

PACKAGE LEAFLET: INFORMATION FOR THE USER

Methotrexate 10 mg Tablets

Methotrexate

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, 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 symptoms are the same as yours.
- If you get any side effects talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.
- **This medicine should only be taken once a week.**
- **Do not exceed the weekly dose as incorrect dosing may lead to serious toxic effects, including death.**

What is in this leaflet:

1. What Methotrexate is and what it is used for
2. What you need to know before you take Methotrexate Tablets
3. How to take Methotrexate Tablets
4. Possible side effects
5. How to store Methotrexate Tablets
6. Contents of the pack and other information

1. What Methotrexate is and what it is used for

Methotrexate 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 to treat severe psoriasis (a skin disease with thickened patches of inflamed red skin, often covered by silvery scales) when other treatments are not effective, severe arthritis due to psoriasis, and rheumatoid arthritis (a disease that causes inflammation of the joints).

You must talk to a doctor if you do not feel better or if you feel worse.

2. What you need to know before you take Methotrexate Tablets

Your doctor may perform several tests such as blood tests, x-rays and physical examinations before treatment with Methotrexate tablets is started, and at regular intervals during treatment.

Do not take Methotrexate Tablets if you

- are allergic to methotrexate or any of the other ingredients of this medicine (listed in section 6);
- you have significant kidney disease;
- you have significant liver disease (including fibrosis, cirrhosis and recent or active hepatitis);
- have disorders of the blood-forming system;
- have increased alcohol consumption;
- have severe or existing infections;

- have a condition that stops your immune system working as well as it should;
- have gastro-intestinal ulcers or ulcers of the oral cavity;
- inflammation of mouth or lips;
- are pregnant or breast-feeding (see section “Pregnancy, breast-feeding and fertility”).

You should not be given live vaccines during treatment with Methotrexate Tablets.

Tell your doctor before you take Methotrexate Tablets if you think any of the above applies to you.

Warnings and precautions

Talk to your doctor before taking Methotrexate Tablets if you

- have a stomach ulcer or ulcerative colitis (inflammation and ulceration of the gut);
- have severe mouth ulcers;
- have/had any liver or kidney disease;
- have problems with your lung function;
- have an abnormal accumulation of liquid in the abdomen or in the cavity between the lungs and chest wall (ascites, pleural effusions);
- are having radiotherapy or UV radiation (the risk of tissue and bone damage may be increased);
- are dehydrated or suffer from conditions leading to dehydration (vomiting, diarrhoea, stomatitis);
- have diabetes mellitus treated with insulin;
- have inactive, prolonged infections (e.g. tuberculosis, hepatitis B or C, shingles (herpes zoster));
- experience any sign or symptoms suggestive of infection, e.g. fever.

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

Special care is also needed in children, the elderly and in those who are in poor physical condition.

You should avoid solariums and direct sun light during treatment, as the skin is more sensitive.

Special precautionary measures for treatment with Methotrexate:

Methotrexate temporarily affects sperm and egg production, which is reversible in most cases. Methotrexate can cause miscarriage and severe birth defects. You must avoid becoming pregnant when using methotrexate and for at least six months after treatment has stopped. See also section “Pregnancy, breast-feeding and fertility”.

Even if methotrexate is administered at low dosage, severe side effects can occur. In order to diagnose them early, **regular monitoring by the doctor at short-term intervals is necessary.**

Before treatment is started your doctor may carry out blood tests, 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. Do not miss appointments for blood tests.

If the results of any of these tests are abnormal, treatment will only be resumed when all readings are back to normal.

Other medicines and Methotrexate Tablets

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription and herbal or natural medicinal products. Remember to tell your doctor about your treatment with Methotrexate Tablets, if you are prescribed other medicine while the treatment is still ongoing.

It is especially important to tell your doctor if you are using:

- other treatments for rheumatoid arthritis or psoriasis such as leflunomide, sulphasalazine (also used for ulcerative colitis), salicylates such as acetylsalicylic acid, phenylbutazone, or amidopyrine
- alcohol (should be avoided)
- live vaccinations
- azathioprine (used to prevent rejection after an organ transplant)
- retinoids, such as acitretin (used to treat skin disorders)
- anticonvulsant drugs (prevents fits)
- cancer treatments
- barbiturates (sleeping injection)
- tranquillisers
- oral contraceptives
- probenecid (for gout)
- antibiotics including sulphonamide antibiotics
- pyrimethamine (used to prevent and treat malaria)
- vitamin preparations which contain folic acid
- nitrous oxide (a gas used as an anaesthetic) 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 the mouth). You can receive treatment to reduce these effects
- proton-pump inhibitors (used to treat severe heartburn or ulcers)
- theophylline (used to treat asthma)
- diuretics (water tablets)
- hypoglycaemic tablets (used to treat diabetes)
- radiotherapy

Methotrexate Tablets with food, drink and alcohol

During Methotrexate Tablet treatment you should avoid any alcohol consumption as it increases the risk of liver damage, as well as excessive consumption of coffee, caffeine-containing beverages or black tea. Also make sure you drink plenty of liquids during treatment with Methotrexate Tablets because dehydration (reduction in body water) can increase the toxicity of Methotrexate Tablets.

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.

Do not use Methotrexate during pregnancy or if you are trying to become pregnant. Methotrexate can cause birth defects, harm the unborn child or cause miscarriage. It is associated with malformations of the skull, face, heart and blood vessels, brain and limbs. Therefore, it is very important that Methotrexate is not given to pregnant patients or patients planning to become pregnant. In women of child-bearing age any possibility of pregnancy must be excluded with appropriate measures, e.g. a pregnancy test before starting treatment. You must avoid becoming pregnant whilst taking methotrexate and for at least 6 months after treatment is stopped by using reliable contraception throughout this time (see also section “Warnings and precautions”).

If you do become pregnant during treatment or suspect you might be pregnant, speak to your doctor as soon as possible. You should be offered advice regarding the risk of harmful effects on the child through treatment.

If you wish to become pregnant you should consult your doctor, who may refer you for specialist advice before the planned start of treatment.

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. Methotrexate may be genotoxic. This means that the medicine may cause genetic mutations. Methotrexate can affect sperm production with the potential to cause birth defects. Therefore, you should avoid fathering a child or donating semen whilst taking methotrexate and for at least 6 months after treatment is stopped.

In women of child-bearing age, any existing pregnancy must be excluded with certainty by taking appropriate measures, e.g. pregnancy test prior to therapy.

As methotrexate may cause genetic mutations, all women who wish to become pregnant are advised to consult a genetic counselling centre, if possible already prior to therapy, and men should seek advice about the possibility of sperm preservation before starting therapy. Methotrexate passes into breast milk. Breast-feeding should be stopped prior to and during treatment with Methotrexate Tablets.

Driving and using machines

Tiredness and dizziness can occur during treatment. If affected you should not drive or operate machinery.

Methotrexate Tablets contains lactose

These tablets contain lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

3. How to take Methotrexate Tablets

Always take these tablets exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.

The tablets should be swallowed whole with a drink of water whilst sitting upright or standing.

Important warning about the dose of Methotrexate Tablets:

Take Methotrexate Tablets **only once a week** for the treatment of psoriasis and rheumatoid arthritis. Taking too much of Methotrexate Tablets may be fatal. Please read section 3 of this leaflet very carefully. If you have any questions, please talk to your doctor or pharmacist before you take this medicine.

Recommended Dose is:

Adults

Rheumatoid Arthritis:

Take methotrexate tablets only **once a week**. In adults, the dose usually starts at 7.5 - 15 mg per week but may rise to 20 mg per week (not exceeding 20mg per week), and the tablets will

be taken once a week and usually on the same day each week. The dose must be given all at once.

Methotrexate will be used with extreme caution in elderly patients and the dosage may need to be reduced.

Psoriasis and Psoriatic arthritis:

Take methotrexate tablets only **once a week**. Patients may be given a test dose of 2.5-5mg by their doctor first to exclude unexpected toxicities. The usual dose may range between 7.5 -15mg (up to a maximum of 25 mg per week). The dose is taken once a week on the same day each week. The dose must be given all at once.

Use in children: This medicine can be used to treat children with severe psoriasis, but should not be used in those under 3 years of age.

If you take more Methotrexate Tablets than you should

See your doctor or go to a hospital Accident and Emergency (Casualty) Department at once. Take your medicine container and show it to the doctor or nurse who treats you. An overdose of methotrexate can lead to severe toxic reactions. Overdose symptoms may include easy bruising or bleeding, unusual weakness, mouth sores, nausea, vomiting, vomiting blood or black or bloody stools. The antidote in case of an overdose is calcium folinate.

If you forget or stop taking Methotrexate Tablets

You should not interrupt or discontinue Methotrexate Tablet treatment, unless you have discussed this with your doctor. Do not take a double dose to make up for forgotten tablets. If you suspect severe side effects, contact your doctor for advice.

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

4. Possible side effects

Like all medicines, Methotrexate Tablets can cause side effects, although not everybody gets them.

Serious side effects

If you develop any of the following side effects, contact your doctor immediately:

- sudden wheeziness, difficulty in breathing, swelling of the eyelids, face or lips, rash or itching (especially affecting your whole body)
- lung complaints (symptoms may be general illness; dry, irritating cough; shortness of breath, breathlessness at rest, chest pain or fever)
- spitting or coughing blood
- severe peeling or blistering of the skin
- unusual bleeding (including vomiting blood) or bruising
- severe diarrhoea
- Inflammation and ulcers in the mouth and throat
- black or tarry stools
- blood in the urine or stools
- tiny red spots on the skin
- signs of infection, such as fever, chills and feeling ill
- yellowing of the skin (jaundice)
- pain or difficulty in passing urine
- thirst and/or frequent urination (diabetes)
- fits (convulsions)
- loss of consciousness

- blurred or decreased vision

The following side effects have also been reported:

Very common (more than 1 in 10):

- Indigestion, loss of appetite
- Nausea (feeling sick), vomiting
- Tummy pain
- Increase in liver enzymes (can be detected by a test carried out by a doctor).

Common (between 1 in 100 and 1 in 10):

- Changes in the number of blood cells and platelets (can be detected by a test carried out by a doctor).
- Headache
- Tiredness, sleepiness
- Diarrhoea
- Measles-like rash (alone), redness and itching.

Uncommon (between 1 in 1000 and 1 in 100):

- Spinning sensation
- Confusion
- Depression
- Brain disorder (leukoencephalopathy/encephalopathy).
- Liver disorders (can be detected by a test carried out by a doctor)
- Decreased blood protein (can be detected by a test carried out by a doctor)
- Nettle rash (alone), light sensitivity, darkening of skin
- Hair loss
- Increase of rheumatic nodules (lumps of tissues)
- Shingles
- Painful psoriasis
- Joint or muscle pain
- Brittle bones, inflammation.
- Inflammation and ulcers of the vagina
- Cancer of the lymph nodes (lymphoma)

Rare (between 1 in 1000 and 1 in 10,000):

- Inflammation of the lining of the heart, fluid around the heart.
- Severe visual disturbance
- Mood alterations
- Low blood pressure
- Blood clots
- Sore throat
- Interruption of breathing
- Asthma
- Weakness in muscles associated with breathing
- Inflammation of the digestive tract
- Inflamed gums
- Changes colour of the nails, acne, red or purple spots
- Bone fracture
- Kidney problems with little or no urine produced and waste products in the blood.

Very rare (less than 1 in 10,000 and unknown):

- Severe failure of the bone marrow (can be detected by a test carried out by a doctor)
- Swollen glands
- Sleeplessness
- Pain
- Muscle weakness
- Sensation of numbness or tingling, having less sensitivity to stimulation than normal
- Changes in the sense of taste (metallic taste)
- Inflammation of the lining of the brain causing paralysis or vomiting
- Red eyes, damage to the retina of the eye
- Fluid on the lungs
- Protein in the urine (can be detected by a test carried out by a doctor)
- Loss of sex drive, problems having an erection
- Low sperm production
- Abnormal periods, vaginal discharge, infertility
- Infection around a fingernail
- Fungal and widespread viral infections
- Boils
- Dilated small blood vessels in the skin
- Damage to the blood vessels of the skin
- Lumps in the armpit or groin
- Slow wound healing
- Impaired thought or emotion
- Ringing in the ears
- Inflammation of the pancreas which causes severe pain in the abdomen and back
- Slurred or slow speech
- Pneumonia
- Lymphoproliferative disorders (excessive growth of white blood cells)

Not known (frequency cannot be estimated from the available data):

- Changes in your body's metabolism
- Dizziness
- Unusual head sensations
- Inability to speak or understand speech
- Effects on learning and memory
- Weakness on one side of your body
- Eye irritation
- Periods stop
- Death
- Skin reaction at the site of previous radiotherapy or sun exposure
- Redness and shedding of skin
- Nose bleed
- Bleeding from the lungs
- Bone damage in the jaw (secondary to excessive growth of white blood cells)
- Swelling

Reporting of side effects

If you get any side effects, talk to your doctor. This includes any side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance Website: www.hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Methotrexate Tablets

Keep this medicine out of the sight and reach of children

Expiry

Do not use this medicine after the expiry date which is stated on the 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

Keep the tablet container in the outer carton in order to protect from light.

Disposal

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information**What Methotrexate Tablets contain**

The active substance is methotrexate. Each tablet contains 10 milligrams (mg) of methotrexate.

The other ingredients are maize starch, lactose monohydrate (see section 2 “Maxtrex Tablets contains lactose”), pre-gelatinized starch, polysorbate 80, microcrystalline cellulose and magnesium stearate.

What Methotrexate Tablets look like and contents of the pack

Methotrexate 10 mg Tablets are scored yellow capsule shaped tablets marked ‘M10’ on one side.

Methotrexate 10 mg Tablets are supplied in plastic bottles containing 100 tablets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

Pfizer Healthcare Ireland
9 Riverwalk, National Digital Park
Citywest Business Campus
Dublin 24, Ireland

Manufacturer

Orion Corporation
Tengstrominkatu 8,
Turku, FI-20360,
Finland

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