Depo-Medrone® 40 mg/ml Injection

(methylprednisolone acetate)

PATIENT INFORMATION LEAFLET

The name of your medicine is Depo-Medrone 40mg/ml Injection and will be referred to as Depo-Medrone in this leaflet.

Read all of this leaflet carefully before you start taking this medicine
- Keep this leaflet. You may need to read it again
- If you have any further questions please ask your doctor or pharmacist
- This medicine has been prescribed for you. Do not pass it to others. It may harm them even if their symptoms are the same as yours
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, tell your doctor or pharmacist

In this leaflet:

1. WHAT DEPO-MEDRONE IS AND WHAT IT IS USED FOR

Depo-Medrone contains Methylprednisolone Acetate.
Methylprednisolone belongs to a group of medicines called corticosteroids or steroids.
Corticosteroids are produced naturally in your body and are important for many body functions.
Boosting your body with extra corticosteroid such as Depo-Medrone can help when injected into the body by a doctor or nurse, such as in or near a joint, to treat local symptoms caused by inflammatory or rheumatic conditions such as:
- **Bursitis:** inflammation in the fluid containing spaces around the shoulder, knee and/or elbow joints. For this condition this medicine will be injected directly into one or more of these spaces.
- **Osteoarthritis and rheumatoid arthritis:** inflammation located in between the joints. For these conditions this medicine will be injected directly into one or more joint spaces.
- **Plantar fasciitis**: inflammation of the tissues of the sole of the foot.
- **Skin problems**: such as alopecia areata (patchy baldness), keloids (scar tissue), lichen planus or simplex (small, purplish raised patches of skin or spots), discoid lupus (round-shaped patches, often on the face) or granuloma annulare (circular warty growths).
- **Epicondylitis (tennis elbow) and tenosynovitis:** For these conditions this medicine will be injected into the tendon sheath.

Alternatively this medicine may be injected into a muscle to help treat more general (systemic) problems affecting the whole body (e.g. symptoms caused by a hypersensitivity to a medicine), or allergic, inflammatory or rheumatic problems affecting the:
- **brain** e.g. meningitis caused by tuberculosis
- **bowel** and **gut** e.g. Crohn's disease (inflammation of the gut) or ulcerative colitis (inflammation of the lower bowel)
- **joints** e.g. rheumatoid arthritis
- **lungs** e.g. asthma, severe hay fever or rhinitis, tuberculosis or inflammation caused by breathing in (aspirating) vomit or stomach contents
- **skin** e.g. Stevens-Johnson syndrome (an 'auto-immune disorder in which an immune system causes the skin to blister and peel) or systemic lupus erythematosus (lupus),

Your doctor may use this medicine to treat conditions other than those listed above. Ask your doctor if you are unsure why you have been given this medicine.

2. BEFORE YOU ARE GIVEN DEPO-MEDRONE

Do not use Depo-Medrone if:
- You think you have ever suffered an **allergic** reaction, or any other type of reaction after being given Depo-Medrone, or any other medicine containing a corticosteroid or any of the ingredients in this medicine (Section 6 of this leaflet contains a list of ingredients).An allergic reaction may cause a skin rash or reddening, swollen face or lips or shortness of breath.
- You get a **rash**, or another symptom of an infection.

See your doctor immediately if you have any of the above.

Do not inject this medicine into:
- the **Achilles tendon** (which is located behind the ankle joint), or
- directly into a **vein (intravenous)**, the spinal cord (intrathecal), the outer covering of the brain (extradural), into the nostrils (intranasal) or in the eye (intraocular).

Take special care before taking Depo-Medrone:
You **must** tell your doctor before you take this medicine if you have any of the following conditions.

Your doctor may also have to monitor your treatment more closely, alter your dose or give you another medicine.

- **Chickenpox, shingles** or a **herpes** eye infection. If you think you have been in contact with someone with chickenpox or shingles and you have not already had these illnesses, or if you are unsure if you have had them.
- Severe **depression** or **manic depression** (bipolar disorder). This includes having had depression before while taking steroid medicines like Depo-Medrone, or having a family history of these illnesses.
- **Diabetes** (or if there is a family history of diabetes).
- **Epilepsy**.
- **Glaucoma** (increased pressure in the eye) or if there is a family history of glaucoma.
- You have recently suffered a **heart attack**.
- **Heart problems**, including heart failure or infections.
- **Hypertension** (high blood pressure).
- **Hypothyroidism** (an under-active thyroid).
- **Joint infection**
- **Kidney** or **liver** disease.
- **Muscle problems** (pain or weakness) have happened while taking steroid medicines in the past.
- **Myasthenia gravis** (a condition causing tired and weak muscles).
- **Osteoporosis** (brittle bones).
- **Skin abscess**.
- **Stomach ulcer** or other serious stomach or intestinal problems.
- **Thrombophlebitis** - vein problems due to thrombosis (clots in the veins) resulting in phlebitis (red, swollen and tender veins).
- **Tuberculosis** (TB) or if you have suffered tuberculosis in the past.

You **must** tell your doctor before you take this medicine if you have any of the conditions listed above.

Taking other medicines
Always tell your doctor or pharmacist if you are taking any medicines (including any you have bought without a prescription) as taking Depo-Medrone with other medicines could be harmful.
You should tell your doctor if you are taking any of the following medicines which can affect the way Depo-Medrone or the other medicine works:
- **Acetazolamide** - used to treat glaucoma and epilepsy
- **Aminoglutethimide** – used for treating cancer
- **Anticoagulants** - used to 'thin' the blood such as acenocoumarol, phenindione and warfarin
- **Anticholinesterase**s - used to treat myasthenia gravis (a muscle condition) such as distigmine and neostigmine
- **Antibiotics** (such as erythromycin)
- **Aspirin** and non-steroidal anti-inflammatory medicines (also called **NSAIDs**) such as ibuprofen used to treat mild to moderate pain
- **Barbiturates, carbamazepine, phenytoin** and **primidone** – used to treat epilepsy
- **Carbenoxolone** - used for heartburn and acid indigestion
- **Ciclosporin** - used to treat conditions such as severe rheumatoid arthritis, severe psoriasis or following an organ or bone marrow transplant
- **Digoxin** - used for heart failure and/or an irregular heart beat
- **Diltiazem** or **mibefradil** – used for heart problems or high blood pressure
- **Diuretics** – sometimes called water tablets.
- **Ketoconazole** or **itraconazole** – used to treat fungal infections
- **Pancuronium** – or other medicines called neuromuscular blocking agents which are used in some surgical procedures
- **Rifampicin** and **rifabutin** – antibiotics used to treat tuberculosis (TB)
- **Vaccines** - tell your doctor or nurse if you have recently had, or are about to have any vaccination. You **should not** have 'live' vaccines while using this medicine. Other vaccines may be less effective

If you are taking long term medication(s)
If you are being treated for diabetes, high blood pressure or water retention (oedema) tell your doctor as he/she may need to adjust the dose of the medicines used to treat these conditions.

Before you have any operation tell your doctor, dentist or anesthetist that you are taking this medicine.

If you require a test to be carried out by your doctor or in hospital it is important that you tell the doctor or nurse that you are taking Depo-Medrone. This medicine can affect the results of some tests.

Pregnancy and breast feeding
You **must** tell your doctor if you are pregnant, think you might be pregnant or are trying to become pregnant as this medicine could slow the baby's growth.
Tell your doctor if you are breast feeding as small amounts of corticosteroid medicines may get into breast milk.

If you continue breast-feeding while you are having treatment, your baby will need extra checks to make sure he or she is not being affected by your medicine.

Driving and Using Machines
There are no special precautions while you are being treated with this medicine.

3. HOW DEPO-MEDRONE IS GIVEN TO YOU

Steroid Cards

Remember to always carry a Steroid Treatment Card. Make sure your doctor or pharmacist has filled out the details of your medicine, including the dose and how long you will require steroid treatment.

You should show your steroid card to **anyone** who gives you treatment (such as a doctor, nurse or dentist) while you are taking this medicine, and for 3 months after your last injection.

If you are admitted to hospital for any reason always tell your doctor or nurse that you are taking this medicine. You can also wear a medic-alert bracelet or pendant to let medical staff know that you are taking a steroid if you have an accident or become unconscious.

Dosage information
Your doctor will decide on the site of injection, how much of the medicine and how many injections you will receive depending on the condition being treated and its severity. Your doctor will inject you with the lowest dose for the shortest possible time to get effective relief of your symptoms.

Adults
Your doctor/nurse will tell you how many injections you will require for the condition you are being treated for, and when you will get them.

Joints - the normal dose for the injections into joint will depend on the size of the joint. Large joints (e.g. knee, ankle and shoulder) may require 20 - 80 mg (0.5 – 2 ml), medium sized joints (e.g. elbow or wrist) 10 - 40 mg (0.25 – 1 ml) and small joints (e.g. finger or toe joints) may require a 4 - 10 mg (0.1 -0.25 ml) dose.
Joint injections may be given weekly over a period of several weeks, depending on how quickly you respond to treatment.

Bursitis and epicondylitis (tennis elbow) – the usual dose is between 4-30 mg (0.1 - 0.75 ml). In most cases repeat injections will not needed for bursitis and epicondylitis.
Repeat injections may be necessary to treat long standing conditions.

Skin conditions – the usual dose is between 20 – 60mg (0.5 – 1.5ml) injected into the affected part or parts of the skin.
For other more general conditions 40 – 120 mg (1 – 3ml) of this medicine may be injected into a large muscle.

Elderly
Treatment will normally be the same as for younger adults. However your doctor may want to see you more regularly to check how you are getting on with this medicine.

Children
Corticosteroids can affect growth in children so your doctor will prescribe the lowest dose that will be effective for your child.

If you are given more Depo-Medrone than you should
If you think you have been given too many injections of this medicine please speak to your doctor immediately.

Stopping/reducing the dose of your Depo-Medrone
Your doctor will decide when it is time to stop your treatment.
You will need to come off this treatment slowly if you:
- have been given Depo-Medrone for more than 3 weeks;
- have been given high doses of Depo-Medrone, over 32 mg (0.8 ml) daily, even if it was only for 3 weeks or less;
- have already had a course of corticosteroid tablets or injections in the last year;
- already have problems with your adrenal glands (adrenocortical insufficiency) before you started this treatment.

You will need to come off this medicine slowly to avoid **withdrawal symptoms**. These symptoms may include itchy skin, fever, muscle and joint pains, runny nose, sticky eyes, sweating and weight loss.

If your symptoms seem to return or get worse as your dose of this medicine is reduced tell your doctor immediately.

Mental problems while taking Depo-Medrone
Mental health problems can happen while taking steroids like Depo-Medrone (see also section 4, **Possible Side Effects**).
- These illnesses can be serious.
- Usually they start within a few days or weeks of starting the medicine.
- They are more likely to happen at high doses.
- Most of these problems go away if the dose is lowered or the medicine is stopped. However if the problems do happen they might need treatment.

Talk to a doctor if you (or someone using this medicine) show any signs of mental problems. This is particularly important if you are depressed, or might be thinking about suicide. In a few cases mental problems have happened when doses are being lowered or stopped.

4. POSSIBLE SIDE-EFFECTS
Like all steroids this medicine can cause side-effects, although not everybody gets them. Your doctor will have given you this medicine for a condition which if not treated properly could become serious.

In certain medical conditions medicines like Depo-Medrone (steroids) should not be stopped abruptly, if you suffer from any of the following symptoms seek IMMEDIATE medical attention, you doctor will then decide whether you should continue taking your medicine:
- **Allergic reactions,** such as skin rash, swelling of the face or wheezing and difficulty breathing. This type of side effect is rare, but can be serious.
- **Acute pancreatitis**, stomach pain spreading to your back, possibly accompanied by vomiting, shock and loss of consciousness.
- **Burst or bleeding ulcers,** symptoms of which are severe stomach pain which may go through to the back and could be associated with bleeding from the back passage, black or blood stained stools and/or vomiting blood.
- **Infections.** This medicine can hide or change the signs and symptoms of some infections, or reduce your resistance to the infection, so that they are hard to diagnose at an early stage. Symptoms might include a raised temperature and feeling unwell. Symptoms of a flare up of a previous TB infection could be coughing blood or pain in the chest. This medicine may also make you more likely to develop a severe infection.
- **Pulmonary embolus** (blood clot in the lung**)** symptoms include sudden sharp chest pain, breathlessness and coughing up blood.
- **Raised pressure within the skull** of children (pseudotumour cerebri) symptoms of which are headaches with vomiting, lack of energy and drowsiness. This side-effect usually occurs after treatment is stopped.
- **Thrombophlebitis (**blood clots or thrombosis in a leg vein), symptoms of which include painful swollen, red and tender veins.

If you experience any of the following side effects, or notice any other unusual effects not mentioned in this leaflet, tell your doctor immediately:

Body water and salts
- Swelling and high blood pressure, caused by increased levels of water and salt content.
- Cramps and spasms, due to the loss of potassium from your body. In rare cases this can lead to congestive heart failure (when the heart cannot pump properly).

Digestive system
- Nausea (feeling sick) or vomiting (being sick).
- Ulcers or thrush in the gullet (discomfort on swallowing).
- Indigestion.
- Bloated stomach.

Eyes
- Glaucoma (raised pressure within the eye, causing pain in the eyes and headaches).
- Swollen optic nerve (causing a condition called papilloedema, and which may cause sight disturbance).
- Damage to the optic nerve or cataracts (indicated by failing eyesight).
- Thinning of the clear part at the front of the eye (cornea) or of the white part of the eye (sclera).
- Worsening of viral or fungal eye infections.
- Protruding of the eyeballs (exophthalmos).

Hormones and metabolic system
- Slowing of normal growth in infants, children and adolescents which may be permanent.
- Irregular or no periods in women.
- Increased hair on the body and face in women (hirsutism).
- Round or moon-shaped face (Cushingoid facies).
- Increased appetite and weight gain.
- Diabetes or worsening of existing diabetes.
- Prolonged therapy can lead to lower levels of some hormones which in turn can cause low blood pressure and dizziness. This effect may persist for months.
- The amount of certain chemicals (enzymes) called alanine transaminase, aspartate transaminase and alkaline phosphatase that help the body digest drugs and other substances in your body may be raised after treatment with a corticosteroid. The change is usually small and the enzyme levels return to normal after your medicine has cleared naturally from your system. You will not notice any symptoms if this happens, but it will show up if you have a blood test.

Immune system
- Increased susceptibility to infections which can hide or change normal reactions to skin tests, such as that for tuberculosis.

Muscles, bones and joints
- Muscle weakness or wasting.
- Brittle bones (bones that break easily).
- Broken bones or fractures.
- Breakdown of bone due to poor circulation of blood, this causes pain in the hip.
- Torn muscle tendons causing pain and/or swelling.
- Muscle cramps or spasms.
- Swollen or painful joints due to infection.

Nerves and mood issues
Steroids including methylprednisolone can cause serious mental health problems.
These are common in both adults and children. They can affect about 5 in every 100 people taking medicines like methylprednisolone.
- Feeling depressed, including thinking about suicide.
- Feeling high (mania) or moods that go up and down.
- Feeling anxious, having problems sleeping, difficulty in thinking or being confused and losing your memory.
- Feeling, seeing or hearing things which do not exist. Having strange and frightening thoughts, changing how you act or having feelings of being alone.
- Other nervous system side effects may include breathing problems, convulsions, dizziness, drowsiness, difficulty breathing, sensation of cold, heat or numbness, tinnitus or unconsciousness.

Skin
- Abscess, especially near injection sites
- Acne.
- Poor wound healing.
- Thinning of skin with stretch marks.
- Bruising.
- Small purple/red patches on the skin.
- Pale or darker patches on your skin, or raised patches which are an unusual color.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.
By reporting side effects, you can help provide more information on the safety of this medicine.

5. HOW TO STORE DEPO-MEDRONE
This medicine must not be used after the expiry date 'EXP' shown on the container.
The doctor or pharmacist will keep the medicine in a safe place where children cannot see or reach it.
This medicine must be stored in a cool place, but must not be frozen.
Keep out of the sight and reach of children.
Do not store above 25ºC. Do not freeze.
Each vial is for single use only.
After use, your doctor should take the container and syringe away. If anything is left behind, return it to your pharmacy for safe disposal. This medicine should not be used if the product is any colour other than white, or if particles can be seen in it.

6. FURTHER INFORMATION
What Depo-Medrone contains:
Each 1 ml vial contains 40 mg methyl-prednisolone acetate.
Vial also contains macrogol 3350, sodium chloride, myristyl-gamma-picolinium chloride, sodium hydroxide, hydrochloric acid and water for injection.

What a Depo-Medrone looks like:
Depo-Medrone is available in a glass vial with a rubber cap, metal seal and a green flip-off cap.
Depo-Medrone is available in packs containing 1 or 10 vials, containing 1ml of suspension.

Manufacturer and Product Licence holder
Manufactured by Pfizer Manufacturing Belgium NV, Rijksweg 12, B-2870 Puurs, Belgium.
Procured from the EU by Product Licence holder Star Pharmaceuticals Ltd., 5 Sandridge Close, Harrow, Middlesex HA1 1XD. Repackaged by Servipharm Ltd.

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Depo-Medrone is a trademark of Pfizer.

Depo-Medrone® 40 mg/ml Injection

(methylprednisolone acetate)

Presentation

White, sterile aqueous suspension for injection containing 40 mg per ml methylprednisolone acetate. Also contains macrogol 3350, sodium chloride, myristyl-gamma-picolinium chloride, sodium hydroxide, hydrochloric acid and water for injection.

Uses

Depo-Medrone may be used locally or systemically, particularly where oral therapy is not feasible.

Depo-Medrone may be used by any of the following routes: intramuscular, intraarticular, periarticular, intrabursal, intralesional or into the tendon sheath. **It must not be used by the intrathecal or intravenous routes.** (See Contra-indications and Side-effects).

Intramuscular administration:

1. *Rheumatic disorders*
   Rheumatoid arthritis
2. *Collagen diseases/arthritis*
   Systemic lupus erythematosus
3. *Dermatological diseases*
   Severe erythema multiforme (Stevens-Johnson syndrome)
4. *Allergic states*
   Bronchial asthma
   Severe seasonal and perennial allergic rhinitis
   Drug hypersensitivity reactions
   Angioneurotic oedema
5. *Gastro-intestinal diseases*
   Ulcerative colitis
   Crohn's disease
6. *Respiratory diseases*
   Fulminating or disseminated tuberculosis (with appropriate antituberculous chemotherapy)
   Aspiration of gastric contents
7. *Miscellaneous*
   TB meningitis (with appropriate antituberculous chemotherapy)

Intra-articular administration:

Rheumatoid arthritis
Osteo-arthritis with an inflammatory component

Soft tissue administration (intrabursal, periarticular, into tendon sheath):

Synovitis not associated with infection
Epicondylitis
Tenosynovitis
Plantar fasciitis
Bursitis

Intralesional:

Keloids
Localized lichen planus
Localized lichen simplex
Granuloma annulare
Discoid lupus erythematosus
Alopecia areata

Dosage and administration

Depo-Medrone should not be mixed with any other suspending agent or solution. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever suspension and container permit. Depo-Medrone may be used by any of the following routes: intramuscular, intra-articular, periarticular, intrabursal, intralesional and into the tendon sheath.
It must not be used by the intrathecal or intravenous routes (see Contra-indications and Side-effects).

Undesirable effects may be minimized by using the lowest effective dose for the minimum period (see special warnings and precautions).

Depo-Medrone vials are intended for single dose use only.

Intramuscular-for sustained systemic effect. Allergic conditions (severe seasonal and perennial allergic rhinitis, asthma, drug reactions).
80 - 120 mg (2 - 3 ml).

Dermatological conditions, 40 - 120 mg (1 - 3 ml)

Rheumatic disorders and collagen diseases (rheumatoid arthritis, SLE), 40 -120 mg (1 - 3 ml) per week.
Dosage must be individualised and depends on the condition being treated and its severity.

Note: Depo-Medrone is not intended for the prophylaxis of severe seasonal and perennial allergic rhinitis or other seasonal allergies and should be administered only when symptoms are present.

The frequency of intramuscular injections should be determined by the duration of the clinical response.
In the case of seasonal allergic rhinitis a single injection is frequently sufficient. If necessary, however, a second injection may be given after two to three weeks.

On average the effect of a single 2 ml (80 mg) injection may be expected to last approximately two weeks.

Infra-articular: Rheumatoid arthritis, osteo-arthritis. The dose of Depo- Medrone depends upon the size of the joint and the severity of the condition. Repeated injections, if needed, may be given at intervals of one to five or more weeks depending upon the degree of relief obtained from the initial injection. A suggested dosage guide is: large joint (knee, ankle, shoulder), 20 - 80mg (0.5 - 2 ml); medium joint (elbow, wrist), 10 - 40 mg (0.25 - 1 ml): small joint (metacarpophalangeal, interphalangeal, sternoclavicular, acromioclavicular), 4 -10 mg (0.1 - 0.25 ml).

Intrabursal: Subdeltoid bursitis, prepatellar bursitis, olecranon bursitis.
For administration directly into bursae, 4-30 mg (0.1 - 0.75 ml). In most cases, repeat injections are not needed.

Intralesional: Keloids, localized lichen planus, localized lichen simplex, granuloma annulare, alopecia areata, and discoid lupus erythematosus.
For administration directly into the lesion for local effect in dermatological conditions, 20 - 60 mg (0.5 -1.5 ml). For large lesions, the dose may be distributed by repeated local injections of 20 - 40 mg
(0.5 -1 ml). One to four injections are usually employed. Care should be taken to avoid injection of sufficient material to cause blanching, since this may be followed by a small slough.

Periarticulac Epicondylitis. Infiltrate 4-30 mg (0.1 - 0.75 ml) into the affected area.

Into the tendon sheath: Tenosynovitis, epicondylitis. For administration directly into the tendon sheath, 4 - 30 mg (0.1 - 0.75 ml). In recurrent or chronic conditions, repeat injections may be necessary.

Special precautions should be observed when administering
Depo-Medrone. Intramuscular injections should be made deeply into the gluteal muscles. The usual technique of aspirating prior to injection should be employed to avoid intravascular administration. Doses recommended for intramuscular injection must not be administered superficially or subcutaneously.

Intra-articular injections should be made using precise, anatomical localisation into the synovial space of the joint involved. 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.
Suitable sites for intra-articular injection are the knee, ankle, wrist, elbow, shoulder, phalangeal and hip joints. The spinal joints, unstable joints and those devoid of synovial space are not suitable. Treatment failures age most frequently the result of failure to enter the joint space.
Intro-articular injections should be made with care as follows: ensure correct positioning of the needle into the synovial space and aspirate a few drops of joint fluid. The aspirating syringe should then be replaced by another containing Depo-Medrone. To ensure position of the needle, synovial fluid should be aspirated and the injection made. After injection the joint is moved slightly to aid mixing of the synovial fluid and the suspension. Subsequent to therapy care should be taken for the patient not to overuse the joint in which 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.

Intrabursal injections should be made as follows: the area around the injection site is prepared in a sterile way and a wheal at the site made with 1 per cent 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. In the treatment of tenosynovitis care should be taken to inject Depo-Medrone into the tendon sheath rather than into the substance of the tendon. Due to the absence of a true tendon sheath, the Achilles tendon should not be injected with Depo-Medrone.

Children: Dosage may be reduced for infants and children but should be governed more by the severity of the condition and response of the patient, than by age or size.

Elderly patients: When used according to instructions, there is no information to suggest that a change in dosage is warranted in the elderly. However, treatment of elderly patients, particularly if long-term, should be planned bearing in mind the more serious consequences of the common side-effects of corticosteroids in old age and close clinical supervision is required (see Special warnings and precautions).

Contra-indications, warnings, etc.

Contra-indications: Depo-Medrone is contra-indicated where there is known hypersensitivity to components and in systemic infection unless specific anti-infective therapy is employed.

Due to its potential for neurotoxicity, Depo-Medrone *must not* be given by the intrathecal route. In addition, as the product is a suspension it *must not* be given by the intravenous route (see Side-effects).
Interactions:

1. Convulsions have been reported with concurrent use of methylprednisolone and cyclosporin. Since concurrent administration of these agents results in a mutual inhibition of metabolism, it is possible that convulsions and other adverse effects associated with the individual use of either drug may be more apt to occur.
2. Drugs that induce hepatic enzymes, such as rifampicin, rifabutin, carbamazepine, phenobarbitone, phenytoin, primidone and aminoglutethimide enhance the metabolism of corticosteroids and their therapeutic effect may be reduced.
3. Drugs such as erythromycin and ketoconazole may inhibit the metabolism of corticosteroids and thus decrease their clearance.
4. Steroids may reduce the effects of anticholinesterases in myasthenia gravis. The desired effects of hypoglycaemic agents (including insulin), anti-hypertensives and diuretics are antagonized by corticosteroids, and the hypokalaemic effects of acetazolamide, loop diuretics, thiazide diuretics and carbenoxolone are enhanced.
5. The efficacy of coumarin anticoagulants may be enhanced by concurrent corticosteroid therapy and close monitoring of the INR or prothrombin time is required to avoid spontaneous bleeding.
6. The renal clearance of salicylates is increased by corticosteroids and steroid withdrawal may result in salicylate intoxication. Salicylates and non-steroid anti-inflammatory agents should be used cautiously in conjunction with corticosteroids in hypothrombinaemia.
7. Steroids have been reported to interact with neuromuscular blocking agents such as pancuronium with partial reversal of the neuromuscular block.

Effects on ability to drive and to use machines: None stated.

Other undesirable effects (frequency and seriousness)

Side-effects: The incidence of predictable undesirable side-effects associated with the use of corticosteroids, including hypothalamicpituitary- adrenal suppression correlates with the relative potency of the drug, dosage, timing of administration and duration of treatment (see Special warnings and precautions)

PARENTERAL CORTICOSTEROID THERAPY - Anaphylactic reaction or allergic reactions, hypopigmentation or hyperpigmentation, subcutaneous and cutaneous atrophy, sterile abscess, post injection flare (following intra- articular use), Charcot-like arthropathy, rare instances of blindness associated with intralesional therapy around the face and head.

GASTRO-INTESTINAL - Dyspepsia, peptic ulceration with perforation and haemorrhage, abdominal distension, oesophageal ulceration, oesophageal candidiasis, acute pancreatitis, perforation of bowel.

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.

ANTI-INFLAMMATORY AND IMMUNOSUPPRESSIVE EFFECTS -
Increased susceptibility and severity of infections with suppression of clinical symptoms and signs, opportunistic infections, may suppress reactions to skin tests, recurrence of dormant tuberculosis (see Special warnings and precautions).

MUSCULOSKELETAL - Proximal myopathy, osteoporosis, vertebral and long bone fractures, avascular osteonecrosis, tendon rupture, aseptic necrosis, muscle weakness.

FLUID AND ELECTROLYTE DISTURBANCE - Sodium and water retention, potassium loss, hypertension, hypokalaemic alkalosis, congestive heart failure in susceptible patients.

DERMATOLOGICAL- Impaired healing, petechiae and ecchymosis, thin fragile skin, skin atrophy, bruising, striae, telangiectasia, acne.

ENDOCRINE/METABOLIC - Suppression of the hypothalamo-pituitaryadrenal axis, growth suppression in infancy, childhood and adolescence, menstrual irregularity and amenorrhoea. Cushingoid fades, hirsutism, weight gain, impaired carbohydrate tolerance with increased requirement for antidiabetic therapy, negative nitrogen and calcium balance, increased appetite.

NEUROPSYCHIATRIC - A wide range of psychiatric reactions including affective disorders (such as irritable, euphoric, depressed and labile mood psychological dependence and suicidal thoughts), psychotic reactions (including mania, delusions, hallucinations and aggravation of schizophrenia), behavioural disturbances, irritability, anxiety, sleep disturbances, and cognitive dysfunction including confusion and amnesia have been reported for all corticosteroids. Reactions are common and may occur in both adults and children. In adults, the frequency of severe reactions was estimated to be 5-6%. Psychological effects have been reported on withdrawal of corticosteroids; the frequency is unknown. Increased intra-cranial pressure with papilloedema in children (pseudotumour cerebri) has been reported, usually after treatment withdrawal of methylprednisolone.

OPHTHALMIC - Increased intra- ocular pressure, glaucoma, papilloedema, cataracts with possible damage to the optic nerve, corneal or sclera! thinning, exacerbation of ophthalmic viral or fungal disease, exophthalmos.

GENERAL - Leucocytosis, hypersensitivity including anaphylaxis,
thrombo-embolism, nausea, vertigo.

WITHDRAWAL SYMPTOMS-too rapid a reduction of corticosteroid dosage following prolonged treatment can lead to acute adrenal insufficiency, hypotension and death. However, this is more applicable to corticosteroids with an indication where continuous therapy is given (see Special warnings and precautions).

A 'withdrawal syndrome' may also occur including fever, myalgia, arthralgia, rhinitis, conjunctivitis, painful itchy skin nodules and loss of weight.

CERTAIN SIDE-EFFECTS REPORTED WITH SOME NON RECOMMENDED ROUTES OF ADMINISTRATION

Intrathecal: Usual systemic corticoid adverse reactions, headache, meningismus, meningitis, paraplegia, spinal fluid abnormalities, nausea, vomiting, sweating, arachnoiditis, convulsions.

Extradural: Wound dehiscence, loss of sphincter control.

Intranasal: Permanent/temporary

Ophthalmic: (Subconjunctival) - Redness and itching, abscess, slough at injection site, residue at injection site, increased intra-ocular pressure, decreased vision - blindness, infection.
Miscellaneous injection sites- Scalp, tonsillar fauces, sphenopalatine ganglion: blindness.

Special warnings and precautions
Warnings and Precautions:

1. A Patient Information Leaflet is provided in the pack by the manufacturer.
2. Undesirable effects may be minimized by using the lowest effect dose for the minimum period. Frequent patient review is required to appropriately titrate the dose against disease activity (see Dosage and administration).
3. Patients should carry 'Steroid Treatment' cards which give clear guidance on the precautions to be taken to minimize risk and which provide details of prescriber, drug, dosage and the duration of treatment.
4. Depo-Medrone vials are intended for single dose use only. Any multidose use of the product may lead to contamination.
5. Depo-Medrone is not recommended for epidural, intranasal, infra-ocular, or any other unapproved route of administration. See Side-effects section for details of side-effects reported from some non- recommended routes of administration.
6. Due to the absence of a true tendon sheath, the Achilles tendon should not be injected with Depo-Medrone.
7. 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 minimize 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.
8. Intralesional doses should not be placed too superficially, particularly in easily visible sites in patients with deeply pigmented skins, since there have been rare reports of subcutaneous atrophy and depigmentation.
9. Systemic absorption of methylprednisolone occurs following intra-articular injection of Depo-Medrone. Systemic as well as local effects can therefore be expected.
10. Intra-articular corticosteroids are associated with a substantially increased risk of inflammatory response in the joint, particularly bacterial infection introduced with the injection. Charcot-like arthropathies have been reported particularly after repeated injections. Appropriate examination of any joint fluid present is necessary to exclude any bacterial infection, prior to injection.
11. Following a single dose of Depo-Medrone, plasma corfisol levels are reduced and there is evidence of hypothalamic-pituitary- adrenal (HPA) axis suppression. This suppression lasts for a variable period of up to 4 weeks. The usual dynamic tests of HPA axis function can be used to diagnose evidence of impaired activity (e.g. Synacthen test).
12. Adrenal cortical atrophy develops during prolonged therapy and may persist for months after stopping treatment. In patients who have received more than physiological doses of systemic corticosteroids (approximately 6 mg methylprednisolone) for greater than 3 weeks, withdrawal should not be abrupt. How dose reduction should be carried out depends largely on whether the disease is likely to relapse as the dose of systemic corticosteroids is reduced. Clinical assessment of disease activity may be needed during withdrawal. If the disease is unlikely to relapse on withdrawal of systemic corticosteroids, but there is uncertainty about HPA suppression, the dose of systemic corticosteroid may be reduced rapidly to physiological doses. Once a daily dose of 6 mg methylprednisolone is reached, dose reduction should be slower to allow the HPA-axis to recover.
    Abrupt withdrawal of systemic corticosteroid treatment, which has continued up to 3 weeks is appropriate if it is considered that the disease is unlikely to relapse. Abrupt withdrawal of doses up to 32 mg daily of methylprednisolone for 3 weeks is unlikely to lead to clinically relevant HPA-axis, in the majority of patients. In the following patient groups, gradual withdrawal of systemic corticosteroid therapy should be considered even after courses lasting 3 weeks or less:
    - Patients who have had repeated courses of systemic corticosteroids, particularly if taken for greater than 3 weeks.
    - When a short course has been prescribed within one year of cessation of long-term therapy (months or years).
    - Patients who may have reasons for adrenocortical insufficiency other than exogenous corticosteroid therapy.
    - Patients receiving doses of corticosteroid greater than 32 mg daily of methylprednisolone.
    - Patients repeatedly taking doses in the evening.
13. Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticoid should be administered concurrently.
14. Because rare instances of anaphylactic 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 drug allergy.
15. Corticosteroids may mask some signs of infection, and new infections may appear during their use. Suppression of the inflammatory response and immune function increases the susceptibility to fungal, viral and bacterial infections and their severity. The clinical presentation may often be atypical and may reach an advanced stage before being recognised.
16. Chickenpox is of serious concern since this normally minor illness may be fatal in immunosuppressed patients. Patients (or parents of children) without a definite history of chickenpox should be advised to avoid close personal contact with chickenpox or herpes zoster and if exposed they should seek urgent medical attention. Passive immunisation with varicella/zoster immunoglobulin (VZIG) is needed by exposed non-immune patients who are receiving systemic corticosteroids or who have used them within the previous 3 months; this should be given within 10 days of exposure to chickenpox. If a diagnosis of chickenpox is confirmed, the illness warrants specialist care and urgent treatment. Corticosteroids should not be stopped and the dose may need to be increased.
17. Live vaccines should not be given to individuals with impaired immune responsiveness. The antibody response to other vaccines may be diminished.
18. The use of Depo-Medrone in active tuberculosis should be restricted to those cases of fulminating or disseminated tuberculosis in which the corticosteroid is used for the management of the disease in conjunction with an appropriate antituberculous 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.
19. Care should be taken for patients receiving cardioactive drugs such as digoxin because of steroid induced electrolyte disturbance/ potassium loss (see Side-effects).
20. *The following precautions apply for parenteral corticosteroids:*
    Following infra-articular injection, the occurrence of a marked increase in pain accompanied by local swelling, further restriction of joint motion, 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 injected 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.

Special Precautions:
Particular care is required when considering the use of systemic corticosteroids in patients with the following conditions and frequent patient monitoring is necessary.

1. Osteoporosis (post-menopausal females are particularly at risk).
2. Hypertension or congestive heart failure.
3. Existing or previous history of severe affective disorders (especially previous steroid psychosis).
4. Diabetes mellitus (or a family history of diabetes).
5. History of tuberculosis.
6. Glaucoma (or a family history of glaucoma).
7. Previous corticosteroid-induced myopathy
8. Liver failure or cirrhosis.
9. Renal insufficiency.
10. Epilepsy.
11. Peptic ulceration.
12. Fresh intestinal anastomoses.
13. Predisposition to thrombophlebitis.
14. Abscess or other pyogenic infections.
15. Ulcerative colitis.
16. Diverticulitis.
17. Myasthenia gravis.
18. Ocular herpes simplex, for fear of corneal perforation.
19. Hypothyroidism.
20. Patients and/or carers should be warned that potentially severe psychiatric adverse reactions may occur with systemic steroids (see section 4.8). Symptoms typically emerge within a few days or weeks of starting treatment. Risks may be higher with high doses/ systemic exposure (see also section 4.5 Interaction with Other Medicaments and Other Forms of Interaction that can increase the risk of side effects), although dose levels do not allow prediction of the onset, type, severity or duration of reactions. Most reactions recover after either dose reduction or withdrawal, although specific treatment may be necessary. Patients/carers should be encouraged to seek medical advice if worrying psychological symptoms develop, especially if depressed mood or suicidal ideation is suspected. Patients/carers should be alert to possible psychiatric disturbances that may occur either during or immediately after dose tapering/ withdrawal of systemic steroids, although such reactions have been reported infrequently.

    Particular care is required when considering the use of systemic corticosteroids in patients with existing or previous history of severe affective disorders in themselves or in their first degree relatives. These would include depressive or manic-depressive illness and previous steroid psychosis.

Use in Pregnancy and Lactation:
Pregnancy
The ability of corticosteroids to cross the placenta varies between drugs, however, methylprednisolone does cross the placenta.
Administration of corticosteroids to pregnant animals can cause abnormalities of foetal development including cleft palate, intra-uterine growth retardation and affects on brain growth and development. There is no evidence that corticosteroids result in an increased incidence of congenital abnormalities, such as cleft palate in man, however, when administered for long periods or repeatedly during pregnancy, corticosteroids may increase the risk of intro-uterine growth retardation. Hypoadrenalism may, in theory, occur in the neonate following prenatal exposure to corticosteroids but usually resolves spontaneously following birth and is rarely clinically important. As with all drugs, corticosteroids should only be prescribed when the benefits to the mother and child outweigh the risks. When corticosteroids are essential, however, patients with normal pregnancies may be treated as though they were in the non-gravid state.

Lactation
Corticosteroids are excreted in small amounts in breast milk, however, doses of up to 40 mg daily of methylprednisolone are unlikely to cause systemic effects in the infant. Infants of months taking higher doses than this may have a degree of adrenal suppression, but the benefits of breastfeeding are likely to outweigh any theoretical risk.

Use in Children: Corticosteroids cause growth retardation in infancy, childhood and adolescence which may be irreversible. Treatment should be limited to the minimum dosage for the shortest possible time.

Use in the Elderly: The common adverse effects of systemic corticosteroids may be associated with more serious consequences in old age, especially osteoporosis, hypertension, hypokalaemia, diabetes, susceptibility to infection and thinning of the skin.
Close clinical supervision is required to avoid life-threatening reactions.

Overdosage: There is no clinical syndrome of acute overdosage with Depo-Medrone. Following overdosage the possibility of adrenal suppression should be guarded against by gradual diminution of dose levels over a period of time. In such event the patient may require to be supported during any further traumatic episode.

Incompatibilities (major):
None stated.

Pharmaceutical precautions
Do not store above 25ºC. Do not freeze. Depo-Medrone should not be mixed with any other fluid.
Discard any remaining suspension after use.

Legal Category
POM

Package quantities
1ml vials or 10 x 1ml vials

Product licence number
PL 20636/2587

Manufacturer and Product Licence Holder
Depo-Medrone is made by Pfizer Manufacturing Belgium NV,
Rijksweg 12, B-2870 Puurs, Belgium.

Procured from within the EU by Product Licence holder
Star Pharmaceuticals Ltd., 5 Sandridge Close, Harrow, Middlesex, UK, HA1 1XD. Repackaged by Servipharm Ltd.

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