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. 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, pharmacist or nurse. This includes any possible side effects not listed in this leaflet.

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

1. What Methotrexate is and what it is used for

The active substance of Methotrexate tablets, methotrexate, is an antimetabolite and immunosuppressant (medicine which affects the reproduction of the body's cells and reduces the activity of the immune system).

Methotrexate is used to treat:
- active rheumatoid arthritis in adult patients,
- severe resistant disabling psoriasis, which is not adequately responsive to other forms of therapy such as phototherapy, PUVA, and retinoids,
- severe psoriatic arthritis in adult patients.

Your doctor will be able to explain how Methotrexate tablets might help in your particular condition.

2. What you need to know before you take Methotrexate

Do not take Methotrexate:
- if you have significant liver disease (your doctor decides the severity of your disease).
- if you have significant kidney disease (your doctor decides the severity of your disease).
- if you have or have had a bone marrow disease or serious blood disorders.
- if you are allergic (hypersensitive) to methotrexate or any of the other ingredients of Methotrexate tablets.
- if you are pregnant or breast-feeding (see also section “Pregnancy, breast-feeding and fertility”).
- if you have severe acute or chronic infections or immunodeficiency syndrome.
- if you suffer from alcoholism.

Warnings and precautions

Please tell your doctor or pharmacist if any of the following conditions concern or have concerned you:
- Diabetes mellitus treated with insulin.
- You have received any vaccinations recently or are you due to have any
- You are using any other medicines or vitamin products (Please see section “Other medicines and Methotrexate”)
- You have infections
- You have ulcerations in your stomach or bowel (peptic ulcer or ulcerative colitis)
- You are in poor general condition
- You have or have had any liver or kidney disease.

Methotrexate temporarily affects sperm and egg production. You and your partner should avoid conception (becoming pregnant or fathering children) if currently receiving methotrexate and for at least six months after your treatment with methotrexate has stopped. See also section “Pregnancy, breast-feeding and fertility”.

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.

**Other medicines and Methotrexate**

Other concomitant medication may affect the efficacy and safety of this medicine. Methotrexate may also affect the efficacy and safety of other medications.

Please 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, if you are prescribed another medicine while the treatment is still ongoing. It is especially important to tell your doctor if you are using:
- certain antibiotics (such as penicillins, sulfonamides, trimethoprim/sulfamethoxazole, tetracycline and chloramphenicol);
- agents that may be harmful to kidneys and liver [e.g. sulfasalazine and leflunomide (medicines for rheumatic diseases), vitamin A and its derivatives, alcohol];
- anticancer agents (e.g. cisplatin, mercaptopurine);
- phenytoin (medicine often used to treat epilepsy);
- aspirin or similar medicines (known as salicylates);
- non-steroidal anti-inflammatory medicines (medicines taken for pain relief) e.g. ibuprofen and pyrazoles;
- medicines taken to help control rheumatism e.g. azathioprine;
- omeprazole or pantoprazole (medicine used to stop the production of stomach acid);
- diuretics, triamterene (water tablets);
- probenecid (medicine used to treat gout);
- folic acid (vitamin preparation);
- theophylline (medicine used to treat respiratory diseases);
- cyclosporine (an agent that can suppress or prevent the immune response).

Tell your physician about use of Methotrexate during your next visits.

**Methotrexate with food, drink and alcohol**

Alcohol should be avoided during methotrexate therapy.

**Pregnancy, breast-feeding and fertility**

**Pregnancy**

Do **not** use Methotrexate during pregnancy or if you are trying to become pregnant. Methotrexate can cause birth defects, harm unborn babies or cause miscarriages and so it is very important that it is not given to pregnant patients or patients planning to become pregnant. Therefore, 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. Therefore you must ensure reliable contraception during this whole period (see also section “Take special care with Methotrexate”).

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 wish to become pregnant you should consult a genetic information centre before the planned start of treatment, because methotrexate may be genotoxic, which means that the medicine may cause genetic mutation.

Breast-feeding

Do not breastfeed during treatment, because methotrexate passes into breast milk. If your attending doctor considers treatment with methotrexate absolutely necessary during the lactation period, you must stop breast-feeding.

Fertility

Male fertility
Methotrexate may be genotoxic. This means that the medicine may cause genetic mutation. Methotrexate can affect sperm and egg production with the potential to cause birth defects. Therefore, you must avoid fathering a child whilst taking methotrexate and for at least 6 months after treatment is stopped. Since treatment with methotrexate may lead to infertility, it might be advisable for male patients to look into the possibility of sperm preservation before starting treatment (see also section “Take special care with Methotrexate”).

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

Driving and using machines

You can feel fatigue and dizziness during Methotrexate treatment. Do not drive or use machines if you have such symptoms.

Methotrexate 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 medicinal product.

3. **How to take Methotrexate**

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

- Take Methotrexate once a week.
- Patients with rheumatoid arthritis or psoriasis will usually take their tablets orally **once a week** on the same day each week.
- Do not take tablets more often than your doctor has told you to.
- **Daily administration can lead to serious toxic effects, including death.**
- Take the tablets with a glass of water whilst sitting upright or standing.

**Dosage for rheumatoid arthritis, psoriasis and severe psoriatic arthritis:**
The recommended dose is 7.5 - 15 mg **orally, once weekly.**
This should be adjusted according to your response to treatment and side effects. Your doctor may also instruct you to take the weekly dose in three divided doses over 24 or 36 hours.
If you take more Methotrexate than you should

If you take (or someone else has taken) more of the medicine than you should, a physician or nearest hospital casualty department must be contacted immediately.

An overdose of methotrexate can lead to severe toxic reactions, including death. Overdose symptoms may include easy bruising or bleeding, unusual weakness, mouth sores, nausea, vomiting, black or bloody stools, coughing up blood or vomit that looks like coffee grounds, and decreased urinating. See also section 4.

Take your medicine package with you if you go to a doctor or hospital.

If you forget to take Methotrexate

Take the forgotten dose 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 a forgotten dose.

Make sure before your holiday or trip that you have enough of your medicine.

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

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. In general, the incidence and severity of adverse reactions of methotrexate are related to dose and frequency of administration. Most adverse reactions are reversible if detected early.

Most of the effects listed below will only be seen in patients who are receiving high doses of methotrexate to treat cancer. They are not seen as often and are not as severe at the doses used in the treatment of psoriasis or rheumatoid arthritis.

Serious side effects
Contact your doctor or hospital emergency department immediately if you have any of the following symptoms:

- A cough producing a thick mucus, difficulty breathing, fever or shortness of breath. You may be suffering from pneumonitis, pulmonary fibrosis or pneumonia. (Common: may affect up to 1 in 10 people)
- Tightness in your chest, difficulty breathing, swelling of the face, throat or hands, feeling dizzy or faint. These could be signs of a severe allergic reaction. (Uncommon: may affect up to 1 in 100 people)
- Severe skin reactions, including peeling and blistering of the skin, mouth, eyes and genitals and numerous pus filled spots with a fever. You could be suffering from Stevens-Johnson syndrome or toxic epidermal necrolysis. (Uncommon: may affect up to 1 in 100 people)
- Fever and deterioration of your general condition, or fever with local infections such as in the throat or mouth. You may have a reduced number of white blood cells (possibly due to bone marrow depression) and your resistance to infection may be decreased. (Uncommon: may affect up to 1 in 100 people)
- Loss of appetite, nausea, itchy skin, yellowing of the skin or eyes, fever, swollen or tender stomach. You may be suffering from inflammation or damage of the liver. (Rare: may affect up to 1 in 1,000 people)
- Vomiting blood, passing black tar-like stools and pain in the stomach. You may have a stomach ulcer or bleeding. (Rare: may affect up to 1 in 1,000 people)
- Cramping pain, heavy ache or swelling in the leg, redness, breathlessness, chest pain or sudden collapse. You may have a blood clot. (Rare: may affect up to 1 in 1,000 people)
- Blood in the urine, more or less frequent urination or difficulty urinating, itching, fever, tenderness of the stomach or pain in the back or side. You may be suffering from kidney damage. (Very rare: may affect up to 1 in 10,000 people)
• A high temperature, chills and shivering, a fast heartbeat, rapid breathing, confusion or dizziness. You may have sepsis as the result of an infection. (Not known: frequency cannot be estimated from the available data)

**Common side effects** (may affect up to 1 in 10 people):
Nausea, vomiting, diarrhoea, exhaustion, tiredness, headache, dizziness, loss of appetite, rash or large red spots on the skin, hair loss, inflamed or sore mouth and lips, an increase in liver enzymes.

**Uncommon side effects** (may affect up to 1 in 100 people):
Reduced blood clotting, changes to your blood count, anaemia, nosebleed, itching, vaginal ulcers, swelling of the lymph nodes.

**Rare side-effects** (may affect up to 1 in 1,000 people):
Depression, confusion, weakness on one side of the body, diabetes, low blood pressure, shortness of breath, inflamed gums, sore throat, acne, whitening of the skin, raised itchy rash, sensitivity to light, burning in psoriatic lesions on the skin, skin ulcers, appearance of local tissue lumps, shingles or painful skin rash, osteoporosis, pain in joints or muscles, menstrual disorders, difficulty having an erection, reduced sex drive.

**Very rare side-effects** (may affect up to 1 in 10,000 people):
Reduced levels of antibodies, feeling irritable, difficulty speaking or communicating, lack of energy, blurred vision, eye infection, fluid or swelling around the heart or lungs, inflammation of blood vessels, chronic obstructive lung disease, dry cough, vomiting of blood, boils, blood like bruises or small blood vessels on the surface of the skin, painful urination, bladder inflammation, fertility problems, low sperm count, infertility, vaginal bleeding, enlargement of male breast tissue.

**The following have also been reported but the frequency is not known:**
Abnormally low number of blood cells, sepsis resulting in death, miscarriage, foetal damages, increased risk of toxic reactions during radiotherapy, increase in the number of white blood cells and inflammation of the lung tissue. Scaly, red skin patches associated with psoriasis may get worse when exposed to sources of ultraviolet light, such as the sun, and taking Methotrexate.

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any side effects not listed in this leaflet. Please note, some of these side effects may only be detectable by your doctor.

**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 the national reporting system, see below. By reporting side effects you can help provide more information on the safety of this medicine.

**United Kingdom**
Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard

**Ireland**
HPRA Pharmacovigilance
Earlsfort Terrace
IRL - Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: www.hpra.ie
e-mail: medsafty@hpra.ie

5. **How to store Methotrexate**

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 tablet container/blister and the outer carton. The expiry date refers to the last day of that month.

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

Proper procedures for safe handling of cytotoxic agents should be administered. Disposable gloves should be used when handling methotrexate tablets. Pregnant women should avoid handling methotrexate tablets, if possible.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements for cytotoxic agents.

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 contains

- The active substance is methotrexate, each tablet contains 2.5 mg.
- The other ingredients are: Lactose monohydrate, maize starch, starch, pregelatinised (potato starch), polysorbate 80, cellulose, microcrystalline and magnesium stearate.

What Methotrexate looks like and contents of the pack

Tablet: Yellow, round, convex, engraved with M 2.5 on one side, diameter 6 mm.

Methotrexate tablets are supplied in HDPE containers of 12, 16, 24, 28, 30 and 100 tablets.
Methotrexate tablets are supplied in blister packs containing 24 or 100 tablets

Not all pack sizes may be marketed.

Marketing Authorisation Holder

Orion Corporation
Orionintie 1
FIN-02200 Espoo
Finland

Manufacturer

Orion Corporation, Orion Pharma
Orionintie 1
FIN-02200 Espoo
Finland

This medicinal product is authorised in the Member States of the EEA under the following names:

Czech Republic Trexan
Latvia
Lithuania
Slovakia

Sweden Methotrexate Orion
Germany MTX-Orion 2,5 mg Tabletten
Ireland  
UK  
France  

Methotrexate  
Imeth  

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