

^{Rx} Methotrexate Injection IP TREXOVA 1G

50mg/2mL, 500mg/20mL & 1000mg/40mL

Each mL contains :

Methotrexate IP 25 mg
Water for Injections IP q.s.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you

1.0 What Methotrexate 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.

2.0 What you need to know before you use 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
- are breast-feeding and additionally, for non-oncological indications (for non-cancer treatment) if you are pregnant (see section 'Pregnancy, breast-feeding and fertility')

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

Warnings and precautions:

Acute bleeding from the nose in patients with underlying rheumatological disease has been reported with methotrexate. If you experience symptoms of spitting or coughing up blood you should contact your doctor immediately.

Methotrexate temporarily affects sperm and egg production.

Methotrexate can cause miscarriage and severe birth defects. You and your partner should avoid having a baby if you Page 2 of 7 are being given methotrexate at the time and for at least 6 months after the end of your treatment with methotrexate. See also section 'Pregnancy, breast-feeding and fertility'.

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 aciclovir (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 cause 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).

Using Methotrexate Injection and drinking alcohol

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

Pregnancy, breast-feeding and fertility

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

Pregnancy

Do not use Methotrexate during pregnancy except if your doctor has prescribed it for oncology treatment. Methotrexate can cause birth defects, harm the unborn child or cause miscarriage. It is also associated with malformations of the skull, face, heart and blood vessels, brain, and limbs. It is therefore very important that

methotrexate is not given to pregnant women or to women who are planning to become pregnant unless used for oncology treatment.

For non-oncological indications, in women of child-bearing age the possibility of a pregnancy must be ruled out, e.g. by pregnancy tests, before treatment is started.

Do not use Methotrexate if you are trying to become pregnant. You must avoid becoming pregnant during treatment with methotrexate and for at least 6 months after the end of treatment. Therefore, you must ensure that you are taking effective contraception for the whole of this period (see also section 'Warnings and precautions').

If you become pregnant during treatment or suspect you might be pregnant, speak to your doctor as soon as possible. If you do become pregnant during treatment, you should be offered advice regarding the risk of harmful effects on the child through treatment. If you want to become pregnant, you should speak with your doctor, who may refer you for specialist advice before the planned start of treatment.

Mothers should not breast-feed whilst treatment with methotrexate is ongoing.

Male fertility

The available evidence does not indicate an increased risk of malformations or miscarriage if the father takes methotrexate less than 30 mg/week. However, a risk cannot be completely excluded and there is no information regarding higher methotrexate doses. Methotrexate can have a genotoxic effect. This means that the medicine can cause genetic mutations. Methotrexate can affect the production of sperm, which is associated with the possibility of birth defects.

You should avoid fathering a child or donating semen during treatment with methotrexate and for at least 6 months after the end of treatment. As treatment with methotrexate at higher doses commonly used in cancer treatment can cause infertility and genetic mutations, it may be advisable for male patients treated with methotrexate doses higher than 30 mg/week to consider sperm preservation before the beginning of treatment (see also section 'Warnings and precautions').

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.

3.0 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 injection (drop) into a vein. It may be diluted before it is given.

Recommended 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.

4.0 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.
- spitting or coughing 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 Page 5 of 7
- 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)
- bleeding from the lungs (frequency not known)*
- lymphoproliferative disorders (excessive growth of white blood cells (frequency very rare)
- bone damage in the jaw (secondary to excessive growth of white blood cells) (frequency not known)

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

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.

5.0 Instructions for use and handling:

Incompatibilities:

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

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

6.0 How to store Methotrexate Injection

Keep this medicine out of the sight and reach of children

Do not use this medicine after the expiry date which is stated on the carton and label (EXP). The expiry date refers to the last day of that month.

For single use only.

Storage :

Store protected from light at a temperature not exceeding 30°C

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.

7.0 Contents of the pack and other information

What Methotrexate contains

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

What Methotrexate looks like and contents of the pack.

Methotrexate Injection is a clear, yellow solution which comes in glass vial.

Marketed by:
NEOVA BIOGENE PRIVATE LIMITED
Wentle Plaza, Malviya Marg,
Mulund (w), Mumbai-80, India

Manufactured in India by:
BETA DRUGS LTD.
Kharun-Lothimajra Road, VII, Nandpur,
Baddi, Distt Solan, Himachal Pradesh-173205