Package Leaflet: Information for the patient

METHYLPREDNISOLONE 500 MG POWDER AND SOLVENT FOR SOLUTION FOR INJECTION/INFUSION
METHYLPREDNISOLONE 1000 MG POWDER AND SOLVENT FOR SOLUTION FOR INJECTION/INFUSION

Methylprednisolone sodium succinate

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you
- 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 on to others. It may harm them even if their signs of illness are the same as yours
- If you get any side effects, talk to your doctor or pharmacist. This includes any side effects not listed in this leaflet.

What is in this leaflet:

1. WHAT METHYLPREDNISOLONE IS AND WHAT IT IS USED FOR

Methylprednisolone contains methylprednisolone sodium succinate. Methylprednisolone belongs to a group of medicines called corticosteroids (steroids). Corticosteroids are produced naturally in your body and are important for many body functions.

Boosting your body with extra corticosteroid such as Methylprednisolone can help following surgery (e.g. organ transplants), flare-ups of the symptoms of multiple sclerosis or other stressful conditions.

These include inflammatory or allergic conditions affecting the:
- **brain** caused by a tumour or meningitis
- **bowel** and **gut** e.g. 'Crohn's disease' and 'ulcerative colitis'
- **lungs** caused by asthma, severe allergy or hypersensitivity, tuberculosis or breathing in (aspirating) vomit or stomach contents
- **skin** e.g. Stevens-Johnson Syndrome.

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

2. WHAT YOU NEED TO KNOW BEFORE YOU ARE GIVEN METHYLPREDNISOLONE

Do not use Methylprednisolone if:
• you think you have ever suffered an **allergic reaction,** or any other type of reaction after being given Methylprednisolone, 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 have any **fungal infection** (such as thrush), other than on the skin which is not being treated
- you have recently had, or are about to have any **vaccination**
- you are suffering from, or receiving treatment for malaria
- you are suffering from a head injury or stroke.

See your doctor immediately if any of the above applies to you.

Warnings and precautions

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

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

- **Chickenpox, measles, shingles** or a **herpes** eye infection. If you think you have been in contact with someone with chickenpox, measles or shingles and you have not already had these illnesses, or if you are unsure if you had them. If you are not immune or you are a parent of a child receiving this medicine, avoid close contact with anyone with these infections. **Seek medical advice** if you think you have been exposed to one of these infections or if a member of your household develops one of them
- Heart failure for which you are being treated with **digoxin**
- **Worm infestation** (e.g. threadworm)
- Severe **depression** or **manic depression** (bipolar disorder). This includes having had depression before while taking steroid medicines like Methylprednisolone, or having a family history of these illnesses or problems such as delusions, hallucinations or disorganised speech after taking steroids
- **Diabetes** (or if there is a family history of diabetes). If you have diabetes, you should closely monitor blood sugar while taking methylprednisolone.
- **Epilepsy, fits** or **seizures**
- **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**
- **Kaposi's sarcoma** (a type of skin cancer)
- **Kidney** or **liver** disease
- **Muscle problems** (pain or weakness) have happened while taking steroids
- **Myasthenia gravis** (a condition causing tired and weak muscles)
- **Osteoporosis** (brittle bones) or if you are a women who has gone through the menopause
- **Skin abscess**
- **Stomach ulcer, diverticulitis** (inflammation of the bowel wall) 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.
- Unusual **stress**
- **Cushing's disease** (condition caused by an excess of cortisol hormone in your body)
- **Acute pancreatitis** (inflammation of the pancreas).

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

Other medicines and Methylprednisolone

Always tell your doctor or pharmacist if you are taking any other medicines (including any you have bought without a prescription) as taking Methylprednisolone 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 Methylprednisolone or other medicines works:

- **Acetazolamide** – used to treat glaucoma, epilepsy and water retention
- **Aminoglutethimide** or **Cyclophosphamide** – used for treating cancer
- **Anticoagulants** – used to 'thin' the blood such as acenococoumarol, phenindione and warfarin
- **Anticholinesterases** – used to treat myasthenia gravis (a muscle condition) such as distigmine and neostigmine
- **Antibiotics** (such as erythromycin, clarithromycin or troleandomycin)
- **Antidiabetics** – medicines used to treat high blood sugar. If you have diabetes, you may need to check your blood sugar more closely when using methylprednisolone
- **Antihypertensives** – medicines used to treat high blood pressure
- **Aprepitant** and **Fosaprepitant** – used to prevent nausea and vomiting
- **Aspirin** and non-steroidal anti-inflammatory medicines (also called **NSAIDs**) such as ibuprofen, naproxen and diclofenac used to treat mild to moderate pain
- **Barbiturates, carbamazepine, phenytoin** and **primidone** – used to treat epilepsy
- **Carbenoxolone** and **cimetidine** – 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 irregular heart beat
- **Diltiazem** or **mibefradil** – used for heart problems or high blood pressure
- **Ethinylestradiol** and **norethisterone** – an oral contraceptive
- **Isoniazid** – used to treat bacterial infections
- **Ketoconazole** or **itraconazole** – used to treat fungal infections
- **Mifepristone** – used for the medical termination of pregnancy
- **Pancuronium** or **vercuronium** – other medicines called neuromuscular blocking agents which are used in some surgical procedures
- Potassium depleting agents – such as diuretics (sometimes called water tablets), **amphotericin B, xanthenes** or **beta2 agonists** (e.g. medicines to treat asthma)
- **Rifampicin** and **rifabutin** – antibiotics used to treat tuberculosis (TB)
- **Tacrolimus** – used following an organ transplant to prevent rejection of the organ
- Some medicines may increase the effect of Methylprednisolone and your doctor may wish to monitor you carefully if you are taking these medicines (including some medicines for HIV: ritonavir, cobicistat).
- **Vaccines** – tell your doctor or nurse if you have recently had, or 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 medicine used to treat these conditions.

Before you have any operation tell your doctor, dentist or anaesthetist that you are being treated with Methylprednisolone.

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 Methylprednisolone as this medicine could affect the test results.

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.

Cataracts have been observed in infants born to mothers undergoing long-term treatment with corticosteroids during pregnancy.
Tell your doctor if you are breast-feeding as small amounts of corticosteroid medicines may get into breast milk.

Methylprednisolone contains sodium
This medicine contains 1.6 mmol (37.2 mg) of sodium in each 500mg vial of methylprednisolone and 3.2 mmol (74.4mg) of sodium in each 1000mg vial of methylprednisolone. If you are on a controlled sodium (salt) diet tell your doctor in case your sodium intake needs to be adjusted.

3. HOW METHYLPREDNISOLONE 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 Methylprednisolone. 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 many injections you will receive depending on the condition being treated and its severity. Your doctor will inject the lowest dose for the shortest possible time to get effective relief of your symptoms.

Adults
Methylprednisolone will be given, as an injection by your doctor or nurse, either into a vein (intravenous) or into a muscle (intramuscular). Usually the first dose is given into a vein, especially in an emergency. It will be given slowly over at least 5 minutes. For larger doses may take 30 minutes or more. Large doses should normally be used for only 2 to 3 days. The medicine is first dissolved in water for injections. If the medicine is to be given by infusion (using a pump or drip) it is then mixed with another suitable fluid. No other medicines should be mixed with it.

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.

Do not drink grapefruit juice while being treated with Methylprednisolone.

If you are given more Methylprednisolone than you should
If you think you have been given too many injections please speak to your doctor immediately.

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

Information for the Healthcare Professional
Methylprednisolone 500mg & 1000mg powder and solvent for solution for injection/infusion
For full prescribing information please read the Summary of Product Characteristics.
Presentation: Each vial of powder contains the equivalent of either 500mg or 1000mg of methylprednisolone as the sodium succinate salt. The 500mg vials come with an ampoule containing 7.8ml of water for injections. The 1000mg vials come with a vial containing 15.6ml of water for injections
Therapeutic Indications
Treatment of any condition in which rapid and intense corticosteroid effect is required.
Dosage and Method of Administration:
Methylprednisolone may be administered i.v. or i.m. For emergency use the preferred method is i.v. injection; doses above 250mg should be given over at least 30 minutes; doses up to 250mg should be given over at least 5 minutes. Subsequent doses may be given i.v. or i.m. at intervals dictated by the patient's response and clinical condition.
Corticosteroid therapy is an adjunct to, and not replacement for, conventional therapy.
Undesirable effects may be minimised by using the lowest effective dose for the minimum period.
Parenteral drug products should wherever possible be visually inspected for particulate matter and discoloration prior to administration.
Adults: initial dosage will vary from 10 to 500mg depending on the severity of the condition, up to 1g/day for graft rejection reactions following transplantation.
Doses of 500mg to 1000mg should be limited to 48 to 72 hours until the patient's condition has stabilised, to avoid serious side effects. In anaphylactic reactions adrenaline or noradrenaline should be administered first for an immediate haemodynamic effect, followed by i.v. injection of methylprednisolone with other accepted procedures.
In sensitivity reactions methylprednisolone provides relief within one half to two hours.
In status asthmaticus, it may be given at a dose of 40mg i.v., repeated as dictated by patient response. In some asthmatic patients administration by slow i.v. drip over a period of hours is recommended.

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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 health problems while taking Methylprednisolone
Mental health problems can happen while taking steroids like Methylprednisolone (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.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, 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 Methylprednisolone (steroids) should not be stopped abruptly. If you suffer from any of the following symptoms seek IMMEDIATE medical attention. Your 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
- **Pancreatitis**, stomach pain spreading to your back, possibly accompanied by vomiting, shock and loss of consciousness
- **Burst or bleeding ulcers**, symptoms of which are stomach pain (especially if it seems to spread to your back), bleeding from the back passage, black or bloodstained 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. Symptoms of a previous malaria infection could involve chills and fever. Methylprednisolone may also make you more likely to develop a severe infection
- **Pulmonary embolus** (blood clots in the lung), symptoms include sudden sharp chest pain, breathlessness and coughing up blood
- **Raised pressure within the skull** of children (pseudotumor 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 straight away.

The side effects may occur with certain frequencies, which are defined as follows:

- *common*: affects 1 to 10 users in 100
- *not known*: frequency cannot be estimated from the available data.

Blood, heart and circulation
common

- High blood pressure, symptoms of which are headaches, or generally feeling unwell.

not known

- Problems with the pumping of your heart (heart failure) symptoms of which are swollen ankles, difficulty in breathing and palpitations (awareness of heart beat) or irregular or very fast or slow pulse
- Low blood pressure symptoms may include dizziness, fainting, light-headedness, blurred vision, a rapid, or irregular heartbeat (palpitations), general weakness
- Increased numbers of white blood cells (leucocytisis)
- Increased clotting of the blood.

Body water and salts
common

- Swelling and high blood pressure, caused by increased levels of water and salt content.

not known

- 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
common

- Ulcers.

not known

- Nausea (feeling sick) or vomiting (being sick)
- Diarrhoea
- Thrush in the gullet (discomfort when swallowing)
- Indigestion
- Bloated stomach
- Abdominal pain
- Hiccups.

Ears
not known

- A feeling of dizziness or spinning (vertigo).

Eyes
common

- Cataracts (indicated by failing eyesight).

not known

- Glaucoma (raised pressure within the eye, causing pain in the eyes and headaches)
- Swollen optic nerve (papillioedema, indicated by sight disturbances).
- 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)
- Disease of the retina and choroid membrane.

General disorders
common

- Poor wound healing.

not known

- Feeling tired or unwell
- Skin reactions at the site of injection.

Hormones and metabolic system
common

- Slowing of normal growth in infants, children and adolescents which may be permanent
- Round or moon-shaped face (Cushingoid facies).

not known

- Irregular or no periods in women
- 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 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.
- A disorder causing accumulation of fat tissue on local parts of the body (lipomatosis).

Immune system
common

- Increased susceptibility to infections.

not known

- Suppression of reactions to skin tests, such as that for tuberculosis.

Liver
not known

- Methylprednisolone can damage your liver, hepatitis and increase of liver enzymes have been reported.

Muscle and bone issues
common

- Brittle bones (bones break easily)
- Muscle weakness.

not known

- Muscle wasting
- 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.

Nerves and mood issues
common
Steroids including methylprednisolone can cause serious 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
- 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.

Skin
common

- Acne
- Bruising
- Thinning of skin (skin atrophy).

not known

- Stretch marks (skin striae)
- Small purple/red patches on the skin
- Pale or darker patches on your skin, or raised patches which are unusual colour
- Excessive growth of bodily and facial hair
- Rash, itching, hives
- Increased sweating.

Additionally the tearing of heart muscles has been observed in patients taking methylprednisolone following a heart attack.

Withdrawal symptoms
A 'withdrawal syndrome' may occur, see Section 3 for more information

If you experience any of the side effects listed above tell your doctor straight away.

Reporting of side effects
If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet.
You can also report side effects directly (see details below). By reporting side effects you can help provide more information on the safety of this medicine.

United Kingdom
Report any unwanted side-effects via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

Ireland
Reports may be made to HPRA Pharmacovigilance, Earlsfort Centre, Earlsfort Terrace, IRL - Dublin 2
Tel: +353 1 6764971; Fax: +353 1 6762517
Website: www.hpra.ie;
E-mail: medsafety@hpra.ie.

5. How to store Methylprednisolone

This medicine must not be used after the expiry date shown on the packaging. The expiry date refers to the last day of the month.
Keep vials/ampoules in the outer carton to protect from light.
The doctor or pharmacist will keep the medicine in a safe place where children cannot reach or see it.
The reconstituted methylprednisolone solution and water for injections should be used immediately and any remainder discarded.
Your doctor or nurse will ensure that your medicine is used and disposed of correctly.

6. Contents of the pack and other information

What Methylprednisolone powder for solution for injection/infusion contains
This medicine contains methylprednisolone sodium succinate as the active ingredient:

Methylprednisolone 500mg powder and solvent for solution for injection/infusion:
Each vial of powder contains 663mg methylprednisolone sodium succinate (equivalent to 500mg methylprednisolone).
Each ampoule of solvent contains 7.8ml of water for injections.

Methylprednisolone 1000mg powder and solvent for solution for injection/infusion:
Each vial of powder contains 1326mg methylprednisolone sodium succinate (equivalent to 1000mg methylprednisolone).
Each vial of solvent contains 15.6ml of water for injections.
Methylprednisolone powder for solution for injection/infusion also contains the inactive ingredient sodium phosphate.

What Methylprednisolone looks like and contents of the pack:
Methylprednisolone 500mg/1000mg powder for solution for injection/infusion is a white powder which comes in a clear glass vial. Each pack contains one vial of methylprednisolone 500mg/1000mg powder and one vial or ampoule of Sterilised Water for Injections.

Marketing Authorisation Holder
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In graft rejection reactions following transplantation doses of up to 1000mg per day have been used to suppress rejection crises, with 500mg to 1000mg most commonly used for acute rejection.
Refer to the Summary of Product Characteristics for the suggested dosage schedules for oedemas due to brain tumour.
In the treatment of acute exacerbations of multiple sclerosis in adults, the recommended dose is 1000mg daily for 3 days, given as an i.v. infusion over at least 30 minutes.
Children: In the treatment of haematological, rheumatic, renal and dermatological conditions, 30mg/kg/day to a maximum of 1 g/day is recommended. This may be repeated for three pulses either daily or on alternate days.

For graft rejection reactions following transplantation, 10 to 20mg/kg/day for up to 3 days, to a maximum of 1 g/day, is recommended.
In the treatment of status asthmaticus, 1 to 4mg/kg/day for 1 to 3 days is recommended.
Elderly: Methylprednisolone is primarily used in acute short term conditions. Treatment should consider the more serious consequences of the common side-effects and close clinical supervision is required.
Pharmaceutical Information: Contains sodium phosphate as buffer. The powder should be reconstituted in the water for injections supplied. **After reconstitution in water for injections, each ml of solution contains the equivalent of 59.6 mg of Methylprednisolone.** The reconstituted solution may be diluted with 5% dextrose in water, isotonic saline solution, or 5% dextrose in isotonic saline solution. To avoid compatibility problems with other drugs the reconstituted solution should be administered separately, only in the diluents mentioned.
Storage Precautions: Keep vials/ampoules in the outer carton to protect from light. **Nature of Container:** Type I glass vials with butyl rubber stopper and aluminium flip-cap. Type I glass ampoules. **Instructions for Use and Handling:** Please refer to Dosing instructions. For single use only. Unused solution must be discarded immediately.