

Package leaflet: Information for the patient
Methotrexate 2.5 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, pharmacist or nurse.

This medicine has been prescribed for you only. 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 or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Methotrexate 2.5 mg Tablets are and what they are used for
2. What you need to know before you take Methotrexate 2.5 mg Tablets
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1. What Methotrexate 2.5 mg Tablets are and what they are used for

Methotrexate 2.5 mg Tablets are one of a group of medicines called antimetabolites which affect cell growth, including the growth of cancer cells.

Methotrexate can be used to treat severe cases of psoriasis (a skin disease) and rheumatoid arthritis (a disease of the joints). It is usually used for patients who have tried other treatments but their illness has not improved. It helps patients with psoriasis by killing the cells in the skin which are growing too quickly. It is these fast growing cells which cause the raised patches of skin in psoriasis.

In the treatment of rheumatoid arthritis, methotrexate is thought to stop or reduce inflammation in the joints by altering the body's defence mechanisms in the immune system.

Methotrexate can also be used to treat several kinds of cancer when it and can be given alone or in combination with other medicines. It is usually used in much higher doses when it is used to treat cancer and it will often be given as an injection rather than tablets.

2. What you need to know before you take Methotrexate 2.5 mg Tablets

Do not take Methotrexate 2.5 mg Tablets:

- if you are allergic to methotrexate or any of the other ingredients of this medicine (listed in section 6)
- if you are breast-feeding and additionally, for non-oncologic indications (for non-cancer treatment)
- if you are pregnant (see section: Pregnancy, breast-feeding and fertility)
- if you suffer from a problem of excessive drinking (alcoholism)
- if you have severe liver problems, including alcoholic liver disease, fibrosis, cirrhosis, and recent or active hepatitis (inflammation of the liver)

- if you have severe kidney problems
- if you have any serious blood disorders including serious cases of anaemia or abnormal counts of blood cells such as a reduction in white cell count (leucopenia) or platelet number (thrombocytopenia)
- if you have a medical condition or are receiving medication which lowers your resistance to infection
- if you have symptoms which may suggest an active infectious disease (e.g. fever, chills, achiness)
- if you have been told you have a hereditary intolerance of galactose, the Lapp lactase deficiency or glucose-galactose malabsorption
- if you have an ulcer in your mouth or if you have been told by your doctor that you have an ulcer in your gut
- if you have a condition that stops your immune system working as well as it should
- if you have or are due to be given a vaccine recently.

Even though some of the above may be obvious, it is important that your doctor is aware if any of them apply to you.

Warnings and precautions

Important warning about the dose of Methotrexate 2.5 mg Tablets (methotrexate):

Take Methotrexate 2.5 mg Tablets **only once a week** for the treatment of rheumatic or skin diseases (RA, JIA and psoriasis or psoriatic arthritis).

Taking too much of Methotrexate 2.5 mg Tablets (methotrexate) 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.

Talk to your doctor, pharmacist or nurse before taking Methotrexate 2.5 mg Tablets if you:

- have any mild or moderate kidney problems, liver problems or blood disorders
- have stomach ulcers or suffer from inflammation and ulceration of the gut
- have severe mouth ulcers
- have problems with your lungs
- have diarrhoea or severe vomiting
- are weak or infirm
- have excess fluid between the lungs and chest wall (pleural effusion) causing breathlessness or in the abdomen causing swelling of the stomach (ascites). These may affect the levels of methotrexate in your blood
- are receiving or intend to receive any vaccine, as methotrexate can reduce their effect
- have diabetes mellitus and taking insulin
- are an elderly patient
- are having radiotherapy (due to the risk of skin and bone damage)
- are or regularly suffer from dehydration

- have any long-term infections such as tuberculosis, hepatitis B or C, shingles (herpes zoster)
- 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.

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 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”.

Special care is also needed in children 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.

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 2.5 mg 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 2.5 mg Tablets, if you are prescribed other medicine while the treatment is still ongoing.

It is especially important to tell your doctor if you are taking or have recently taken:

- NSAIDs (non-steroidal anti-inflammatory drugs) e.g. ibuprofen, indomethacin or aspirin (for relief of pain or inflammation)
- diuretics (water pills)
- phenytoin (for seizures)
- antibiotics including penicillins, ciprofloxacin, sulphonamides, tetracyclines, chloramphenicol
- retinoids e.g. acitretin (for psoriasis or skin disorders)
- other treatments for rheumatoid arthritis or psoriasis such as leflunomide or azathioprine (used for suppression of inflammatory conditions) or ciclosporin, aspirin, phenylbutazone or amidopyrine
- sulphasalazine (for inflammation of the bowel)
- cisplatin or mercaptopurine (used for cancer)
- probenecid (for gout)
- omeprazole (for stomach ulcers, heartburn, reflux)
- theophylline (for asthma)
- anti-folate drugs (e.g. trimethoprim/sulfamethoxazole)

- vitamin preparations containing folic acid or its derivatives
- alcohol (should be avoided)
- live vaccinations
- barbiturates (sleeping injection)
- tranquillisers
- oral contraceptives
- pyrimethamine (used to prevent and treat malaria)
- nitrous oxide (a gas used as an anaesthetic)
- hypoglycaemic tablets (used to treat diabetes).

Methotrexate 2.5 mg Tablets with food, drink and alcohol

You should not drink alcohol whilst you are taking this medicine. You should also avoid drinking too much coffee containing beverages while taking this medicine. Also make sure you drink plenty of liquids during treatment with Methotrexate 2.5 mg Tablets because dehydration (reduction in body water) can increase the risk of side effects.

Pregnancy, breast feeding and fertility

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

Pregnancy

Do not use Methotrexate 2.5 mg Tablets 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 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 2.5 mg Tablets 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.

Breast-feeding

Methotrexate 2.5 mg Tablets should not be used during breast-feeding. Methotrexate passes into breast milk. Breast-feeding should be stopped prior to and during treatment with Methotrexate 2.5 mg Tablets.

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 to donate 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").

Driving and using machines

Methotrexate 2.5 mg Tablets may make you feel tired, dizzy or may give you blurred vision. You should not drive or use machines when you first start to take this medicine until you are certain that you are not getting these side effects. If in any doubt, speak to your doctor before you drive or use machines.

Methotrexate 2.5 mg Tablets contains lactose and sodium

This medicine contains lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

3. How to take Methotrexate 2.5 mg Tablets

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Do not take more tablets than your doctor has told you to. It will not make you better any faster and it may harm you.

ADULTS

Important warning about the dose of Methotrexate 2.5 mg Tablets (methotrexate):

Use Methotrexate 2.5 mg Tablets only once a week for the treatment of rheumatoid arthritis, psoriasis etc. Using too much of Methotrexate 2.5 mg Tablets (methotrexate) 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.

Dose in psoriasis

Take Methotrexate 2.5 mg Tablets only once a week.

The recommended dose is between 10 and 25 mg taken once a week on the same day each week. Take Methotrexate 2.5 mg tablets once a week.

Dose in rheumatoid arthritis

Take Methotrexate 2.5 mg Tablets only once a week.

The recommended dose is between 7.5 and 20 mg taken once a week on the same day each week. These doses may alter as your condition changes. Take Methotrexate 2.5 mg tablets once a week.

- daily administration can lead to serious toxic effects, including death.

Patients with cancer

Your doctor will decide the dose depending on your condition. Methotrexate may be the only drug given or it may be given with other drugs.

Your doctor will want to monitor your progress, usually every 1-2 months, whilst you are receiving Methotrexate 2.5 mg Tablets.

Before, during and after your treatment you may have tests, such as a chest X-ray, physical examination and blood tests to check that your liver and kidneys are working properly.

Do not miss your appointments as these are necessary to ensure that Methotrexate 2.5 mg Tablets are used safely.

Your doctor may give you additional medication to help make sure that methotrexate does not collect in the kidneys.

Use in children

Patients with Cancer

Your doctor will decide the most appropriate dose depending on your condition.

Methotrexate 2.5 mg Tablets should be used in children for any other indication.

Blood monitoring should be done for all patients treated with methotrexate.

Close monitoring of the blood levels should be done including the complete blood counts, urine tests and in some cases blood methotrexate monitoring along with liver and kidney function tests to detect any problems.

If you take more Methotrexate 2.5 mg Tablets than you should

If you have taken more Methotrexate 2.5 mg Tablets than the doctor has told you to, you should get medical help immediately either by calling your doctor or by going to the nearest hospital casualty department. Always take the labelled medicine container with you, whether there are any Methotrexate 2.5 mg Tablets left or not.

If you forget to take Methotrexate 2.5 mg Tablets

Take it as soon as you remember if this is within two days. However, if you have missed a dose by more than two days, please contact your doctor for advice. Do not take a double dose to make up for a forgotten dose.

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

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects

All medicines can cause allergic reactions although serious allergic reactions are rare. If you develop any of the following side effects, stop taking this medicine and contact your doctor immediately:

- serious allergic reaction which causes difficulty in breathing or dizziness
- serious illness with blistering of the skin, mouth, eyes and genitals. These could be signs of a condition known as Steven Johnsons Syndrome
- severe peeling or blistering of the skin. These could be signs of a condition known as Toxic Epidermal Necrolysis
- lung complaints (symptoms may be general illness; dry, irritating cough; shortness of breath, breathlessness at rest, chest pain or fever)
- symptoms of altered mental state, inability to concentrate, drowsiness, headaches and tremors. These could be signs of a condition known as encephalopathy
- a serious infection affecting the whole body (sepsis) characterized by fever, chills, rapid breathing and low blood pressure
- symptoms of shortness of breath, weakness, light headedness and cough. These could be signs of a condition known as cardiac tamponade
- symptoms of chest pains after regular activity such as eating, exercise. This could be signs of heart disease
- symptoms of fever, headache and neck stiffness. These could be signs of a condition known as aseptic meningitis
- 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
- 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
- if you have a miscarriage or if you believe there may be damage to your unborn child
- spitting or coughing blood*.

*(has been reported for methotrexate used in patients with underlying rheumatologic disease).

The following side effects have also been reported:

Very Common: may affect more than 1 in 10 people

- indigestion

- loss of appetite
- nausea (feeling sick), vomiting (being sick)
- stomach pain
- increase in liver enzymes (can be detected by a test carried out by a doctor)
- mouth ulcers
- swelling of your mouth.

Common: may affect up to 1 in 10 people

- a reduction in white blood cells that makes infections more likely
- a reduction in red blood cells which can make the skin pale and cause weakness or breathlessness
- headache
- dizziness
- fatigue
- loose stools
- a skin rash with reddening of the skin
- hair loss.

Uncommon: may affect up to 1 in 100 people

- a lump in your neck, groin or armpits with associated backache, weight loss or night sweats
- decrease in the number of blood cells
- severe reduction in number of white blood cells which makes infections more likely
- confusion
- vertigo
- pale skin, weakness, tiredness or difficulties in breathing
- unusual bleeding or bruising
- nose bleed
- itching
- hives on your arms and legs
- increased sensitivity to light
- skin discolouration
- symptoms of back pain, loss of height over time, stooped posture or broken bones that have occurred too easily. This could be a sign of osteoporosis
- muscle pain
- joint pain
- vaginal ulcers or inflammation
- kidney damage
- swelling around your bladder.

Rare: may affect up to 1 in 1,000 people

- raised blood sugar levels (diabetes mellitus)
- herpes zoster (shingles) which is a viral disease characterized by a painful skin rash with blisters
- feeling of fullness or pressure in the chest or abdomen, difficulty in breathing or eating, an enlarged lump or swelling under the skin in the neck or collarbone or groin or armpit, weight

loss, anemia or a lack of red blood cells, fever, cough, weakness, fatigue, excessive sweating, night sweats, nausea and vomiting (Lymphoproliferative disorders)

- if you are told by your doctor that you have some issues with your red blood cells
- depression
- inability to move one half of the body
- fall in blood pressure
- tenderness and swelling of the lower extremities (clot in the veins)
- swelling of the gums
- acne
- appearance of lightened patches on the skin
- skin ulcers and painful erosions of inflamed areas, in psoriasis patients
- small bruises on the skin caused by blood leaking from broken blood vessels
- an increase in rheumatic nodules
- lowered or absence of urine
- if you have too much urea in your urine (your doctor will inform you)
- loss of interest in, or inability to have sex
- lowered sperm count
- menstrual disorders.

Very Rare: may affect up to 1 in 10,000 people

- reduction in red blood cells which can make the skin pale yellow and cause weakness or breathlessness
- severe reduction in blood cells which can cause weakness, bruising or make infections more likely
- swelling of your lymph nodes around the throat and neck
- altered level of blood cells in your body (your doctor will inform you)
- suppressing your immune system, making you more likely to pick up infections
- insomnia
- drowsiness
- irritation
- difficulty with speech
- weakness
- tingling and numbness in your arms or legs
- blurred vision
- eye infection
- chest pain or tightness of chest, with difficulty in breathing
- lung infection
- vomiting blood
- dry cough
- abdominal pain, feeling bloated or abdominal tenderness
- boils
- dilatation of small blood vessels causing focal red lesions
- pain or difficulty in passing urine
- blood in urine
- elevation of urea and/or creatinine in the blood
- infertility

- enlargement of breasts
- vaginal bleeding
- fever
- delayed healing of cuts and bruises
- sudden nail infections, fungal infections
- lymphoproliferative disorders (excessive growth of white blood cells).

Not known: frequency cannot be estimated from the available data

- increased likelihood of getting infections
- internal bleeding
- issues with the shape of your blood cells (your doctor will inform you)
- issues with your metabolism
- eye irritation
- fluid buildup in your lungs
- serious liver damage
- absence of menstruation
- tiredness
- chills
- bone damage in the jaw (secondary to excessive growth of white blood cells)
- bleeding from the lungs*.

*(has been reported for methotrexate used in patients with underlying rheumatologic disease).

In a small number of patients methotrexate may cause serious side effects and on rare occasions, death.

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie E-mail: medsafety@hpra.ie.

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Methotrexate 2.5 mg Tablets

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 blister after “Exp. Date”.

The expiry date refers to the last day of that month.

Do not store above 25°C. Store in the original container in order to protect from light.

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 2.5 mg Tablets contains

- The active substance is methotrexate. Each tablet contains Methotrexate sodium equivalent to 2.5 mg methotrexate
- The other ingredients are lactose monohydrate, sodium hydroxide, magnesium stearate, and starch, pregelatinised.

What Methotrexate 2.5 mg Tablets looks like and contents of the pack

Methotrexate 2.5 mg Tablets are round, biconvex, yellow tablets, engraved with “2.5” on one side. They are scored in half on the other side with “M” written above the line and “1” below. They are supplied in PVC/aluminium blister packs containing 28 or 30 tablets. Not all pack sizes may be marketed.

Marketing Authorisation Holder:

Amdipharm Limited,
Temple Chambers, 3 Burlington Road,
Dublin 4, Ireland

Manufacturer

Haupt Pharma Wolfratshausen GmbH, Pfaffenrieder Straße 5, D-82515 Wolfratshausen Germany.

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