Methotrexate 25 mg/ml Injection

Read all of this leaflet carefully before you start using this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor.

In this leaflet:

1. What Methotrexate Injection is and what it is used for
2. Before you are given Methotrexate Injection
3. How you are given Methotrexate Injection
4. Possible side effects
5. How to store Methotrexate Injection
6. Further information

1. WHAT METHOTREXATE INJECTION IS AND WHAT IT IS USED FOR

Methotrexate Injection is an anti-metabolite medicine (medicine which affects how the body’s cells grow) and immunosuppressant (medicine which reduces the activity of the immune system).

Methotrexate is used in large doses (on its own or in combination with other medicines) to treat certain types of cancer such as breast cancer. In smaller doses it can be used to treat severe psoriasis (a skin disease with thickened patches of inflamed red skin, often covered by silvery scales), when it has not responded to other treatments.

2. BEFORE YOU ARE GIVEN METHOTREXATE INJECTION

You will not be given Methotrexate Injection if you

- are allergic (hypersensitive) to Methotrexate or any of the other ingredients of Methotrexate Injection
- have significant kidney or liver problems
- have been told you have (or think you have) a blood disorder such as low levels of white blood cells, red blood cells (anaemia) or platelets
- have any infection
- your immune system is not working as well as it should

Tell your doctor if any of the above applies to you before this medicine is used.

Take special care with Methotrexate Injection if you

- have a stomach ulcer or ulcerative colitis (inflammation and ulceration of the gut)
- have an infection
- have mild kidney problems
- have a medical condition which causes a build up of fluid in the lining of your lungs or in your abdomen (the fluid will need to be drained before methotrexate treatment is started)
- are to have radiotherapy (risk of tissue and bone damage may be increased)
• are to have any vaccinations

Tell your doctor if any of the above applies to you before this medicine is used.

Special care will also be taken in children, the elderly and in those who are in poor physical condition.

**Taking/using other medicines**

Special care is needed if you are taking/using other medicines as some could interact with methotrexate, for example:

• non-steroidal anti-inflammatory medicines e.g. ibuprofen (medicines taken for pain relief)
• aspirin or similar medicines (known as salicylates)
• omeprazole, esomeprazole and pantoprazole (medicines used to reduce the production of stomach acid)
• diuretics (water tablets)
• medicines taken for diabetes (including insulin and tablets)
• antibiotics such as penicillins, sulphonamides, co-trimoxazole, trimethoprim, tetracycline, chloramphenicol and para-aminobenzoic acid
• phenytoin (medicine often used to treat epilepsy)
• vitamin supplements containing folic acid
• probenecid (medicine used to treat gout)
• nitrous oxide (used for general anaesthesia and pain relief). Nitrous oxide increases the effect of Methotrexate and can lead to an increase in some side effects (such as reduced number of blood cells and platelets and inflammation of mouth). Following injection into the spine it can have an effect on your nervous system
• retinoids, such as acitretin (a medicine used to treat psoriasis) or isotretinoin (used to treat severe acne)
• other drugs that may cause damage to your kidneys
• other drugs that may case damage to your liver
• live virus vaccines
• mercaptopurine (medicine used in the treatment of blood cell cancer)
• theophylline (medicine used in the treatment of asthma)

Please tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

**Using Methotrexate Injection and drinking alcohol**

Do not drink alcohol whilst being treated with Methotrexate as alcohol increases the risk of liver damage.

**Pregnancy and breast-feeding**

Tell your doctor if you are pregnant, trying to become pregnant or breast-feeding before this medicine is used.

This medicine must not be used during pregnancy.

Mothers should not breast-feed whilst treatment with methotrexate is ongoing.
Due to the risk of birth defects, conception should be avoided during methotrexate treatment and for at least 6 months after treatment is stopped.

Ask your doctor or pharmacist for advice before taking any medicine.

**Driving and using machines**
Do not drive or use machines if you experience any side effect (e.g. dizziness, drowsiness or blurred vision) which may lessen your ability to do so.

**Important information about one of the ingredients of Methotrexate Injection**
This medicinal product contains 0.2 mmol (4.5 mg) sodium per millilitre (ml) of solution. To be taken into consideration by patients on a low sodium diet.

**3. HOW YOU ARE GIVEN METHOTREXATE INJECTION**

This medicine may be given by injection into a vein (intravenous injection), into muscle (intramuscular injection), into an artery (intraarterial injection) or into the spine (intrathecal injection)*. It may also be given by infusion (drip) into a vein. It may be diluted before it is given.

* Of the presentations available (see section 6) only the 50 mg/2 ml is suitable for intrathecal injection.

**Dose**
Your doctor will work out the correct dose of Methotrexate Injection for you and how often it must be given.

The dose of medicine given to you will depend on the disease being treated, your medical condition, your age, your size and how well your kidneys are working.

Before treatment is started your doctor may carry out blood tests to check the levels of cells in your blood, and also to check how well your kidneys and liver are working. You may also have a chest X-ray. Further tests may also be done during and after treatment.

**If you are given too much or too little Methotrexate Injection**
This medicine will be given to you in a hospital, under the supervision of a doctor. It is unlikely that you will be given too much or too little, however, tell your doctor or nurse if you have any concerns.

**4. POSSIBLE SIDE EFFECTS**

Methotrexate is a very toxic medicine and patients have died, or become very ill, whilst being treated with it. During treatment you should watch for any side effects and report them to the doctor.

**If any of the following happen, tell your doctor immediately:**
- severe allergic reaction - you may experience a sudden itchy rash (hives), swelling of the hands, feet, ankles, face, lips, mouth or throat (which may cause difficulty in swallowing or breathing), and you may feel you are going to faint
- inflammation of the lung with breathlessness – you may develop a persistent cough, experience pain or difficulty breathing, or become breathless. This may be associated with changes in a particular type of white cell in your blood.
- symptoms of an infection e.g. fever, chills, achiness, sore throat
• unexpected bleeding e.g. bleeding gums, blood in the urine or in vomit, or the appearance of unexpected bruises or broken blood vessels (broken veins)
• black tarry stools
• a sore mouth, particularly if you have a number of ulcers or blisters inside of the mouth or on the tongue
• skin rashes or blistering to the surfaces of the eyes, nose, vagina or anus (back passage)
• diarrhoea
• stroke/ weakness on one side of the body
• weakness in the legs that spreads to the upper limbs and the face, which may result in paralysis
• abdominal pain, fatty stools, vomiting
• chest pain (which may be due to heart or lung problems)

These are serious side effects. You may need urgent medical attention.

If any of the following happen, tell your doctor as soon as possible:
• low blood pressure (you may feel faint)
• fits
• blurred vision
• dizziness
• difficulty/inability to talk
• muscle weakness
• you may feel the need to drink more than usual (diabetes)
• abnormally easily broken bones (osteoporosis)
• pain or redness of the blood vessels (vasculitis)
• itching or the appearance of lightened patches on the skin, bruises, boils
• increased sensitivity to sunlight
• acne
• yellowing of the skin and whites of the eyes (jaundice)
• pain in the stomach, loins or abdomen
• you may need to pass urine more often than normal, which may be painful (cystitis)
• headaches
• drowsiness
• generally feeling tired or unwell
• reduced appetite, feeling or being sick
• irregular periods in women (periods may stop completely)
• hair loss
• effects on learning and memory
• ringing in the ears
• joint and muscle pain
• blood clot which causes pain, swelling or redness (cerebral, deep vein, retinal vein or arterial vein)
• mood alterations
• inflammation of the lungs, which causes breathlessness, cough and raised temperature, pneumonia
• shingles (Herpes Zoster)

Some different side effects may occur following injection into the spine. These are
• headache
- back or shoulder pain
- difficulty with bending your head down
- fever
- temporary paralysis or weakness
- problems with a particular part of your brain, leading to shaking, abnormal balance or staggering.
- Irritability and confusion
- Stiffness
- Fits
- Confusion and loss of memory
- Sleepiness
- Coma
- Death

Methotrexate may lead to problems with your blood, liver and kidneys. Your doctor will take blood samples to check for these problems and may ask you to have an operation to have a small sample of your liver removed.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor.

Effects on fertility
Treatment with methotrexate may reduce fertility in men and women. Fertility is thought to go back to normal after methotrexate treatment is stopped. Tell your doctor if you have concerns.

5. HOW TO STORE METHOTREXATE INJECTION

Keep out of the reach and sight of children

Expiry
This medicine must not be used after the expiry date which is stated on the vial label and carton after 'EXP'. Where only a month and year is stated, the expiry date refers to the last day of that month.

Storage
The vials should be kept in the outer carton, in order to protect from light, and stored at, or below, 25°C. The vials should not be frozen.
Unused portions of opened vials must not be stored for later use.
Prepared infusions should be used immediately, however, if this is not possible they can, in certain circumstances, be stored for up to 30 days in a refrigerator provided they have been prepared in a way to exclude microbial contamination.

6. FURTHER INFORMATION

What Methotrexate Injection contains
The active substance is methotrexate. Each millilitre (ml) of solution contains 25 milligrams (mg) of methotrexate.

The other ingredients are sodium chloride, sodium hydroxide and Water for Injections.

What Methotrexate Injection looks like and contents of the pack
Methotrexate Injection is a clear, yellow solution for injection which comes in glass containers called vials.

It may be supplied in packs containing:
- 5 x 50 mg/2 ml vials
- 1 x 500 mg/20 ml vial

Not all packs may be marketed.

Marketing authorisation holder and manufacturer responsible for batch release in Europe
Hospira UK Limited, Horizon, Honey Lane, Hurley, Maidenhead, SL6 6RJ, UK

Manufacturer
Hospira Australia Pty Ltd, 1-5, 7-23 and 25-39 Lexia Place,
MULGRAVE VIC 3170, Australia

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Methotrexate 25 mg/ml Injection
The following information is intended for medical or healthcare professionals only

Further to the information included in section 3, practical information on the preparation/handling of the medicinal product is provided here.

Incompatibilities
Immediate precipitation or turbidity results when combined with certain concentrations of droperidol, heparin sodium, metoclopramide hydrochloride, ranitidine hydrochloride in syringe.

Instructions for use and handling
Only the 50 mg/2 ml presentation is suitable for intrathecal administration.
Single use only

Discard any unused contents

After dilution, chemical and physical in-use stability has been demonstrated in dextrose 5% and sodium chloride 0.9% infusion solutions for 30 days at 4°C in PVC containers when protected from light.

From a microbiological point of view the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2-8°C, unless dilution has taken place in controlled and validated aseptic conditions.