDROL Suspension for Injection 40 mg per mL supplied as 5 x 1 mL and 1 x 1 mL single dose vials.

DEPO-MEDROL is for single use in a single patient only. Discard any unused product.
Store below 30°C. Protect from freezing.

NAME AND ADDRESS OF THE SPONSOR

Pfizer Australia Pty Ltd
ABN 50 008 422 348
38-42 Wharf Road
West Ryde NSW 2114

POISON SCHEDULE OF THE MEDICINE

S4, PRESCRIPTION ONLY MEDICINE.

DATE OF TGA APPROVAL

30 March 2011

DATE OF MOST RECENT AMENDMENT

26 September 2012

* Please note changes to product information

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