Methotrexate Sandoz®

20 mg/ml solution for injection, pre-filled syringe

CONSUMER MEDICINE INFORMATION

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

In this leaflet:

1. What Methotrexate Sandoz is and what it is used for

Methotrexate Sandoz is a drug with the following properties:

- it interferes with the growth of certain cells in the body that reproduce quickly (anti-tumour agent)
- it reduces undesired reactions of the body's own defence mechanism (immunosuppressant), and
- it has anti-inflammatory effects

Methotrexate Sandoz is used in patients with:

- Active rheumatoid arthritis (RA) in adult patients where treatment with disease modifying antirheumatic drugs (DMARDs) is indicated.
- Polyarthritic forms (when five or more joints are involved) of severe, active, juvenile idiopathic arthritis (JIA) when the response to non-steroidal anti-inflammatory drugs (NSAIDs) has been inadequate
- Severe forms of psoriasis particularly of the plaque type, which cannot be sufficiently treated with conventional therapy such as phototherapy, PUVA, and retinoids, and severe psoriasis affecting the joints (psoriatic arthritis)

2. Before you use Methotrexate Sandoz

Do not use Methotrexate Sandoz if you

- are allergic (hypersensitive) to the active substance methotrexate or to any of the other ingredients of Methotrexate Sandoz,
- have significant kidney disease (your doctor decides the severity of your disease)
- have significant liver disease (your doctor decides the severity of your disease)
- have disorders of the blood-forming system
- have increased alcohol consumption
- have an impaired immune system
- have severe or existing infections
- have gastro-intestinal ulcers
- are pregnant or breast-feeding (see section "Pregnancy and lactation") You should not be given live vaccines during treatment with Methotrexate Sandoz.

Take special care with Methotrexate Sandoz if you

- have diabetes mellitus treated with insulin
- have inactive, prolonged infections (e.g. tuberculosis, hepatitis B or C, shingles (herpes zoster))
- have/had any liver or kidney disease
- have problem with your lung function
- are severely overweight
- have abnormal accumulation of liquid in the abdomen or in the cavity between the lungs and chest wall (ascites, pleural effusions)
- are dehydrated or suffer from conditions leading to dehydration (vomiting, diarrhoea, stomatitis)

If you have experienced problems with your skin after radiation therapy (radiation induced dermatitis) and sun-burn these conditions can reappear under methotrexate therapy (recall-reaction).

Use in children, adolescents and elderly

Dosage instructions depend on patient‟ s body weight. Use in children < 3 years of age is not recommended due to the insufficient experience in this age group.

Children and the elderly under **Methotrexate Sandoz** treatment should be kept under particularly close, medical surveillance, in order to identify possible side effects as early as possible.

Dosage for elderly patients should be relatively low due to age-related reduced liver and kidney function and low folate reserves.

Special precautionary measures during treatment of Methotrexate Sandoz

Methotrexate Sandoz should only be prescribed by doctors with sufficient experience in the Methotrexate Sandoz treatment of the disease concerned.

Methotrexate temporarily affects sperm and egg production. You and your partner must 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 and lactation".

Skin changes caused by psoriasis can worsen during treatment with Methotrexate Sandoz if exposure to UV irradiation occurs at the same time.

Recommended examinations

Even if **Methotrexate Sandoz** 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.

Using other medicines

Please tell your doctor or pharmacist if you are taking, or have recently taken 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 Sandoz, if you are prescribed another 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), aspirin, phenylbutazone, or amidopyrine
- alcohol (should be avoided)
- live vaccinations
- azathioprine (used to prevent rejection after an organ transplant)
- retinoids (used to treat skin disorders)
- anticonvulsant drugs (prevent fits)
- cancer treatments
- barbiturates (sleeping injection)
- tranquillisers
- oral contraceptives
- probenecid (for gout)
- antibiotics
- pyrimethamine (used to prevent and treat malaria)
- vitamin preparations, which contain folic acid
- proton-pump inhibitors (used to treat severe heartburn or ulcers)
- theophylline (used to treat asthma)

Using Methotrexate Sandoz with food and drink

During Methotrexate Sandoz treatment you should avoid any alcohol consumption 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 Sandoz because dehydration (reduction in body water) can increase the toxicity of Methotrexate Sandoz.

Pregnancy and lactation

Pregnancy

Do not use Methotrexate Sandoz 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 Sandoz").

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 your doctor, who may refer you for specialist advice,before the planned start of treatment, because methotrexate may be genotoxic, which means that the medicine may cause genetic mutation.

Breast-feeding

Do not breast-feed 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.

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 Sandoz").

Driving and using machines

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

Important information about some of the ingredients of sodium

This medicinal product contains less than 1 mmol sodium (23 mg) per weekly dosage, i.e. essentially "sodium - free".

3. How to use Methotrexate Sandoz

Methotrexate Sandoz should only be prescribed by physicians, who are familiar with the various characteristics of the medicinal products and its mode of action.

Always use Methotrexate Sandoz exactly as your doctor has told you. You should check with your doctor or pharmacist if you are unsure.

The usual dosage is:

Dosage in patients with rheumatoid arthritis

The recommended starting dose for methotrexate is 7.5 mg once a week. Methotrexate Sandoz is given in a single application as injection under the skin, into a muscle or a vein (see section "Method and duration of administration").

In case of inadequate action and if tolerated well, Methotrexate Sandoz doses may be gradually increased by 2.5 mg.

Alternatively, treatment can also be started using higher doses. The mean weekly dose is 15-20 mg. Generally, a weekly dose of 20 mg Methotrexate Sandoz should not be exceeded. Upon achieving desired therapeutic results, the dose should – if possible – be gradually reduced to the lowest possible effective maintenance dose.

Dosage in children and adolescents with polyarthritic forms of juvenile idiopathic arthritis

The recommended dose is 10-15 mg/m² body surface area **per** week. In cases with inadequate response, the weekly dosage may be increased up to 20 mg/m2 body surface area/week. However, regular check-ups should be done more often. As there is very little data about giving the drug intravenously (into a vein) in children and adolescents, it should only be given by subcutaneous (under the skin) or intramuscular (into the muscle) injection.

Use in children < 3 years of age is not recommended due to the insufficient experience in this age group.

Adults with psoriasis or psoriatic arthritis

Recommended initial dose (for an average adult of 70 kg body weight):

It is recommended to administer a single test dose of 5-10 mg, in order to assess possibly damaging effects.

This dose can be administered subcutaneously (under the skin), intramuscularly (into a muscle) or intravenously (into a vein).

If, one week later, no blood count changes are observed, therapy is continued with a dose of approximately 7.5 mg. The dose may be gradually increased (in steps of 5-7.5 mg per week and under blood count surveillance) until ideal therapeutic results are obtained. Generally, a weekly dose of 30 mg should not be exceeded.

Upon achieving desired therapeutic results, the dose should be weekly reduced to the lowest possible effective maintenance dose for the individual patient.

Patients with a kidney disorder

Patients with a kidney disorder may need a reduced dose.

Method and duration of administration

The duration of the treatment is determined by the treating physician. Methotrexate Sandoz is injected once weekly! It is recommended to specify a certain day of the week as "day for injection".

Methotrexate Sandoz is given as injection under the skin, into a muscle or a vein, in children and adolescents it must not be given intravenously.

Treatment of rheumatoid arthritis, juvenile idiopathic arthritis, psoriasis vulgaris and psoriatic arthritis with Methotrexate Sandoz is a long-term treatment.

Rheumatoid arthritis

Generally, improvement of the symptoms can be expected after 4-8 weeks of treatment. Symptoms may return after Methotrexate Sandoz discontinuation.

Severe types of psoriasis vulgaris and psoriatic arthritis (psoriasis arthropatica) Generally, response to treatment can be expected after 2-6 weeks.

Depending on symptoms severity and on laboratory parameters, the therapy is then continued or discontinued.

At the start of your therapy, Methotrexate Sandoz may be injected by medical staff. However, your doctor may decide that it is right for you to learn how to inject Methotrexate Sandoz under the skin yourself. You will receive appropriate training for you to do this. Under no circumstances should you attempt to inject yourself unless you have been trained to do so.

If you use more Methotrexate Sandoz than you should

Do not change the dosage by yourself! Use Methotrexate Sandoz according to the doctor's orders or according to the dosage directions stated in this package leaflet.

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. 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. The antidote in case of an overdose is calcium folinate.

If you forget to take Methotrexate Sandoz

Do not take a double dose to make up for forgotten individual doses, but continue taking the ordered dose. Ask your doctor for advice.

If you stop taking Methotrexate Sandoz

You should not interrupt or discontinue Methotrexate Sandoz treatment, unless you have discussed this with your doctor. If you suspect severe side effects, contact your doctor immediately 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 Sandoz can cause side effects, although not everybody gets them.

Tell your doctor straight away if you get any sudden wheeziness, difficulty in breathing, swelling of the eyelids, face or lips, rash or itching (especially affecting your whole body).

Serious side effects

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

- lung complaints (symptoms may be general illness; dry, irritating cough; shortness of breath, breathlessness at rest, chest pain, or fever)
- Severe peeling or blistering of the skin.
- Unusual bleeding (including vomiting blood) or bruising
- severe diarrhoea
- ulcers in mouth
- black or tarry stools
- blood in the urine or stools
- tiny red spots on the skin
- fever
- yellowing of the skin (jaundice)
- pain or difficulty in passing urine
- thirst and/or frequent urination
- fits (convulsions)
- loss of consciousness
- blurred or decreased vision

The following side effects have also been reported:

Very common (more than 1 in 10):

Inflammation of the mouth, indigestion, loss of appetite, nausea (feeling sick), vomiting, tummy pain,

inflammation and ulcers in the mouth and throat, and 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, measle-like rash (alone), redness, and itching.

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

Spinning sensation, confusion, depression, fits, lung damage, ulcers and bleeding in the digestive tract, liver disorders (can be detected by a test carried out by a doctor), diabetes, decreased blood protein (can be detected by a test carried out by a doctor), nettle rash (alone), light sensitivity, brown skin, hair loss, increase of rheumatic nodules (lumps of tissues), shingles, painful psoriasis, Joint or muscle pain, brittle bones, inflammation and ulcers in the bladder (possibly with blood in the urine), painful urination, severe allergic reactions, inflammation and ulcers of the vagina.

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

Inflammation of the lining of the heart, fluid around the heart, severely visual disturbance, mood alterations, low blood pressure, blood clots, sore throat, interruption of breathing, asthma, inflammation of the digestive tract, bloody stools, inflamed gums, abnormal digestion, changed colour of nails, acne, red or purple spots, bone fracture, kidney failure, little or no urine produced, waste products in the blood.

Very rare (less than 1 in 10000 and unknown):

Infections, severe failure of the bone marrow (can be detected by a test carried out by a doctor), swollen glands, sleeplessness, pain, muscle weakness, pins and needles, changes in 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, vomiting blood, cold sores, protein in the urine (can be detected by a test carried out by a doctor), loss of sex drive, problems having an erection, infection around a fingernail, severe complication of the digestive tract, boils, small blood vessels in the skin, fungal infections, damage to the blood vessels of the skin, lumps in the armpit or groin, slow wound healing, low sperm production, abnormal periods, vaginal discharge, infertility

Other: After injection into a muscle, there may be a burning sensation or damage at the injection site. After injection under the skin there may be a mild skin reaction.

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

5. How to store EBETREXAT

Keep out of the reach and sight of children.

Do not use this medicinal product after the expiry date which is stated on the label of the pre-filled syringe and the carton after EXP. The expiry date refers to the last day of that month.

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

The product has to be used immediately after opening.

You must not use Methotrexate Sandoz, if the solution is not clear and contains particles.

For single use only. Any unused solution should be discarded!

This medicine and its packaging must not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines or packaging no longer required. These measures will help to protect the environment.

6. Further information

What Methotrexate Sandoz contains:

The active substance is: Methotrexate.

1 ml of solution for injection contains 20 mg methotrexate (as 21.94mg methotrexate disodium).

1 pre-filled syringe of 0.375 ml solution for injection contains 7.5 mg methotrexate.

1 pre-filled syringe of 0.5 ml solution for injection contains 10 mg methotrexate.

1 pre-filled syringe of 0.75 ml solution for injection contains 15 mg methotrexate.

1 pre-filled syringe of 1 ml solution for injection contains 20 mg methotrexate.

1 pre-filled syringe of 1.25 ml solution for injection contains 25 mg methotrexate.

1 pre-filled syringe of 1.5 ml solution for injection contains 30 mg methotrexate.

1 pre-filled syringe of 2.0 ml solution for injection contains 40 mg methotrexate.

The other ingredients are: sodium chloride, sodium hydroxide for pH adjustment and water for injections.

What Methotrexate Sandoz looks like and contents of the pack:

Methotrexate Sandoz is solution for injection available in pre-filled syringes as a clear, yellowish solution for injection.

Each box contains pre-filled syringes with 0.375mL, 0.5mL, 0.75mL, 1mL, 1.25mL, 1.5mL or 2mL solution for injection, single-use injection needles and alcohol pads.

Each box may contain 1, 4, 5, 6 or 12 pre-filled syringes. Not all pack sizes may be marketed.

Instructions for use and handling and disposal

The solutions should be clear and without particles.

Handling and disposal must be consistent with that of other cytotoxic preparations in accordance with local requirements. Pregnant health care personnel should not handle and/or administer Methotrexate Sandoz.

For single use only. Any unused solution should be discarded.

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

Incompatibilities

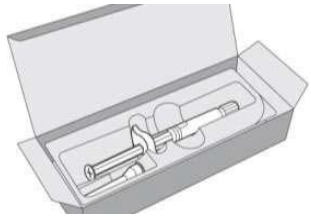
In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

Special precautions for storage

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

Step-by-step instructions for subcutaneous injection:

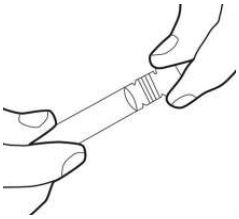
- Open the box and read the package leaflet carefully.



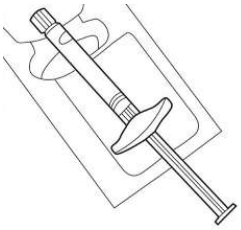
- Take out the inner-package, containing the pre-filled syringe and cannula package.

- Open the inner-package by pulling the corner flap. Take out the pre-filled syringe.

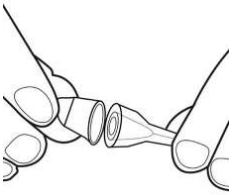
- Remove (twist) the grey rubber cap from the syringe, without touching the opening of the pre-filled syringe.



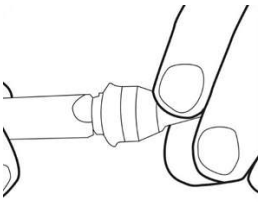
- Place the syringe back into the inner-package. The yellow solution will be unable to escape.



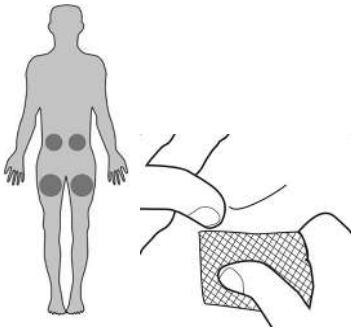
- Now, open the cannula packaging by pulling the flap. Do not touch the round sterile opening. To avoid this, keep hold of the bottom end of the cannula packaging.



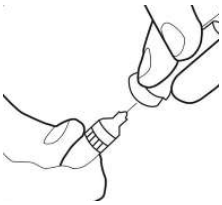
- Attach the cannula, with its packaging, onto the syringe and fix it (clockwise). Put the syringe in a readily accessible place.



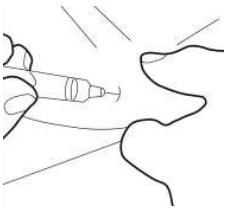
- Choose an injection site. Wipe the injection site with the alcohol pad, using a circular motion. Do not touch this area before injecting.



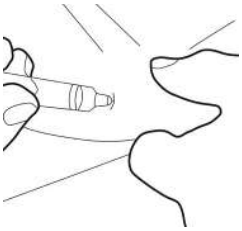
- Pull the packaging from the cannula. Put aside the cannula packaging.



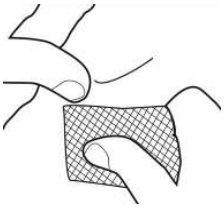
- Do not touch the sterile cannula. If this should happen, ask your doctor or pharmacist about using of another cannula. With two fingers, form a skin fold and puncture it almost vertically.



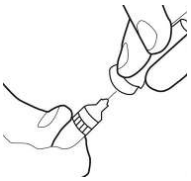
- Push the cannula completely into the skin fold. Then, slowly push the plunger down and inject all the fluid underneath the skin.



- Carefully remove the cannula and dab the injection site with a swab. Do not rub, as this will cause irritation at the injection site.



- To avoid any injuries, carefully put the cannula packaging back on to the cannula by gently pressing it into place.



Manufacturer

Methotrexate Sandoz® is made by:

EBEWE Pharma GmbH, Unterach, Austria

Sponsor

Methotrexate Sandoz® is distributed in New Zealand by:

Novartis New Zealand Limited

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