

## **PACKAGE LEAFLET: INFORMATION FOR THE USER**

# Metoject<sup>®</sup> PEN 7.5 mg solution for injection in pre-filled pen (methotrexate)

**Read all of this leaflet carefully before you start using 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 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. This includes any possible side effects not listed in this leaflet. See section 4.
- Your medicine is called Metoject PEN 7.5 mg solution for injection in pre-filled pen but will be referred to as Metoject PEN throughout the remainder of this leaflet.
- Metoject PEN is also available in other strengths.

### **What is in this leaflet**

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

## **1. WHAT METOJECT PEN IS AND WHAT IT IS USED FOR**

Metoject PEN is indicated for the treatment of

- active rheumatoid arthritis in adult patients.
- polyarthritic forms of severe, active juvenile idiopathic arthritis, when the response to nonsteroidal anti-inflammatory drugs (NSAIDs) has been inadequate.
- moderate to severe psoriasis in adult patients, and severe psoriatic arthritis in adults.
- mild to moderate Crohn’s disease in adult patients when adequate treatment with other medicines is not possible.

**Rheumatoid arthritis** (RA) is a chronic collagen disease, characterised by inflammation of the synovial membranes (joint membranes). These membranes produce a fluid which acts as a lubricant for many joints. The inflammation causes thickening of the membrane and swelling of the joint.

**Juvenile arthritis** concerns children and adolescents less than 16 years. Polyarthritic forms are indicated if 5 or more joints are affected within the first 6 months of the disease.

**Psoriasis** is a common chronic skin disease, characterised by red patches covered by thick, dry, silvery, adherent scales.

**Psoriatic arthritis** is a kind of arthritis with psoriatic lesions of the skin and nails, especially at the joints of fingers and toes.

Metoject PEN modifies and slows down the progression of the disease.

Crohn’s disease is a type of inflammatory bowel disease that may affect any part of the gastrointestinal tract causing symptoms such as abdominal pain, diarrhoea, vomiting or weight loss.

## **2. WHAT YOU NEED TO KNOW BEFORE YOU USE METOJECT PEN**

### **Do not use Metoject PEN**

- if you are allergic to methotrexate or any of the other ingredients of this medicine (listed in section 6).
- if you suffer from liver or severe kidney diseases or blood diseases.
- if you regularly drink large amounts of alcohol.

- if you suffer from a severe infection, such as tuberculosis, HIV or other immunodeficiency syndromes.
- if you suffer from mouth ulcers, stomach ulcer or intestinal ulcer.
- if you are pregnant or breast-feeding (see section “Pregnancy, breast-feeding and fertility”).
- if you receive vaccinations with live vaccines at the same time.

### **Warnings and precautions**

Talk to your doctor or pharmacist before taking Metoject PEN if

- you are elderly or if you feel generally unwell and weak.
- you have problems with the way your liver works.
- you suffer from dehydration (water loss).
- you have diabetes mellitus and are being treated with insulin.

### **Special precautionary measures for treatment with Metoject PEN**

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 6 months after treatment has stopped if you are a woman. If you are a man you should avoid fathering a child if you are being given methotrexate at the time and for at least 3 months after the end of your treatment. See also section “Pregnancy, breast-feeding and fertility”.

### **Recommended follow-up examinations and precautions**

Even if methotrexate is used in low doses, serious side effects can occur. In order to detect them in time, your doctor must perform monitoring examinations and laboratory tests.

### **Prior to the start of therapy**

Before you start treatment, your blood will be checked to see if you have enough blood cells. Your blood will also be tested to check your liver function and to find out if you have hepatitis. Furthermore, serum albumin (a protein in the blood), hepatitis (liver infection) status and kidney function will be checked. The doctor may also decide to run other liver tests, some of these may be images of your liver and others may need a small sample of tissue taken from the liver in order to examine it more closely. Your doctor may also check to see if you have tuberculosis and they may X-ray your chest or perform a lung function test.

### **During the treatment**

Your doctor may perform the following examinations:

- Examination of the oral cavity and the pharynx for changes in the mucous membrane such as inflammation or ulceration.
- Blood tests/blood count with number of blood cells and measurement of serum methotrexate levels.
- Blood test to monitor liver function.
- Imaging tests to monitor liver condition.
- Small sample of tissue taken from the liver in order to examine it more closely.
- Blood test to monitor kidney function.
- Respiratory tract monitoring and, if necessary, lung function test.

It is very important that you appear for these scheduled examinations. If the results of any of these tests are conspicuous, your doctor will adjust your treatment accordingly.

### **Elderly patients**

Elderly patients under treatment with methotrexate should be monitored closely by a physician so that possible side effects can be detected as early as possible.

Age-related impairment of liver and kidney function as well as low body reserves of the vitamin folic acid in old age require a relatively low dosage of methotrexate.

### **Other precautions**

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 may affect your immune system and vaccination results. It may also affect the result of immunological tests. Inactive, chronic infections (such as herpes zoster [shingles], tuberculosis, hepatitis B or C) may flare up. **During therapy with Metoject PEN you must not be vaccinated with live vaccines.**

Methotrexate may make your skin more sensitive to sunlight. Avoid intense sun and do not use sun-beds or a sun-lamp without medical advice. To protect your skin from intense sun, wear adequate clothing or use a sunscreen with a high protection factor.

Radiation-induced dermatitis and sunburn can reappear under methotrexate therapy (recall-reaction). Psoriatic lesions can exacerbate during UV-irradiation and simultaneous administration of methotrexate.

Enlarged lymph nodes (lymphoma) may occur and if this is the case, therapy must be stopped.

Diarrhoea can be a possible side effect of Metoject PEN and requires an interruption of therapy. If you suffer from diarrhoea, please speak to your doctor.

Certain brain disorders (encephalopathy/leukoencephalopathy) have been reported in cancer patients receiving methotrexate. Such side effects cannot be excluded when methotrexate is used to treat other diseases.

If you, your partner or your caregiver notice new onset or worsening of neurological symptoms including general muscle weakness, disturbance of vision, changes in thinking, memory and orientation leading to confusion and personality changes contact your doctor immediately because these may be symptoms of a very rare, serious brain infection called progressive multifocal leukoencephalopathy (PML).

### **Other medicines and Metoject PEN**

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. Please note that this also applies to medicines that you will take **in the future**.

The effect of the treatment may be affected if Metoject PEN is administered at the same time as certain other medicines:

- **Antibiotics** such as: tetracyclines, chloramphenicol, non-absorbable broad-spectrum antibiotics, penicillins, glycopeptides, sulphonamides, ciprofloxacin and cefalotin (medicines to prevent/fight certain infections).
- **Non-steroidal anti-inflammatory** drugs or **salicylates** (medicines against pain and/or inflammation such as acetylsalicylic acid, diclofenac and ibuprofen or pyrazole).
- Metamizole (synonyms novaminsulfon and dipyrone) (medicine against severe pain and/or fever).
- **Probenecid** (medicine against gout).
- Weak organic acids like loop **diuretics** (“water tablets”).
- Medicines, which may have adverse effects on the **bone marrow**, such as trimethoprim-sulfamethoxazole (an antibiotic) and pyrimethamine.
- Other **medicines used to treat rheumatoid arthritis** such as leflunomide, sulphasalazine and azathioprine.
- Cyclosporine (for suppressing the immune system).
- Mercaptopurine (a **cytostatic** medicine).
- Retinoids (medicine against **psoriasis** and other dermatological diseases).
- Theophylline (medicine against **bronchial asthma** and other lung diseases).
- Some medicines against **stomach trouble** such as omeprazole and pantoprazole.
- Hypoglycaemics (medicines that are used to **lower the blood sugar**).

Vitamins containing **folic acid** may impair the effect of your treatment and should only be taken when advised by your doctor.

**Vaccination with live vaccine must be avoided.**

### **Metoject PEN with food, drink and alcohol**

Alcohol as well as large amounts of coffee, caffeine-containing soft drinks and black tea should be avoided during treatment with Metoject PEN.

### **Pregnancy, breast-feeding and fertility**

#### **Pregnancy**

Do not use Metoject PEN 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. pregnancy test before starting treatment.

You must avoid becoming pregnant while 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.

#### **Breast-feeding**

Stop breast-feeding prior to and during treatment with Metoject PEN.

#### **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 mutation. Methotrexate can affect sperm production with the potential to cause birth defects. Therefore, you should avoid fathering a child or to donate semen while taking methotrexate and for at least 3 months after treatment is stopped.

### **Driving and using machines**

Treatment with Metoject PEN may cause adverse reactions affecting the central nervous system, such as tiredness and dizziness. Thus, the ability to drive a vehicle and/or to operate machines may, in certain cases, be compromised. If you feel tired or drowsy do not drive or use machines.

### **Metoject PEN contains sodium**

This medicine contains less than 1 mmol sodium (23 mg) per dose; that is to say essentially “sodium-free”.

## **3. HOW TO USE METOJECT PEN**

### **Important warning about the dose of Metoject PEN (methotrexate):**

Use Metoject PEN **only once a week** for the treatment of rheumatoid arthritis, juvenile idiopathic arthritis, psoriasis and psoriatic arthritis, and Crohn’s disease. Using too much of Metoject PEN (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.

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

Your doctor decides on the dose, which is adjusted individually to you. Usually it takes 4 – 8 weeks before there is any effect of the treatment.

Metoject PEN is administered subcutaneously (under the skin) by or under the supervision of a physician or healthcare staff as an injection **once a week only**. Together with your doctor you decide on a suitable weekday each week on which you receive your injection.

### **Use in children and adolescents**

The doctor decides on the appropriate dose in children and adolescents with polyarthritic forms of juvenile idiopathic arthritis.

**Metoject PEN is not recommended in children less than 3 years of age** due to insufficient experience in this age group.



## **Instructions for Use**

### **Recommendations**

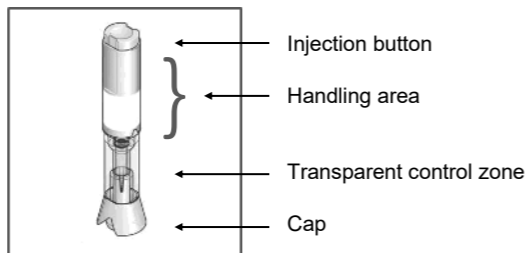
- Carefully read the instructions below before starting your injection.
- Always use the injection technique advised by your doctor, pharmacist or nurse.

### **Additional information**

The manner of handling and throwing away of the medicine and pre-filled pen must be in accordance with local requirements. Pregnant healthcare personnel should not handle and/or administer Metoject PEN.

Methotrexate should not come into contact with the surface of the skin or mucosa. In the event of contamination, the affected area must be rinsed immediately with plenty of water.

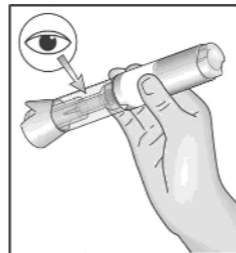
### **Metoject PEN pre-filled pen components:**



- a) With cap before injection
- b) After cap removal before injection
- c) After injection

What you need to do before administering your injection

1. Wash your hands very carefully.
2. Remove the system from its packaging.
3. Check the Metoject PEN pre-filled pen before using it:



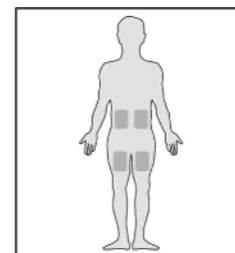
If the Metoject PEN pre-filled pen appears to be damaged **do not use** it. Use another one and contact your doctor, pharmacist or nurse.

In case a small air bubble is visible through the transparent control zone, this will not affect your dose nor will it harm you.

If you are not able to see or to check the system correctly prior to injection, ask someone around you for assistance.

4. Set the Metoject PEN pre-filled pen on a clean flat surface (such as a table).

### **Where you should administer the injection**



The most appropriate zones for your injection are:

- upper thighs,
- abdomen except around the navel.

- If someone around you administers the injection for you, the person may also use the top of the zone at the back of the arm, just below the shoulder.
- Change the injection area with each injection. This will minimise any reactions at the injection site.
- Never inject into areas where the skin is tender, bruised, red or hard or where you have psoriasis, you should not try to inject directly into any raised, thick, red or scaly skin patches or lesions.

## Method and duration of administration

Metoject PEN is injected **once weekly!**

The duration of the treatment is determined by the treating physician. Treatment of rheumatoid arthritis, juvenile idiopathic arthritis, psoriasis vulgaris, psoriatic arthritis and Crohn's disease with Metoject PEN is a long-term treatment.

At the start of your treatment, Metoject PEN may be injected by medical staff. However, your doctor may decide that you can learn how to inject Metoject PEN 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.**

Read the Instructions for Use at the end of this leaflet to find guidance on how to correctly use Metoject PEN.

Please note that all of the contents have to be used.

The manner of handling and throwing away of the medicine and pre-filled pen must be in accordance with local requirements. Pregnant healthcare personnel should not handle and/or administer Metoject PEN.

Methotrexate should not come into contact with the surface of the skin or mucosa. In the event of contamination, the affected area must be rinsed immediately with plenty of water.

### If you use more Metoject PEN than you should

If you use more Metoject PEN than you should, talk to your doctor immediately.

### If you forget to use Metoject PEN

Do not take a double dose to make up for a forgotten dose.

### If you stop using Metoject PEN

If you stop using Metoject PEN, talk to your doctor immediately.

If you have the impression that the effect of Metoject PEN is too strong or too weak, talk to your doctor or pharmacist.

## 4. POSSIBLE SIDE EFFECTS

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

The frequency as well as the degree of severity of the side effects depends on the dosage level and the frequency of administration. As severe side effects may occur even at low dosage, it is important that you are monitored regularly by your doctor. Your doctor will do **tests to check for abnormalities** developing in the blood (such as low white blood cells, low platelets, lymphoma) and changes in the kidneys and the liver.

**Tell your doctor immediately** if you experience any of the following symptoms, as these may indicate a serious, potentially life-threatening side effect, which require urgent specific treatment:

- **persistent dry, non-productive cough, shortness of breath and fever;** these may be signs of an inflammation of the lungs [common]
- **spitting or coughing blood;** these might be signs of bleeding from the lungs [not known]
- **symptoms of liver damage such as yellowing of the skin and whites of the eyes;** methotrexate can cause chronic liver damage (liver cirrhosis), formation of scar tissue in the liver (liver fibrosis), fatty degeneration of the liver [all uncommon], inflammation of the liver (acute hepatitis) [rare] and liver failure [very rare]
- **allergy symptoms such as skin rash including red itchy skin, swelling of the hands, feet, ankles, face, lips, mouth or throat (which may cause difficulty in swallowing or breathing) and feeling you are going to faint;** these may be signs of severe allergic reactions or an anaphylactic shock [rare]
- **symptoms of kidney damage such as swelling of the hands, ankles or feet or changes in frequency of urination or decrease (oliguria) or absence of urine (anuria);** these may be signs of kidney failure [rare]
- **symptoms of infections, e.g. fever, chills, achiness, sore throat;** methotrexate can make you more susceptible to infections. Severe infections like a certain type of pneumonia (*Pneumocystis jirovecii pneumonia*) or blood poisoning (sepsis) may occur [rare]

- **symptoms such as weakness of one side of the body (stroke) or pain, swelling, redness and unusual warmth in one of your legs (deep vein thrombosis); this may happen when a dislodged blood clot causes a blockage of a blood vessel** (thromboembolic event) [rare]
- **fever and serious deterioration of your general condition, or sudden fever accompanied by a sore throat or mouth, or urinary problems;** methotrexate can cause a sharp fall in certain white blood cells (agranulocytosis) and severe bone marrow suppression [very rare]
- **unexpected bleeding, e.g. bleeding gums, blood in the urine, vomiting blood or bruising,** these can be signs of a severely reduced number of blood platelets caused by severe courses of bone marrow depression [very rare]
- **symptoms such as severe headache often in combination with fever, neck stiffness, feeling sick, vomiting, disorientation and sensitivity to light** may indicate an inflammation of the membranes of the brain (acute aseptic meningitis) [very rare]
- certain brain disorders (encephalopathy/leukoencephalopathy) have been reported in cancer patients receiving methotrexate. Such side effects cannot be excluded when methotrexate therapy is used to treat other diseases. Signs of this kind of brain disorders may be **altered mental state, movement disorders (ataxia), visual disturbances or disturbances of memory [not known]**
- **severe skin rash or blistering of the skin (this can also affect your mouth, eyes and genitals);** these may be signs of conditions called Stevens Johnson syndrome or burned skin syndrome (toxic epidermal necrolysis/Lyell's syndrome) [very rare]

In the following, please find the other side effects that may occur:

**Very common:** may affect more than 1 in 10 people

- Inflammation of the mouth lining, indigestion, feeling sick, loss of appetite, abdominal pain.
- Abnormal liver function test (ASAT, ALAT, bilirubin, alkaline phosphatase).

**Common:** may affect up to 1 in 10 people

- Mouth ulcers, diarrhoea.
- Rash, reddening of the skin, itching.
- Headache, tiredness, drowsiness.
- Reduced blood cell formation with decrease in white and/or red blood cells and/or platelets.

**Uncommon:** may affect up to 1 in 100 people

- Throat inflammation.
- Inflammation of the bowels, vomiting, inflammation of pancreas, black or tarry stools, gastrointestinal ulcers and bleeding.
- Sunburn-like reactions due to increased sensitivity of the skin to sunlight, loss of hair, increased number of rheumatic nodules, skin ulcer, shingles, inflammation of blood vessels, herpes-like skin rash, hives.
- Onset of diabetes mellitus.
- Dizziness, confusion, depression.
- Decrease in serum albumin.
- Decrease in the number of all blood cells and platelets.
- Inflammation and ulcer of the urinary bladder or vagina, reduced kidney function, disturbed urination.
- Joint pain, muscle pain, reduction of bone mass.

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

- Inflammation of gum tissue.
- Increased skin pigmentation, acne, blue spots on the skin due to vessel bleeding (ecchymosis, petechiae), allergic inflammation of blood vessels.
- Decreased number of anti-bodies in the blood.
- Infection (incl. reactivation of inactive chronic infection), red eyes (conjunctivitis).
- Mood swings (mood alterations).
- Visual disturbances.
- Inflammation of the sac around the heart, accumulation of fluid in the sac around the heart, obstruction of cardiac filling due to fluid in the sac around the heart.

- Low blood pressure.
- Formation of scar tissue in the lung (pulmonary fibrosis), shortness of breath and bronchial asthma, accumulation of fluid in the sac around the lung.
- Stress fracture.
- Electrolyte disturbances.
- Fever, wound-healing impairment.

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

- Acute toxic dilatation of the gut (toxic megacolon).
- Increased pigmentation of the nails, inflammation of the cuticles (acute paronychia), deep infection of hair follicles (furunculosis), visible enlargement of small blood vessels.
- Pain, loss of strength or sensation of numbness or tingling / having less sensitivity to stimulation than normal, changes in taste (metallic taste), convulsions, paralysis, meningism.
- Impaired vision, non-inflammatory eye disorder (retinopathy).
- Loss of sexual drive, impotence, male breast enlargement, defective sperm formation (oligospermia), menstrual disorder, vaginal discharge.
- Enlargement of lymphatic nodes (lymphoma).
- Lymphoproliferative disorders (excessive growth of white blood cells).

**Not known:** frequency cannot be estimated from the available data

- Increased number of certain white blood cells.
- Nosebleed.
- Proteins in urine.
- Feeling of weakness.
- Bone damage in the jaw (secondary to excessive growth of white blood cells).
- Tissue destruction at injection site.
- Redness and shedding of skin.
- Swelling.

Subcutaneous application of methotrexate is locally well tolerated. Only mild local skin reactions (such as burning sensations, erythema, swelling, discolouration, severe itching, pain) were observed, decreasing during therapy.

### 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 Yellow Card Scheme at: [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard) or search for MHRA Yellow Card in the **Google Play** or **Apple App Store**.

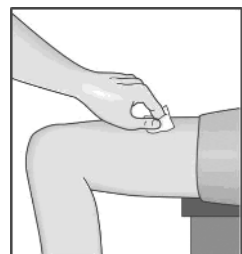
By reporting side effects you can help provide more information on the safety of this medicine.

## 5. HOW TO STORE METOJECT PEN

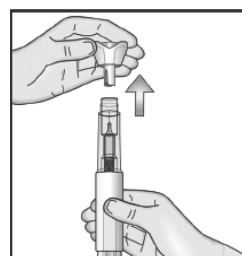
- Keep out of the sight and reach of children.
- Do not store above 25°C.
- Keep the pre-filled pen in the outer carton in order to protect from light.
- Do not use Metoject PEN after the expiry date which is stated on the pre-filled pen and carton after EXP. The expiry date refers to the last day of that month.
- If your medicine becomes discoloured or if your Metoject PEN shows any sign of deterioration or doesn't work properly, take it back to your pharmacist.
- Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.



### How to prepare the injection

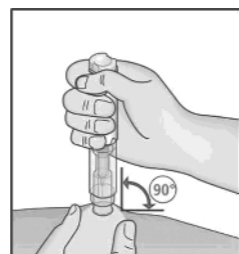


5. Choose an injection site and clean the area of and around the chosen injection site.

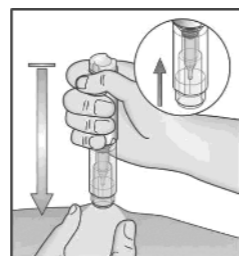


- Do not remove the cap before you are ready to administer the injection.
- 6. Hold the pen with one hand in the handling area with the cap pointing upwards. Use your other hand to gently pull the cap straight off (do not bend or twist the cap). The cap has a small needle shield that should come off with the cap automatically. If the needle shield does not come off, use another pen and contact your doctor, pharmacist or nurse.
- If you are unable to remove the cap, ask someone around you for assistance.

**Note: Once you have removed the cap, perform your injection without delay.**

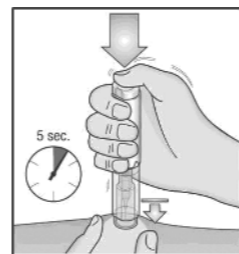


7. With your free hand, build a skin fold by gently squeezing the area of the cleaned skin at the injection site.
  - The fold must be held pinched until the Metoject PEN pre-filled pen is removed from the skin after the injection.



8. Position the uncapped transparent end of Metoject PEN pre-filled pen perpendicular to the fold of skin.
9. **Without pressing the button,** push the Metoject PEN pre-filled pen firmly onto your skin in order to unlock the button.
  - If you are unable to push the Metoject PEN pre-filled pen to the stop-point, ask someone around you for assistance.

### How to administer the injection:



10. While holding the Metoject PEN pre-filled pen firmly against the skin, **now press the button** with your thumb.
11. You will hear a click which indicates the start of the injection. Keep holding the pen against the raised skin until all of the medicine is injected. This can take up to **5 seconds**.

### Note:

Do not remove the Metoject PEN pre-filled pen from the skin before the end of the injection to avoid incomplete injection. If the injection is not triggered, release the button, make sure that the Metoject PEN pre-filled pen is pressed firmly against the skin and push hard on the button. If you have troubles with your hearing, count 5 seconds from the moment you have pressed the button and then lift the Metoject PEN pre-filled pen from the injection site.

## 6. CONTENTS OF THE PACK AND OTHER INFORMATION

### What Metoject PEN contains

1 pre-filled pen with 0.15 ml solution contains 7.5 mg methotrexate.

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

### What Metoject PEN looks like and contents of the pack

Metoject PEN is a pre-filled pen containing a clear, yellow-brown solution in colourless glass pre-filled syringe with a rubber plunger stopper and embedded injection needle. The syringe is externally equipped with a device for self-administration.

Metoject PEN is available in packs of 1 pre-filled pen.

Manufactured by medac Gesellschaft für klinische Spezialpräparate mbH, Theaterstr. 6, 22880 Wedel, Germany.

Procured from within the EU. Repackaged by the Product Licence Holder: MPT Pharma Ltd., Westgate Business Park, Unit 5-7 Tintagel Way, Aldridge, Walsall WS9 8ER.

PL: 33532/1521

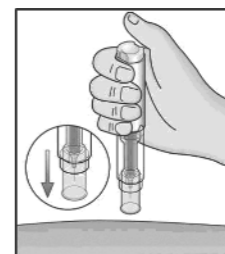
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Leaflet dated 28<sup>th</sup> May 2025

Leaflet coded xxxxxxxxxx

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To request a copy of this leaflet in Braille, large print or audio please call 01922 745645 and ask for the Regulatory Department.



12. Remove the Metoject PEN pre-filled pen from the injection site, perpendicular to the skin (pull up).

13. The protective shield automatically moves into place over the needle. The protective shield is then locked and the needle is protected.

14. In case of a slight bleeding use a plaster.

Before throwing away the Metoject PEN pre-filled pen, check visually that there is no liquid left in the pen, at the bottom of the **transparent control zone**. If there is liquid left in the pen, not all of the medicine has been injected correctly and you should consult your doctor.

### Note

To avoid any injury, **never insert your fingers in the opening of the protective tube** covering the needle. **Do not destroy the pen.**

### Whom should you contact in case of need

- For any problem or question, contact your doctor, pharmacist or nurse.
- If you or someone around you is injured by the needle, consult your doctor immediately and throw away the Metoject PEN pre-filled pen.

## PACKAGE LEAFLET: INFORMATION FOR THE USER

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- If you have any further questions, ask your doctor or pharmacist.
- 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. This includes any possible side effects not listed in this leaflet. See section 4.
- Your medicine is called Metoject PEN 7.5 mg solution for injection in pre-filled pen but will be referred to as Metoject PEN throughout the remainder of this leaflet.
- Metoject PEN is also available in other strengths.

#### What is in this leaflet

- What Metoject PEN is and what it is used for
- What you need to know before you use Metoject PEN
- How to use Metoject PEN
- Possible side effects
- How to store Metoject PEN
- Contents of the pack and other information

## 1. WHAT METOJECT PEN IS AND WHAT IT IS USED FOR

Metoject PEN is indicated for the treatment of

- active rheumatoid arthritis in adult patients.
- polyarthritic forms of severe, active juvenile idiopathic arthritis, when the response to nonsteroidal anti-inflammatory drugs (NSAIDs) has been inadequate.
- moderate to severe psoriasis in adult patients, and severe psoriatic arthritis in adults.
- mild to moderate Crohn’s disease in adult patients when adequate treatment with other medicines is not possible.

**Rheumatoid arthritis** (RA) is a chronic collagen disease, characterised by inflammation of the synovial membranes (joint membranes). These membranes produce a fluid which acts as a lubricant for many joints. The inflammation causes thickening of the membrane and swelling of the joint.

**Juvenile arthritis** concerns children and adolescents less than 16 years. Polyarthritic forms are indicated if 5 or more joints are affected within the first 6 months of the disease.

**Psoriasis** is a common chronic skin disease, characterised by red patches covered by thick, dry, silvery, adherent scales.

**Psoriatic arthritis** is a kind of arthritis with psoriatic lesions of the skin and nails, especially at the joints of fingers and toes.

Metoject PEN modifies and slows down the progression of the disease.

Crohn’s disease is a type of inflammatory bowel disease that may affect any part of the gastrointestinal tract causing symptoms such as abdominal pain, diarrhoea, vomiting or weight loss.

## 2. WHAT YOU NEED TO KNOW BEFORE YOU USE METOJECT PEN

#### Do not use Metoject PEN

- if you are allergic to methotrexate or any of the other ingredients of this medicine (listed in section 6).
- if you suffer from liver or severe kidney diseases or blood diseases.
- if you regularly drink large amounts of alcohol.
- if you suffer from a severe infection, such as tuberculosis, HIV or other immunodeficiency syndromes.
- if you suffer from mouth ulcers, stomach ulcer or intestinal ulcer.
- if you are pregnant or breast-feeding (see section “Pregnancy, breast-feeding and fertility”).
- if you receive vaccinations with live vaccines at the same time.

### INSTRUCTIONS FOR USE

These Instructions for Use contain information on how to inject your Metoject PEN pre-filled pen.

**Read these Instructions for Use until the end before using the pre-filled pen for your subcutaneous injection. Read these Instructions for Use each time you receive a new prescription and keep them for information you may need after the use.**

When receiving a new medicine or a new dose of medicine always check that it matches what your doctor has prescribed you. Before using the pen, your healthcare provider should show you or your caregiver how to use it correctly.

**Do not** use the pen unless you have been taught how to use it by your healthcare provider. If you or your caregiver have any questions, contact your healthcare provider.

#### Important Information You Need to Know Before Injecting With Your Metoject PEN Pre-filled Pen

**Inject with your Metoject PEN pre-filled pen once a week only, and always inject on the same day of the week.**

**Do not inject or handle the product if you are pregnant.**

- Keep the pen in a secure location out of the sight and reach of children.
- If you have any contact with the medicine, wash the affected area with plenty of water right away.

**Do not** remove the protective cap until just before your injection. **Do not** share your pen with another person. **Do not** use the pen if:

- it has dropped onto a hard surface or appears damaged.
- the clear yellow solution got discoloured, looks cloudy or contains particles.
- it has been frozen or stored above 25°C.
- the expiry date has passed.

If you are unsure, contact your healthcare provider.

#### Warnings and precautions

Talk to your doctor or pharmacist before taking Metoject PEN if

- you are elderly or if you feel generally unwell and weak.
- you have problems with the way your liver works.
- you suffer from dehydration (water loss).
- you have diabetes mellitus and are being treated with insulin.

**Special precautionary measures for treatment with Metoject PEN**
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 6 months after treatment has stopped if you are a woman. If you are a man you should avoid fathering a child if you are being given methotrexate at the time and for at least 3 months after the end of your treatment. See also section “Pregnancy, breast-feeding and fertility”.

#### Recommended follow-up examinations and precautions

Even if methotrexate is used in low doses, serious side effects can occur. In order to detect them in time, your doctor must perform monitoring examinations and laboratory tests.

#### Prior to the start of therapy

Before you start treatment, your blood will be checked to see if you have enough blood cells. Your blood will also be tested to check your liver function and to find out if you have hepatitis. Furthermore, serum albumin (a protein in the blood), hepatitis (liver infection) status and kidney function will be checked. The doctor may also decide to run other liver tests, some of these may be images of your liver and others may need a small sample of tissue taken from the liver in order to examine it more closely. Your doctor may also check to see if you have tuberculosis and they may X-ray your chest or perform a lung function test.

#### During the treatment

Your doctor may perform the following examinations:

- Examination of the oral cavity and the pharynx for changes in the mucous membrane such as inflammation or ulceration.
- Blood tests/blood count with number of blood cells and measurement of serum methotrexate levels.
- Blood test to monitor liver function.
- Imaging tests to monitor liver condition.
- Small sample of tissue taken from the liver in order to examine it more closely.
- Blood test to monitor kidney function.
- Respiratory tract monitoring and, if necessary, lung function test.

It is very important that you appear for these scheduled examinations. If the results of any of these tests are conspicuous, your doctor will adjust your treatment accordingly.

#### Elderly patients

Elderly patients under treatment with methotrexate should be monitored closely by a physician so that possible side effects can be detected as early as possible.

Age-related impairment of liver and kidney function as well as low body reserves of the vitamin folic acid in old age require a relatively low dosage of methotrexate.

#### Other precautions

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 may affect your immune system and vaccination results. It may also affect the result of immunological tests. Inactive, chronic infections (such as herpes zoster [shingles], tuberculosis, hepatitis B or C) may flare up. **During therapy with Metoject PEN you must not be vaccinated with live vaccines.**

Methotrexate may make your skin more sensitive to sunlight. Avoid intense sun and do not use sun-beds or a sun-lamp without medical advice. To protect your skin from intense sun, wear adequate clothing or use a sunscreen with a high protection factor.

Radiation-induced dermatitis and sunburn can reappear under methotrexate therapy (recall-reaction). Psoriatic lesions can exacerbate during UV-irradiation and simultaneous administration of methotrexate.

Enlarged lymph nodes (lymphoma) may occur and if this is the case, therapy must be stopped.

Diarrhoea can be a possible side effect of Metoject PEN and requires an interruption of therapy. If you suffer from diarrhoea, please speak to your doctor.

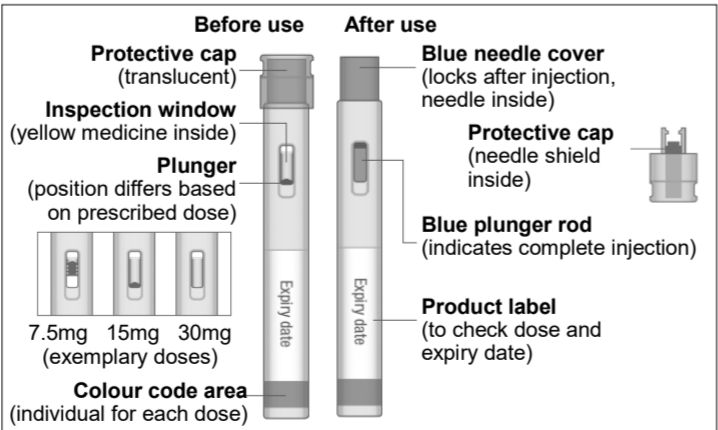
### How to store your Metoject PEN pre-filled pen

- Store below 25°C.
- Transport and keep the pen in the outer carton in order to protect it from light.
- Keep the pen in a secure location out of the sight and reach of children.

**Do not** freeze. **Do not** store above 25°C.

### The Metoject PEN pre-filled pen (Figure A)

The Metoject PEN pre-filled pen is a two-step, fixed-dose, single-use disposable auto-injector. It is available in 10 different doses ranging from 7.5 mg to 30 mg.



**Figure A**

Certain brain disorders (encephalopathy/leukoencephalopathy) have been reported in cancer patients receiving methotrexate. Such side effects cannot be excluded when methotrexate is used to treat other diseases.

If you, your partner or your caregiver notice new onset or worsening of neurological symptoms including general muscle weakness, disturbance of vision, changes in thinking, memory and orientation leading to confusion and personality changes contact your doctor immediately because these may be symptoms of a very rare, serious brain infection called progressive multifocal leukoencephalopathy (PML).

#### Other medicines and Metoject PEN

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. Please note that this also applies to medicines that you will take **in the future**.

The effect of the treatment may be affected if Metoject PEN is administered at the same time as certain other medicines:

- Antibiotics** such as: tetracyclines, chloramphenicol, non-absorbable broad-spectrum antibiotics, penicillins, glycopeptides, sulphonamides, ciprofloxacin and cefalotin (medicines to prevent/fight certain infections).
- Non-steroidal anti-inflammatory drugs** or **salicylates** (medicines against pain and/or inflammation such as acetylsalicylic acid, diclofenac and ibuprofen or pyrazole).
- Metamizole (synonyms novaminsulfon and dipyrone) (medicine against severe pain and/or fever).
- Probenecid** (medicine against gout).
- Weak organic acids like loop **diuretics** ("water tablets").
- Medicines, which may have adverse effects on the **bone marrow**, such as trimethoprim-sulfamethoxazole (an antibiotic) and pyrimethamine.
- Other medicines used to treat rheumatoid arthritis** (such as leflunomide, sulphasalazine and azathioprine).
- Cyclosporine (for suppressing the immune system).
- Mercaptopurine (a **cytostatic** medicine).
- Retinoids (medicine against **psoriasis** and other dermatological diseases).
- Theophylline (medicine against **bronchial asthma** and other lung diseases).
- Some medicines against **stomach trouble** such as omeprazole and pantoprazole.
- Hypoglycaemics (medicines that are used to **lower the blood sugar**).

Vitamins containing **folic acid** may impair the effect of your treatment and should only be taken when advised by your doctor.

**Vaccination with live vaccine must be avoided.**

#### Metoject PEN with food, drink and alcohol

Alcohol as well as large amounts of coffee, caffeine-containing soft drinks and black tea should be avoided during treatment with Metoject PEN.

### Pregnancy, breast-feeding and fertility

#### Pregnancy

Do not use Metoject PEN 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. pregnancy test before starting treatment.

You must avoid becoming pregnant while 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.

#### Breast-feeding

Stop breast-feeding prior to and during treatment with Metoject PEN.

#### 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 mutation. Methotrexate can affect sperm production with the potential to cause birth defects. Therefore, you should avoid fathering a child or to donate semen while taking methotrexate and for at least 3 months after treatment is stopped.

### Supplies needed for your injection (Figure B)

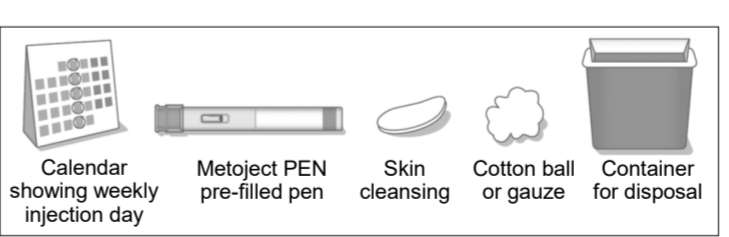
At your weekly injection day find a comfortable place, ensure the area is well lit and you have a clean flat surface, such as a table to place your injection supplies.

You need:

- your Metoject PEN pre-filled pen.

Make sure you have the following additional supplies available to perform your injection as they are not included in the package:

- your calendar to check your once weekly injection day,
- skin cleansing like alcohol disinfection, if not available water and soap,
- cotton ball or gauze to treat your injection site,
- container for disposal in accordance with local requirements.



**Figure B**

#### Driving and using machines

Treatment with Metoject PEN may cause adverse reactions affecting the central nervous system, such as tiredness and dizziness. Thus, the ability to drive a vehicle and/or to operate machines may, in certain cases, be compromised. If you feel tired or drowsy do not drive or use machines.

#### Metoject PEN contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per dose; that is to say essentially "sodium-free".

3. HOW TO USE METOJECT PEN
<p><b>Important warning about the dose of Metoject PEN (methotrexate):</b> Use Metoject PEN <b>only once a week</b> for the treatment of rheumatoid arthritis, juvenile idiopathic arthritis, psoriasis and psoriatic arthritis, and Crohn’s disease. Using too much of Metoject PEN (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.</p>

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

Your doctor decides on the dose, which is adjusted individually to you. Usually it takes 4 – 8 weeks before there is any effect of the treatment.

Metoject PEN is administered subcutaneously (under the skin) by or under the supervision of a physician or healthcare staff as an injection **once a week only**. Together with your doctor you decide on a suitable weekday each week on which you receive your injection.

#### Use in children and adolescents

The doctor decides on the appropriate dose in children and adolescents with polyarthritic forms of juvenile idiopathic arthritis.

**Metoject PEN is not recommended in children less than 3 years of age** due to insufficient experience in this age group.

#### Method and duration of administration

Metoject PEN is injected **once weekly!** The duration of the treatment is determined by the treating physician. Treatment of rheumatoid arthritis, juvenile idiopathic arthritis, psoriasis vulgaris, psoriatic arthritis and Crohn’s disease with Metoject PEN is a long-term treatment.

At the start of your treatment, Metoject PEN may be injected by medical staff. However, your doctor may decide that you can learn how to inject Metoject PEN 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.**

Read the Instructions for Use at the end of this leaflet to find guidance on how to correctly use Metoject PEN.

Please note that all of the contents have to be used.

The manner of handling and throwing away of the medicine and pre-filled pen must be in accordance with local requirements. Pregnant healthcare personnel should not handle and/or administer Metoject PEN.

Methotrexate should not come into contact with the surface of the skin or mucosa. In the event of contamination, the affected area must be rinsed immediately with plenty of water.

#### If you use more Metoject PEN than you should

If you use more Metoject PEN than you should, talk to your doctor immediately.

#### If you forget to use Metoject PEN

Do not take a double dose to make up for a forgotten dose.

#### If you stop using Metoject PEN

If you stop using Metoject PEN, talk to your doctor immediately.

If you have the impression that the effect of Metoject PEN is too strong or too weak, talk to your doctor or pharmacist.

## 4. POSSIBLE SIDE EFFECTS

Like all medicines, this medicine can cause side effects, although not everybody gets them. The frequency as well as the degree of severity of the side effects depends on the dosage level and the frequency of administration. As severe side effects may occur even at low dosage, it is important that you are monitored regularly by your doctor. Your doctor will do **tests to check for abnormalities** developing in the blood (such as low white blood cells, low platelets, lymphoma) and changes in the kidneys and the liver.

Prepare for your injection
----------------------------

### 1. Wash your hands and unpack your pen (Figure C)

- Wash your hands with soap and water.
- Carefully take the pen out of the carton.

**Do not** remove the protective cap until you are ready to inject.



**Figure C**

### 2. Check your pen before use (Figure D)

Carefully check the name and dose on the pen and verify that you have the correct medication. If you are not able to see well enough, ask someone for assistance.

- Check the expiry date on the label of the pen.
- Do not use the pen if it has expired.
- Check the medicine through the inspection window by turning it upside down or gently shaking it. The medicine inside the pen should look clear and yellow.
  - Do not inject if the solution looks cloudy or discoloured or contains particles.
  - It is normal to see one or more air bubbles. Do not try to remove them.
  - You may see a scale in the window; you do not need to consider that.
- Check that the pen is not damaged and that the cap is firmly on. Do not use the pen if it looks damaged or if the cap has been removed or is not firmly attached.

**If the pen is expired, appears damaged, or does not look as expected, do not use it and contact your healthcare provider.**

Carefully place the pen on a clean flat surface, such as a table before performing the next steps.



**Figure D**

**Tell your doctor immediately** if you experience any of the following symptoms, as these may indicate a serious, potentially life-threatening side effect, which require urgent specific treatment:

- **persistent dry, non-productive cough, shortness of breath and fever;** these may be signs of an inflammation of the lungs [common]
- **spitting or coughing blood;** these might be signs of bleeding from the lungs [not known]
- **symptoms of liver damage such as yellowing of the skin and whites of the eyes;** methotrexate can cause chronic liver damage (liver cirrhosis), formation of scar tissue in the liver (liver fibrosis), fatty degeneration of the liver [all uncommon], inflammation of the liver (acute hepatitis) [rare] and liver failure [very rare]
- **allergy symptoms such as skin rash including red itchy skin, swelling of the hands, feet, ankles, face, lips, mouth or throat (which may cause difficulty in swallowing or breathing) and feeling you are going to faint;** these may be signs of severe allergic reactions or an anaphylactic shock [rare]
- **symptoms of kidney damage such as swelling of the hands, ankles or feet or changes in frequency of urination or decrease (oliguria) or absence of urine (anuria);** these may be signs of kidney failure [rare]
- **symptoms of infections, e.g. fever, chills, achiness, sore throat;** methotrexate can make you more susceptible to infections. Severe infections like a certain type of pneumonia (*Pneumocystis jirovecii pneumonia*) or blood poisoning (sepsis) may occur [rare]
- **symptoms such as weakness of one side of the body (stroke) or pain, swelling, redness and unusual warmth in one of your legs (deep vein thrombosis); this may happen when a dislodged blood clot causes a blockage of a blood vessel** (thromboembolic event) [rare]
- **fever and serious deterioration of your general condition, or sudden fever accompanied by a sore throat or mouth, or urinary problems;** methotrexate can cause a sharp fall in certain white blood cells (agranulocytosis) and severe bone marrow suppression [very rare]
- **unexpected bleeding, e.g. bleeding gums, blood in the urine, vomiting blood or bruising,** these can be signs of a severely reduced number of blood platelets caused by severe courses of bone marrow depression [very rare]
- **symptoms such as severe headache often in combination with fever, neck stiffness, feeling sick, vomiting, disorientation and sensitivity to light** may indicate an inflammation of the membranes of the brain (acute aseptic meningitis) [very rare]
- certain brain disorders (encephalopathy/leukoencephalopathy) have been reported in cancer patients receiving methotrexate. Such side effects cannot be excluded when methotrexate therapy is used to treat other diseases. Signs of this kind of brain disorders may be **altered mental state, movement disorders (ataxia), visual disturbances or disturbances of memory [not known]**
- **severe skin rash or blistering of the skin (this can also affect your mouth, eyes and genitals);** these may be signs of conditions called Stevens Johnson syndrome or burned skin syndrome (toxic epidermal necrolysis/Lyell's syndrome) [very rare]

In the following, please find the other side effects that may occur:

- **Very common:** may affect more than 1 in 10 people
- Inflammation of the mouth lining, indigestion, feeling sick, loss of appetite, abdominal pain.
- Abnormal liver function test (ASAT, ALAT, bilirubin, alkaline phosphatase).

**Common:** may affect up to 1 in 10 people

- Mouth ulcers, diarrhoea.
- Rash, reddening of the skin, itching.
- Headache, tiredness, drowsiness.
- Reduced blood cell formation with decrease in white and/or red blood cells and/or platelets.

**Uncommon:** may affect up to 1 in 100 people

- Throat inflammation.
- Inflammation of the bowels, vomiting, inflammation of pancreas, black or tarry stools, gastrointestinal ulcers and bleeding.
- Sunburn-like reactions due to increased sensitivity of the skin to sunlight, loss of hair, increased number of rheumatic nodules, skin ulcer, shingles, inflammation of blood vessels, herpes-like skin rash, hives.
- Onset of diabetes mellitus.
- Dizziness, confusion, depression.
- Decrease in serum albumin.
- Decrease in the number of all blood cells and platelets.
- Inflammation and ulcer of the urinary bladder or vagina, reduced kidney function, disturbed urination.
- Joint pain, muscle pain, reduction of bone mass.

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

- Inflammation of gum tissue.
- Increased skin pigmentation, acne, blue spots on the skin due to vessel bleeding (ecchymosis, petechiae), allergic inflammation of blood vessels.
- Decreased number of anti-bodies in the blood.
- Infection (incl. reactivation of inactive chronic infection), red eyes (conjunctivitis).
- Mood swings (mood alterations).
- Visual disturbances.
- Inflammation of the sac around the heart, accumulation of fluid in the sac around the heart, obstruction of cardiac filling due to fluid in the sac around the heart.
- Low blood pressure.
- Formation of scar tissue in the lung (pulmonary fibrosis), shortness of breath and bronchial asthma, accumulation of fluid in the sac around the lung.
- Stress fracture.
- Electrolyte disturbances.
- Fever, wound-healing impairment.

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

- Acute toxic dilatation of the gut (toxic megacolon).
- Increased pigmentation of the nails, inflammation of the cuticles (acute paronychia), deep infection of hair follicles (furunculosis), visible enlargement of small blood vessels.
- Pain, loss of strength or sensation of numbness or tingling / having less sensitivity to stimulation than normal, changes in taste (metallic taste), convulsions, paralysis, meningism.
- Impaired vision, non-inflammatory eye disorder (retinopathy).
- Loss of sexual drive, impotence, male breast enlargement, defective sperm formation (oligospemia), menstrual disorder, vaginal discharge.
- Enlargement of lymphatic nodes (lymphoma).
- Lymphoproliferative disorders (excessive growth of white blood cells).

**Not known:** frequency cannot be estimated from the available data

- Increased number of certain white blood cells.
- Nosebleed.
- Proteins in urine.
- Feeling of weakness.
- Bone damage in the jaw (secondary to excessive growth of white blood cells).
- Tissue destruction at injection site.
- Redness and shedding of skin.
- Swelling.

Subcutaneous application of methotrexate is locally well tolerated. Only mild local skin reactions (such as burning sensations, erythema, swelling, discolouration, severe itching, pain) were observed, decreasing during therapy.

**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 Yellow Card Scheme at: [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard) or search for MHRA Yellow Card in the **Google Play** or **Apple App Store**.

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

## 5. HOW TO STORE METOJECT PEN

- Keep out of the sight and reach of children.
- Do not store above 25°C. Do not freeze.
- Keep the pre-filled pen in the outer carton in order to protect from light.
- Do not use Metoject PEN after the expiry date which is stated on the pre-filled pen and carton after EXP. The expiry date refers to the last day of that month.
- If your medicine becomes discoloured or if your Metoject PEN shows any sign of deterioration or doesn't work properly, take it back to your pharmacist.
- Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

## 6. CONTENTS OF THE PACK AND OTHER INFORMATION

**What Metoject PEN contains**

1 pre-filled pen with 0.15 ml solution contains 7.5 mg methotrexate.

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

**What Metoject PEN looks like and contents of the pack**

Metoject PEN is a pre-filled pen containing a clear, yellow-brown solution.

Metoject PEN pre-filled pen is a two-step auto-injector with a translucent protective cap and a blue needle cover

Metoject PEN is available in packs of 1 pre-filled pen.

Manufactured by medac Gesellschaft für klinische Spezialpräparate mbH, Theaterstr. 6, 22880 Wedel, Germany.

Procured from within the EU. Repackaged by the Product Licence Holder: MPT Pharma Ltd., Westgate Business Park, Unit 5-7 Tintagel Way, Aldridge, Walsall WS9 8ER.

PL: 33532/1521

POM

Leaflet dated 28<sup>th</sup> May 2025

Leaflet coded xxxxxxxxxx

Metoject<sup>®</sup> is a registered trademark of medac Gesellschaft für klinische Spezialpräparate mbH.

To request a copy of this leaflet in Braille, large print or audio please call 01922 745645 and ask for the Regulatory Department.



### 3. Choose your injection site (Figure E)

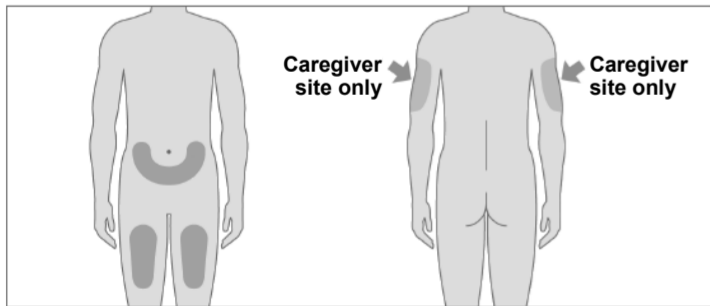


Figure E

- You can inject yourself into your:
  - upper thighs,
  - lower part of the abdomen except within 5 cm around the belly button.
- If a caregiver administers the injection for you, the person may also use the area at the back of the upper arm.
- Use a different site than for your last injection.

When selecting an injection site:

**Do not** inject into other parts of the body.  
**Do not** inject into skin that is bruised, tender, scaly, red or hard.  
**Do not** inject into moles, scars or stretch marks.  
**Do not** inject through clothing.

### 4. Clean your injection site (Figure F)

- Clean your injection site with alcohol disinfection; if not available you may use water and soap.
- Allow the skin to air dry.

**Do not** fan or blow on the clean area.

**Do not** touch your injection site again until you have finished your injection.



Figure F

### Inject your dose

#### 5. Remove the cap (Figure G)

Only remove the protective cap when you are ready to inject.

**Do not** try to put the cap back on the pen once it is removed.

- Hold the pen with the cap pointing upwards and firmly pull the cap straight off.

**Do not** bend or twist the cap while pulling off.

- Dispose of the cap right away.
- You may notice small droplets of the medicine. This is normal.
- Perform your injection immediately after removing the cap.

**Do not** touch the blue needle cover with your fingers. Touching the blue needle cover may accidentally trigger the injection and cause injury.

#### 6. Position your pen (Figure H)

- Position the uncapped blue needle cover at a 90 degree angle against the skin with the inspection window facing towards you so you can see it.
- You may feel more comfortable when grabbing a skin pinch by gently squeezing the area around the injection site with your thumb and forefingers before injecting, but this is not necessary for this pen.

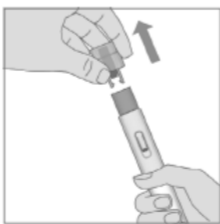


Figure G

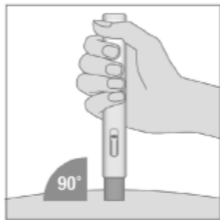


Figure H

#### 7. Start your injection (Figure I)

- To start your injection, push the pen down all the way. This will slide the blue needle cover up into the pen and the injection will start automatically.
- A first "click" hereby indicates the start of the injection. The blue plunger rod will move down.
- Keep holding the pen against the skin until all of the medicine is injected.

**Do not** change the position of the pen once the injection has started.

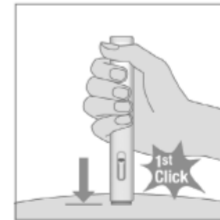


Figure I

#### 8. Hold the pen in place to complete your injection (Figure J)

- Continue holding the pen down against your skin.
- Your injection is complete when either:
  - you hear a second "click", shortly after the first
  - or: the blue plunger rod has stopped moving and fills the inspection window
  - or: 5 seconds have passed.

**Do not** remove the pen until at least 5 seconds have passed.

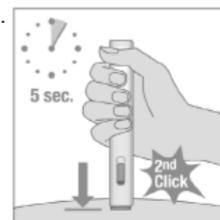


Figure J

#### 9. Finishing your injection (Figure K)

- Remove the pen by pulling it straight up from the injection site.
- The blue needle cover automatically moves into place over the needle. The blue needle cover is then locked.
- Check the inspection window for any leftover yellow medicine inside.

If you still see yellow medicine inside the window you may not have received the full dose. If this happens or if you have any other concerns, contact your healthcare provider.

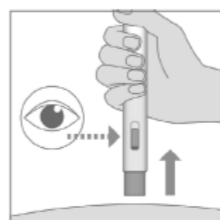


Figure K

**Do not** touch the blue needle cover after injection. This may cause injury.

### After your injection

#### 10. Treat your injection site (Figure L)

- You may notice a small drop of blood at the injection site. This is normal. Press a cotton ball or gauze on the area, if necessary.
- If needed, cover the injection site with a small bandage.

**Do not** rub your injection site.



Figure L

#### 11. Dispose of your pen (Figure M)

Each pen can only be used once.

**Do not** recap the pen.

**Keep your used pen and protective cap out of the sight and reach of children.**

- Dispose of the cap and your pen right away after use.

The manner of throwing away the medicine and the pre-filled pen must be in accordance with local requirements.

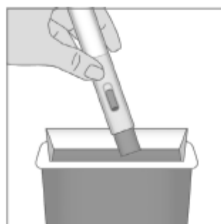


Figure M

- Throw away the used supplies in your household trash. The paper carton can be recycled.

**Safely dispose of Metoject PEN pre-filled pens that are expired, no longer needed, or otherwise unusable.**

## **PACKAGE LEAFLET: INFORMATION FOR THE USER**

# Methotrexate 7.5 mg solution for injection in pre-filled pen

**Read all of this leaflet carefully before you start using 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 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. This includes any possible side effects not listed in this leaflet. See section 4.
- Your medicine is called Methotrexate 7.5 mg solution for injection in pre-filled pen but will be referred to as Methotrexate throughout the remainder of this leaflet.
- Methotrexate is also available in other strengths.

### **What is in this leaflet**

1. What Methotrexate is and what it is used for
2. What you need to know before you use Methotrexate
3. How to use 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**

Methotrexate is indicated for the treatment of

- active rheumatoid arthritis in adult patients.
- polyarthritic forms of severe, active juvenile idiopathic arthritis, when the response to nonsteroidal anti-inflammatory drugs (NSAIDs) has been inadequate.
- moderate to severe psoriasis in adult patients, and severe psoriatic arthritis in adults.
- mild to moderate Crohn's disease in adult patients when adequate treatment with other medicines is not possible.

**Rheumatoid arthritis (RA)** is a chronic collagen disease, characterised by inflammation of the synovial membranes (joint membranes). These membranes produce a fluid which acts as a lubricant for many joints. The inflammation causes thickening of the membrane and swelling of the joint.

**Juvenile arthritis** concerns children and adolescents less than 16 years. Polyarthritic forms are indicated if 5 or more joints are affected within the first 6 months of the disease.

**Psoriasis** is a common chronic skin disease, characterised by red patches covered by thick, dry, silvery, adherent scales.

**Psoriatic arthritis** is a kind of arthritis with psoriatic lesions of the skin and nails, especially at the joints of fingers and toes.

Methotrexate modifies and slows down the progression of the disease.

Crohn's disease is a type of inflammatory bowel disease that may affect any part of the gastrointestinal tract causing symptoms such as abdominal pain, diarrhoea, vomiting or weight loss.

## **2. WHAT YOU NEED TO KNOW BEFORE YOU USE METHOTREXATE**

### **Do not use Methotrexate**

- if you are allergic to methotrexate or any of the other ingredients of this medicine (listed in section 6).
- if you suffer from liver or severe kidney diseases or blood diseases.
- if you regularly drink large amounts of alcohol.
- if you suffer from a severe infection, such as tuberculosis, HIV or other immunodeficiency syndromes.

- if you suffer from mouth ulcers, stomach ulcer or intestinal ulcer.
- if you are pregnant or breast-feeding (see section "Pregnancy, breast-feeding and fertility").
- if you receive vaccinations with live vaccines at the same time.

### **Warnings and precautions**

Talk to your doctor or pharmacist before taking Methotrexate if

- you are elderly or if you feel generally unwell and weak.
- you have problems with the way your liver works.
- you suffer from dehydration (water loss).
- you have diabetes mellitus and are being treated with insulin.

### **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 6 months after treatment has stopped if you are a woman. If you are a man you should avoid fathering a child if you are being given methotrexate at the time and for at least 3 months after the end of your treatment. See also section "Pregnancy, breast-feeding and fertility".

### **Recommended follow-up examinations and precautions**

Even if methotrexate is used in low doses, serious side effects can occur. In order to detect them in time, your doctor must perform monitoring examinations and laboratory tests.

### **Prior to the start of therapy**

Before you start treatment, your blood will be checked to see if you have enough blood cells. Your blood will also be tested to check your liver function and to find out if you have hepatitis. Furthermore, serum albumin (a protein in the blood), hepatitis (liver infection) status and kidney function will be checked. The doctor may also decide to run other liver tests, some of these may be images of your liver and others may need a small sample of tissue taken from the liver in order to examine it more closely. Your doctor may also check to see if you have tuberculosis and they may X-ray your chest or perform a lung function test.

### **During the treatment**

Your doctor may perform the following examinations:

- Examination of the oral cavity and the pharynx for changes in the mucous membrane such as inflammation or ulceration.
- Blood tests/blood count with number of blood cells and measurement of serum methotrexate levels.
- Blood test to monitor liver function.
- Imaging tests to monitor liver condition.
- Small sample of tissue taken from the liver in order to examine it more closely.
- Blood test to monitor kidney function.
- Respiratory tract monitoring and, if necessary, lung function test.

It is very important that you appear for these scheduled examinations. If the results of any of these tests are conspicuous, your doctor will adjust your treatment accordingly.

### **Elderly patients**

Elderly patients under treatment with methotrexate should be monitored closely by a physician so that possible side effects can be detected as early as possible. Age-related impairment of liver and kidney function as well as low body reserves of the vitamin folic acid in old age require a relatively low dosage of methotrexate.

### **Other precautions**

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 may affect your immune system and vaccination results. It may also affect the result of immunological tests. Inactive, chronic infections (such as herpes zoster [shingles], tuberculosis, hepatitis B or C) may flare up. **During therapy with Methotrexate you must not be vaccinated with live vaccines.**

Methotrexate may make your skin more sensitive to sunlight. Avoid intense sun and do not use sun-beds or a sun-lamp without medical advice. To protect your skin from intense sun, wear adequate clothing or use a sunscreen with a high protection factor.

Radiation-induced dermatitis and sunburn can reappear under methotrexate therapy (recall-reaction). Psoriatic lesions can exacerbate during UV-irradiation and simultaneous administration of methotrexate.

Enlarged lymph nodes (lymphoma) may occur and if this is the case, therapy must be stopped.

Diarrhoea can be a possible side effect of Methotrexate and requires an interruption of therapy. If you suffer from diarrhoea, please speak to your doctor.

Certain brain disorders (encephalopathy/leukoencephalopathy) have been reported in cancer patients receiving methotrexate. Such side effects cannot be excluded when methotrexate is used to treat other diseases.

If you, your partner or your caregiver notice new onset or worsening of neurological symptoms including general muscle weakness, disturbance of vision, changes in thinking, memory and orientation leading to confusion and personality changes contact your doctor immediately because these may be symptoms of a very rare, serious brain infection called progressive multifocal leukoencephalopathy (PML).

### **Other medicines and Methotrexate**

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. Please note that this also applies to medicines that you will take **in the future**.

The effect of the treatment may be affected if Methotrexate is administered at the same time as certain other medicines:

- **Antibiotics** such as: tetracyclines, chloramphenicol, non-absorbable broad-spectrum antibiotics, penicillins, glycopeptides, sulphonamides, ciprofloxacin and cefalotin (medicines to prevent/fight certain infections).
- **Non-steroidal anti-inflammatory** drugs or **salicylates** (medicines against pain and/or inflammation such as acetylsalicylic acid, diclofenac and ibuprofen or pyrazole).
- Metamizole (synonyms novaminsulfon and dipyrone) (medicine against severe pain and/or fever).
- **Probenecid** (medicine against gout).
- Weak organic acids like loop **diuretics** ("water tablets").
- Medicines, which may have adverse effects on the **bone marrow**, such as trimethoprim-sulfamethoxazole (an antibiotic) and pyrimethamine.
- Other **medicines used to treat rheumatoid arthritis** such as leflunomide, sulphasalazine and azathioprine.
- Cyclosporine (for suppressing the immune system).
- Mercaptopurine (a **cytostatic** medicine).
- Retinoids (medicine against **psoriasis** and other dermatological diseases).
- Theophylline (medicine against **bronchial asthma** and other lung diseases).
- Some medicines against **stomach trouble** such as omeprazole and pantoprazole.
- Hypoglycaemics (medicines that are used to **lower the blood sugar**).

Vitamins containing **folic acid** may impair the effect of your treatment and should only be taken when advised by your doctor.

**Vaccination with live vaccine must be avoided.**

### **Methotrexate with food, drink and alcohol**

Alcohol as well as large amounts of coffee, caffeine-containing soft drinks and black tea should be avoided during treatment with Methotrexate.

### **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 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. pregnancy test before starting treatment.

You must avoid becoming pregnant while 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.

#### **Breast-feeding**

Stop breast-feeding prior to and during treatment with Methotrexate.

#### **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 mutation. Methotrexate can affect sperm production with the potential to cause birth defects. Therefore, you should avoid fathering a child or to donate semen while taking methotrexate and for at least 3 months after treatment is stopped.

### **Driving and using machines**

Treatment with Methotrexate may cause adverse reactions affecting the central nervous system, such as tiredness and dizziness. Thus, the ability to drive a vehicle and/or to operate machines may, in certain cases, be compromised. If you feel tired or drowsy do not drive or use machines.

### **Methotrexate contains sodium**

This medicine contains less than 1 mmol sodium (23 mg) per dose; that is to say essentially "sodium-free".

## **3. HOW TO USE METHOTREXATE**

### **Important warning about the dose of Methotrexate:**

Use Methotrexate **only once a week** for the treatment of rheumatoid arthritis, juvenile idiopathic arthritis, psoriasis and psoriatic arthritis, and Crohn's disease. Using too much of 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.

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

Your doctor decides on the dose, which is adjusted individually to you. Usually it takes 4 – 8 weeks before there is any effect of the treatment.

Methotrexate is administered subcutaneously (under the skin) by or under the supervision of a physician or healthcare staff as an injection **once a week only**. Together with your doctor you decide on a suitable weekday each week on which you receive your injection.

### **Use in children and adolescents**

The doctor decides on the appropriate dose in children and adolescents with polyarthritic forms of juvenile idiopathic arthritis. **Methotrexate is not recommended in children less than 3 years of age** due to insufficient experience in this age group.



## **Instructions for Use**

### **Recommendations**

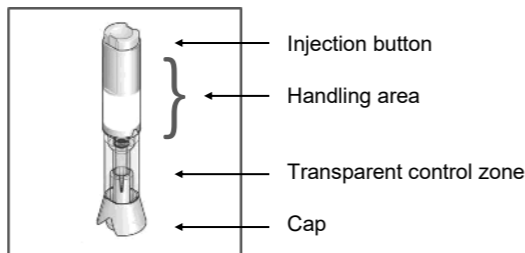
- Carefully read the instructions below before starting your injection.
- Always use the injection technique advised by your doctor, pharmacist or nurse.

### **Additional information**

The manner of handling and throwing away of the medicine and pre-filled pen must be in accordance with local requirements. Pregnant healthcare personnel should not handle and/or administer Methotrexate.

Methotrexate should not come into contact with the surface of the skin or mucosa. In the event of contamination, the affected area must be rinsed immediately with plenty of water.

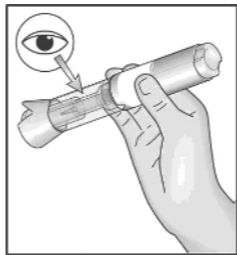
### **Methotrexate pre-filled pen components:**



- a) With cap before injection
- b) After cap removal before injection
- c) After injection

What you need to do before administering your injection

1. Wash your hands very carefully.
2. Remove the system from its packaging.
3. Check the Methotrexate pre-filled pen before using it:



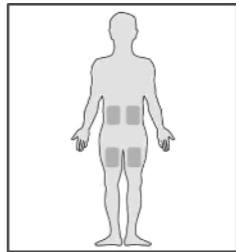
If the Methotrexate pre-filled pen appears to be damaged **do not use** it. Use another one and contact your doctor, pharmacist or nurse.

In case a small air bubble is visible through the transparent control zone, this will not affect your dose nor will it harm you.

If you are not able to see or to check the system correctly prior to injection, ask someone around you for assistance.

4. Set the Methotrexate pre-filled pen on a clean flat surface (such as a table).

### **Where you should administer the injection**



The most appropriate zones for your injection are:

- upper thighs,
- abdomen except around the navel.

- If someone around you administers the injection for you, the person may also use the top of the zone at the back of the arm, just below the shoulder.
- Change the injection area with each injection. This will minimise any reactions at the injection site.
- Never inject into areas where the skin is tender, bruised, red or hard or where you have scars or stretch marks. If you have psoriasis, you should not try to inject directly into any raised, thick, red or scaly skin patches or lesions.

## Method and duration of administration

Methotrexate is injected **once weekly!**

The duration of the treatment is determined by the treating physician. Treatment of rheumatoid arthritis, juvenile idiopathic arthritis, psoriasis vulgaris, psoriatic arthritis and Crohn's disease with Methotrexate is a long-term treatment.

At the start of your treatment, Methotrexate may be injected by medical staff. However, your doctor may decide that you can learn how to inject Methotrexate 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.**

Read the Instructions for Use at the end of this leaflet to find guidance on how to correctly use Methotrexate.

Please note that all of the contents have to be used.

The manner of handling and throwing away of the medicine and pre-filled pen must be in accordance with local requirements. Pregnant healthcare personnel should not handle and/or administer Methotrexate.

Methotrexate should not come into contact with the surface of the skin or mucosa. In the event of contamination, the affected area must be rinsed immediately with plenty of water.

### If you use more Methotrexate than you should

If you use more Methotrexate than you should, talk to your doctor immediately.

### If you forget to use Methotrexate

Do not take a double dose to make up for a forgotten dose.

### If you stop using Methotrexate

If you stop using Methotrexate, talk to your doctor immediately.

If you have the impression that the effect of Methotrexate is too strong or too weak, talk to your doctor or pharmacist.

## 4. POSSIBLE SIDE EFFECTS

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

The frequency as well as the degree of severity of the side effects depends on the dosage level and the frequency of administration. As severe side effects may occur even at low dosage, it is important that you are monitored regularly by your doctor. Your doctor will do **tests to check for abnormalities** developing in the blood (such as low white blood cells, low platelets, lymphoma) and changes in the kidneys and the liver.

**Tell your doctor immediately** if you experience any of the following symptoms, as these may indicate a serious, potentially life-threatening side effect, which require urgent specific treatment:

- **persistent dry, non-productive cough, shortness of breath and fever;** these may be signs of an inflammation of the lungs [common]
- **spitting or coughing blood;** these might be signs of bleeding from the lungs [not known]
- **symptoms of liver damage such as yellowing of the skin and whites of the eyes;** methotrexate can cause chronic liver damage (liver cirrhosis), formation of scar tissue in the liver (liver fibrosis), fatty degeneration of the liver [all uncommon], inflammation of the liver (acute hepatitis) [rare] and liver failure [very rare]
- **allergy symptoms such as skin rash including red itchy skin, swelling of the hands, feet, ankles, face, lips, mouth or throat (which may cause difficulty in swallowing or breathing) and feeling you are going to faint;** these may be signs of severe allergic reactions or an anaphylactic shock [rare]
- **symptoms of kidney damage such as swelling of the hands, ankles or feet or changes in frequency of urination or decrease (oliguria) or absence of urine (anuria);** these may be signs of kidney failure [rare]
- **symptoms of infections, e.g. fever, chills, achiness, sore throat;** methotrexate can make you more susceptible to infections. Severe infections like a certain type of pneumonia (*Pneumocystis jirovecii pneumonia*) or blood poisoning (sepsis) may occur [rare]

- **symptoms such as weakness of one side of the body (stroke) or pain, swelling, redness and unusual warmth in one of your legs (deep vein thrombosis); this may happen when a dislodged blood clot causes a blockage of a blood vessel** (thromboembolic event) [rare]
- **fever and serious deterioration of your general condition, or sudden fever accompanied by a sore throat or mouth, or urinary problems;** methotrexate can cause a sharp fall in certain white blood cells (agranulocytosis) and severe bone marrow suppression [very rare]
- **unexpected bleeding, e.g. bleeding gums, blood in the urine, vomiting blood or bruising,** these can be signs of a severely reduced number of blood platelets caused by severe courses of bone marrow depression [very rare]
- **symptoms such as severe headache often in combination with fever, neck stiffness, feeling sick, vomiting, disorientation and sensitivity to light** may indicate an inflammation of the membranes of the brain (acute aseptic meningitis) [very rare]
- certain brain disorders (encephalopathy/leukoencephalopathy) have been reported in cancer patients receiving methotrexate. Such side effects cannot be excluded when methotrexate therapy is used to treat other diseases. Signs of this kind of brain disorders may be **altered mental state, movement disorders (ataxia), visual disturbances or disturbances of memory [not known]**
- **severe skin rash or blistering of the skin (this can also affect your mouth, eyes and genitals);** these may be signs of conditions called Stevens Johnson syndrome or burned skin syndrome (toxic epidermal necrolysis/Lyell's syndrome) [very rare]

In the following, please find the other side effects that may occur:

**Very common:** may affect more than 1 in 10 people

- Inflammation of the mouth lining, indigestion, feeling sick, loss of appetite, abdominal pain.
- Abnormal liver function test (ASAT, ALAT, bilirubin, alkaline phosphatase).

**Common:** may affect up to 1 in 10 people

- Mouth ulcers, diarrhoea.
- Rash, reddening of the skin, itching.
- Headache, tiredness, drowsiness.
- Reduced blood cell formation with decrease in white and/or red blood cells and/or platelets.

**Uncommon:** may affect up to 1 in 100 people

- Throat inflammation.
- Inflammation of the bowels, vomiting, inflammation of pancreas, black or tarry stools, gastrointestinal ulcers and bleeding.
- Sunburn-like reactions due to increased sensitivity of the skin to sunlight, loss of hair, increased number of rheumatic nodules, skin ulcer, shingles, inflammation of blood vessels, herpes-like skin rash, hives.
- Onset of diabetes mellitus.
- Dizziness, confusion, depression.
- Decrease in serum albumin.
- Decrease in the number of all blood cells and platelets.
- Inflammation and ulcer of the urinary bladder or vagina, reduced kidney function, disturbed urination.
- Joint pain, muscle pain, reduction of bone mass.

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

- Inflammation of gum tissue.
- Increased skin pigmentation, acne, blue spots on the skin due to vessel bleeding (ecchymosis, petechiae), allergic inflammation of blood vessels.
- Decreased number of anti-bodies in the blood.
- Infection (incl. reactivation of inactive chronic infection), red eyes (conjunctivitis).
- Mood swings (mood alterations).
- Visual disturbances.
- Inflammation of the sac around the heart, accumulation of fluid in the sac around the heart, obstruction of cardiac filling due to fluid in the sac around the heart.

- Low blood pressure.
- Formation of scar tissue in the lung (pulmonary fibrosis), shortness of breath and bronchial asthma, accumulation of fluid in the sac around the lung.
- Stress fracture.
- Electrolyte disturbances.
- Fever, wound-healing impairment.

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

- Acute toxic dilatation of the gut (toxic megacolon).
- Increased pigmentation of the nails, inflammation of the cuticles (acute paronychia), deep infection of hair follicles (furunculosis), visible enlargement of small blood vessels.
- Pain, loss of strength or sensation of numbness or tingling / having less sensitivity to stimulation than normal, changes in taste (metallic taste), convulsions, paralysis, meningism.
- Impaired vision, non-inflammatory eye disorder (retinopathy).
- Loss of sexual drive, impotence, male breast enlargement, defective sperm formation (oligospermia), menstrual disorder, vaginal discharge.
- Enlargement of lymphatic nodes (lymphoma).
- Lymphoproliferative disorders (excessive growth of white blood cells).

**Not known:** frequency cannot be estimated from the available data

- Increased number of certain white blood cells.
- Nosebleed.
- Proteins in urine.
- Feeling of weakness.
- Bone damage in the jaw (secondary to excessive growth of white blood cells).
- Tissue destruction at injection site.
- Redness and shedding of skin.
- Swelling.

Subcutaneous application of methotrexate is locally well tolerated. Only mild local skin reactions (such as burning sensations, erythema, swelling, discolouration, severe itching, pain) were observed, decreasing during therapy.

### 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 Yellow Card Scheme at:

[www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard) or search for MHRA Yellow Card in the **Google Play** or **Apple App Store**.

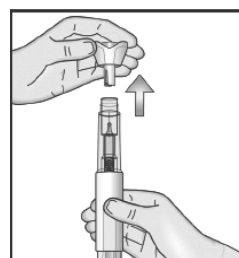
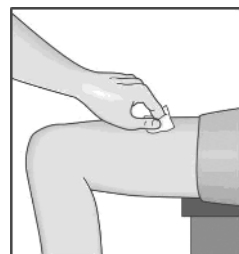
By reporting side effects you can help provide more information on the safety of this medicine.

## 5. HOW TO STORE METHOTREXATE

- Keep out of the sight and reach of children.
- Do not store above 25°C.
- Keep the pre-filled pen in the outer carton in order to protect from light.
- Do not use Methotrexate after the expiry date which is stated on the pre-filled pen and carton after EXP. The expiry date refers to the last day of that month.
- If your medicine becomes discoloured or if your Methotrexate shows any sign of deterioration or doesn't work properly, take it back to your pharmacist.
- Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.



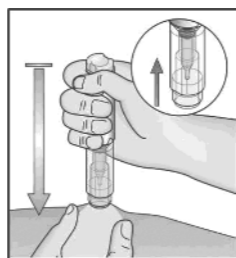
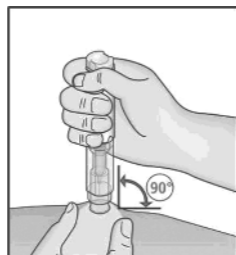
### How to prepare the injection



5. Choose an injection site and clean the area of and around the chosen injection site.

- Do not remove the cap before you are ready to administer the injection.
- 6. Hold the pen with one hand in the handling area with the cap pointing upwards. Use your other hand to gently pull the cap straight off (do not bend or twist the cap). The cap has a small needle shield that should come off with the cap automatically. If the needle shield does not come off, use another pen and contact your doctor, pharmacist or nurse.
- If you are unable to remove the cap, ask someone around you for assistance.

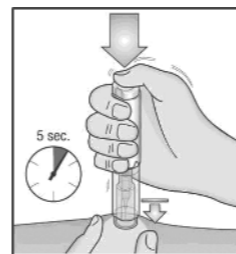
**Note: Once you have removed the cap, perform your injection without delay.**



7. With your free hand, build a skin fold by gently squeezing the area of the cleaned skin at the injection site.
  - The fold must be held pinched until the Methotrexate pre-filled pen is removed from the skin after the injection.

8. Position the uncapped transparent end of Methotrexate pre-filled pen perpendicular to the fold of skin.
9. **Without pressing the button,** push the Methotrexate pre-filled pen firmly onto your skin in order to unlock the button.
  - If you are unable to push the Methotrexate pre-filled pen to the stop-point, ask someone around you for assistance.

### How to administer the injection:



10. While holding the Methotrexate pre-filled pen firmly against the skin, **now press the button** with your thumb.
11. You will hear a click which indicates the start of the injection. Keep holding the pen against the raised skin until all of the medicine is injected. This can take up to **5 seconds**.

### Note:

Do not remove the Methotrexate pre-filled pen from the skin before the end of the injection to avoid incomplete injection. If the injection is not triggered, release the button, make sure that the Methotrexate pre-filled pen is pressed firmly against the skin and push hard on the button. If you have troubles with your hearing, count 5 seconds from the moment you have pressed the button and then lift the Methotrexate pre-filled pen from the injection site.

## 6. CONTENTS OF THE PACK AND OTHER INFORMATION

### What Methotrexate contains

1 pre-filled pen with 0.15 ml solution contains 7.5 mg methotrexate.

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

### What Methotrexate looks like and contents of the pack

Methotrexate is a pre-filled pen containing a clear, yellow-brown solution in colourless glass pre-filled syringe with a rubber plunger stopper and embedded injection needle. The syringe is externally equipped with a device for self-administration.

Methotrexate is available in packs of 1 pre-filled pen.

Manufactured by medac Gesellschaft für klinische Spezialpräparate mbH, Theaterstr. 6, 22880 Wedel, Germany.

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PL: 33532/1521

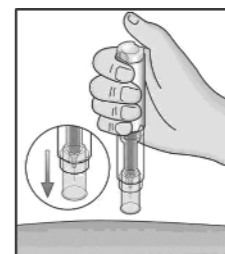
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Leaflet dated 28<sup>th</sup> May 2025

Leaflet coded xxxxxxxxx

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12. Remove the Methotrexate pre-filled pen from the injection site, perpendicular to the skin (pull up).
13. The protective shield automatically moves into place over the needle. The protective shield is then locked and the needle is protected.
14. In case of a slight bleeding use a plaster.

Before throwing away the Methotrexate pre-filled pen, check visually that there is no liquid left in the pen, at the bottom of the **transparent control zone**. If there is liquid left in the pen, not all of the medicine has been injected correctly and you should consult your doctor.

### Note

To avoid any injury, **never insert your fingers in the opening of the protective tube** covering the needle. **Do not destroy the pen.**

### Whom should you contact in case of need

- For any problem or question, contact your doctor, pharmacist or nurse.
- If you or someone around you is injured by the needle, consult your doctor immediately and throw away the Methotrexate pre-filled pen.

## PACKAGE LEAFLET: INFORMATION FOR THE USER

# Methotrexate 7.5 mg solution for injection in pre-filled pen

**Read all of this leaflet carefully before you start using 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 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. This includes any possible side effects not listed in this leaflet. See section 4.
- Your medicine is called Methotrexate 7.5 mg solution for injection in pre-filled pen but will be referred to as Methotrexate throughout the remainder of this leaflet.
- Methotrexate is also available in other strengths.

**What is in this leaflet**

- What Methotrexate is and what it is used for
- What you need to know before you use Methotrexate
- How to use Methotrexate
- Possible side effects
- How to store Methotrexate
- Contents of the pack and other information

## 1. WHAT METHOTREXATE IS AND WHAT IT IS USED FOR

Methotrexate is indicated for the treatment of

- active rheumatoid arthritis in adult patients.
- polyarthritic forms of severe, active juvenile idiopathic arthritis, when the response to nonsteroidal anti-inflammatory drugs (NSAIDs) has been inadequate.
- moderate to severe psoriasis in adult patients, and severe psoriatic arthritis in adults.
- mild to moderate Crohn’s disease in adult patients when adequate treatment with other medicines is not possible.

**Rheumatoid arthritis** (RA) is a chronic collagen disease, characterised by inflammation of the synovial membranes (joint membranes). These membranes produce a fluid which acts as a lubricant for many joints. The inflammation causes thickening of the membrane and swelling of the joint.

**Juvenile arthritis** concerns children and adolescents less than 16 years. Polyarthritic forms are indicated if 5 or more joints are affected within the first 6 months of the disease.

**Psoriasis** is a common chronic skin disease, characterised by red patches covered by thick, dry, silvery, adherent scales.

**Psoriatic arthritis** is a kind of arthritis with psoriatic lesions of the skin and nails, especially at the joints of fingers and toes.

Methotrexate modifies and slows down the progression of the disease.

Crohn’s disease is a type of inflammatory bowel disease that may affect any part of the gastrointestinal tract causing symptoms such as abdominal pain, diarrhoea, vomiting or weight loss.

## 2. WHAT YOU NEED TO KNOW BEFORE YOU USE METHOTREXATE

**Do not use Methotrexate**

- if you are allergic to methotrexate or any of the other ingredients of this medicine (listed in section 6).
- if you suffer from liver or severe kidney diseases or blood diseases.
- if you regularly drink large amounts of alcohol.
- if you suffer from a severe infection, such as tuberculosis, HIV or other immunodeficiency syndromes.
- if you suffer from mouth ulcers, stomach ulcer or intestinal ulcer.
- if you are pregnant or breast-feeding (see section “Pregnancy, breast-feeding and fertility”).
- if you receive vaccinations with live vaccines at the same time.

When receiving a new medicine or a new dose of medicine always check that it matches what your doctor has prescribed you. Before using the pen, your healthcare provider should show you or your caregiver how to use it correctly.

**Do not** use the pen unless you have been taught how to use it by your healthcare provider. If you or your caregiver have any questions, contact your healthcare provider.

### INSTRUCTIONS FOR USE

These Instructions for Use contain information on how to inject your Methotrexate pre-filled pen.

**Read these Instructions for Use until the end before using the pre-filled pen for your subcutaneous injection. Read these instructions for Use each time you receive a new prescription and keep them for information you may need after the use.**

When receiving a new medicine or a new dose of medicine always check that it matches what your doctor has prescribed you. Before using the pen, your healthcare provider should show you or your caregiver how to use it correctly.

**Do not** use the pen unless you have been taught how to use it by your healthcare provider. If you or your caregiver have any questions, contact your healthcare provider.

### Important Information You Need to Know Before Injecting With Your Methotrexate Pre-filled Pen

**Inject with your Methotrexate pre-filled pen once a week only, and always inject on the same day of the week.**

**Do not inject or handle the product if you are pregnant.**

- Keep the pen in a secure location out of the sight and reach of children.
- If you have any contact with the medicine, wash the affected area with plenty of water right away.

**Do not** remove the protective cap until just before your injection. **Do not** share your pen with another person.

**Do not** use the pen if:

- it has dropped onto a hard surface or appears damaged.
- the clear yellow solution got discoloured, looks cloudy or contains particles.
- it has been frozen or stored above 25°C.
- the expiry date has passed.

If you are unsure, contact your healthcare provider.

**Warnings and precautions**

Talk to your doctor or pharmacist before taking Methotrexate if

- you are elderly or if you feel generally unwell and weak.
- you have problems with the way your liver works.
- you suffer from dehydration (water loss).
- you have diabetes mellitus and are being treated with insulin.

**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 6 months after treatment has stopped if you are a woman. If you are a man you should avoid fathering a child if you are being given methotrexate at the time and for at least 3 months after the end of your treatment. See also section “Pregnancy, breast-feeding and fertility”.

**Recommended follow-up examinations and precautions**

Even if methotrexate is used in low doses, serious side effects can occur. In order to detect them in time, your doctor must perform monitoring examinations and laboratory tests.

**Prior to the start of therapy**

Before you start treatment, your blood will be checked to see if you have enough blood cells. Your blood will also be tested to check your liver function and to find out if you have hepatitis. Furthermore, serum albumin (a protein in the blood), hepatitis (liver infection) status and kidney function will be checked. The doctor may also decide to run other liver tests, some of these may be images of your liver and others may need a small sample of tissue taken from the liver in order to examine it more closely. Your doctor may also check to see if you have tuberculosis and they may X-ray your chest or perform a lung function test.

**During the treatment**

Your doctor may perform the following examinations:

- Examination of the oral cavity and the pharynx for changes in the mucous membrane such as inflammation or ulceration.
- Blood tests/blood count with number of blood cells and measurement of serum methotrexate levels.
- Blood test to monitor liver function.
- Imaging tests to monitor liver condition.
- Small sample of tissue taken from the liver in order to examine it more closely.
- Blood test to monitor kidney function.
- Respiratory tract monitoring and, if necessary, lung function test.

It is very important that you appear for these scheduled examinations. If the results of any of these tests are conspicuous, your doctor will adjust your treatment accordingly.

**Elderly patients**

Elderly patients under treatment with methotrexate should be monitored closely by a physician so that possible side effects can be detected as early as possible.

Age-related impairment of liver and kidney function as well as low body reserves of the vitamin folic acid in old age require a relatively low dosage of methotrexate.

**Other precautions**

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 may affect your immune system and vaccination results. It may also affect the result of immunological tests. Inactive, chronic infections (such as herpes zoster [shingles], tuberculosis, hepatitis B or C) may flare up. **During therapy with Methotrexate you must not be vaccinated with live vaccines.**

Methotrexate may make your skin more sensitive to sunlight. Avoid intense sun and do not use sun-beds or a sun-lamp without medical advice. To protect your skin from intense sun, wear adequate clothing or use a sunscreen with a high protection factor.

Radiation-induced dermatitis and sunburn can reappear under methotrexate therapy (recall-reaction). Psoriatic lesions can exacerbate during UV-irradiation and simultaneous administration of methotrexate.

Enlarged lymph nodes (lymphoma) may occur and if this is the case, therapy must be stopped.

Diarrhoea can be a possible side effect of Methotrexate and requires an interruption of therapy. If you suffer from diarrhoea, please speak to your doctor.

When receiving a new medicine or a new dose of medicine always check that it matches what your doctor has prescribed you. Before using the pen, your healthcare provider should show you or your caregiver how to use it correctly.

**Do not** use the pen unless you have been taught how to use it by your healthcare provider. If you or your caregiver have any questions, contact your healthcare provider.

**How to store your Methotrexate pre-filled pen**

- Store below 25°C.

- Transport and keep the pen in the outer carton in order to protect it from light.

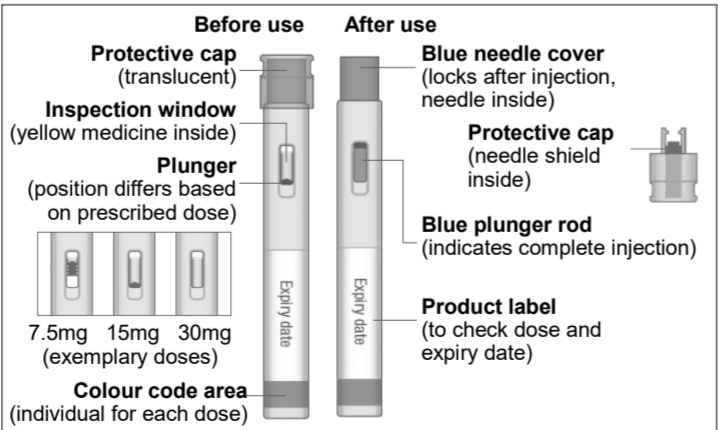
- Keep the pen in a secure location out of the sight and reach of children.

**Do not** freeze.

**Do not** store above 25°C.

**The Methotrexate pre-filled pen (Figure A)**

The Methotrexate pre-filled pen is a two-step, fixed-dose, single-use disposable auto-injector. It is available in 10 different doses ranging from 7.5 mg to 30 mg.



**Figure A**

Certain brain disorders (encephalopathy/leukoencephalopathy) have been reported in cancer patients receiving methotrexate. Such side effects cannot be excluded when methotrexate is used to treat other diseases.

If you, your partner or your caregiver notice new onset or worsening of neurological symptoms including general muscle weakness, disturbance of vision, changes in thinking, memory and orientation leading to confusion and personality changes contact your doctor immediately because these may be symptoms of a very rare, serious brain infection called progressive multifocal leukoencephalopathy (PML).

**Other medicines and Methotrexate**

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. Please note that this also applies to medicines that you will take **in the future**.

The effect of the treatment may be affected if Methotrexate is administered at the same time as certain other medicines:

- Antibiotics** such as: tetracyclines, chloramphenicol, non-absorbable broad-spectrum antibiotics, penicillins, glycopeptides, sulphonamides, ciprofloxacin and cefalotin (medicines to prevent/fight certain infections).
- Non-steroidal anti-inflammatory drugs** or **salicylates** (medicines against pain and/or inflammation such as acetylsalicylic acid, diclofenac and ibuprofen or pyrazole).
- Metamizole (synonyms novaminsulfon and dipyrone) (medicine against severe pain and/or fever).
- Probenecid** (medicine against gout).
- Weak organic acids like loop **diuretics** ("water tablets").
- Medicines, which may have adverse effects on the **bone marrow**, such as trimethoprim-sulfamethoxazole (an antibiotic) and pyrimethamine.
- Other medicines used to treat rheumatoid arthritis** (such as leflunomide, sulphasalazine and azathioprine).
- Cyclosporine (for suppressing the immune system).
- Mercaptopurine (a **cytostatic** medicine).
- Retinoids (medicine against **psoriasis** and other dermatological diseases).
- Theophylline (medicine against **bronchial asthma** and other lung diseases).
- Some medicines against **stomach trouble** such as omeprazole and pantoprazole.
- Hypoglycaemics (medicines that are used to **lower the blood sugar**).

Vitamins containing **folic acid** may impair the effect of your treatment and should only be taken when advised by your doctor.

**Vaccination with live vaccine must be avoided.**

**Methotrexate with food, drink and alcohol**

Alcohol as well as large amounts of coffee, caffeine-containing soft drinks and black tea should be avoided during treatment with Methotrexate.

**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 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. pregnancy test before starting treatment.

You must avoid becoming pregnant while 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.

**Breast-feeding**

Stop breast-feeding prior to and during treatment with Methotrexate.

**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 mutation. Methotrexate can affect sperm production with the potential to cause birth defects. Therefore, you should avoid fathering a child or to donate semen while taking methotrexate and for at least 3 months after treatment is stopped.

When receiving a new medicine or a new dose of medicine always check that it matches what your doctor has prescribed you. Before using the pen, your healthcare provider should show you or your caregiver how to use it correctly.

**Supplies needed for your injection (Figure B)**

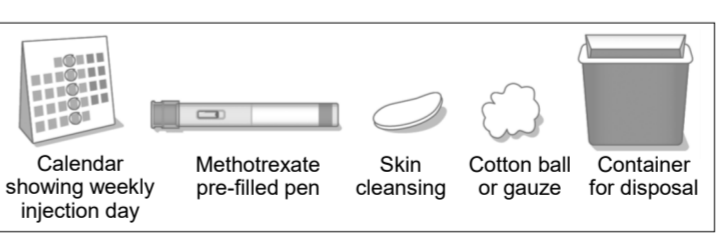
At your weekly injection day find a comfortable place, ensure the area is well lit and you have a clean flat surface, such as a table to place your injection supplies.

You need:

- your Methotrexate pre-filled pen.

Make sure you have the following additional supplies available to perform your injection as they are not included in the package:

- your calendar to check your once weekly injection day,
- skin cleansing like alcohol disinfection, if not available water and soap,
- cotton ball or gauze to treat your injection site,
- container for disposal in accordance with local requirements.



**Figure B**

**Driving and using machines**

Treatment with Methotrexate may cause adverse reactions affecting the central nervous system, such as tiredness and dizziness. Thus, the ability to drive a vehicle and/or to operate machines may, in certain cases, be compromised. If you feel tired or drowsy do not drive or use machines.

**Methotrexate contains sodium**

This medicine contains less than 1 mmol sodium (23 mg) per dose; that is to say essentially "sodium-free".

## 3. HOW TO USE METHOTREXATE

**Important warning about the dose of Methotrexate:**
Use Methotrexate **only once a week** for the treatment of rheumatoid arthritis, juvenile idiopathic arthritis, psoriasis and psoriatic arthritis, and Crohn’s disease. Using too much of 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.

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

Your doctor decides on the dose, which is adjusted individually to you. Usually it takes 4 – 8 weeks before there is any effect of the treatment.

Methotrexate is administered subcutaneously (under the skin) by or under the supervision of a physician or healthcare staff as an injection **once a week only**. Together with your doctor you decide on a suitable weekday each week on which you receive your injection.

**Use in children and adolescents**

The doctor decides on the appropriate dose in children and adolescents with polyarthritic forms of juvenile idiopathic arthritis.

**Methotrexate is not recommended in children less than 3 years of age** due to insufficient experience in this age group.

**Method and duration of administration**

Methotrexate is injected **once weekly!**

The duration of the treatment is determined by the treating physician. Treatment of rheumatoid arthritis, juvenile idiopathic arthritis, psoriasis vulgaris, psoriatic arthritis and Crohn’s disease with Methotrexate is a long-term treatment.

At the start of your treatment, Methotrexate may be injected by medical staff. However, your doctor may decide that you can learn how to inject Methotrexate 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.**

Read the Instructions for Use at the end of this leaflet to find guidance on how to correctly use Methotrexate. Please note that all of the contents have to be used.

The manner of handling and throwing away of the medicine and pre-filled pen must be in accordance with local requirements. Pregnant healthcare personnel should not handle and/or administer Methotrexate.

Methotrexate should not come into contact with the surface of the skin or mucosa. In the event of contamination, the affected area must be rinsed immediately with plenty of water.

**If you use more Methotrexate than you should**

If you use more Methotrexate than you should, talk to your doctor immediately.

**If you forget to use Methotrexate**

Do not take a double dose to make up for a forgotten dose.

**If you stop using Methotrexate**

If you stop using Methotrexate, talk to your doctor immediately.

If you have the impression that the effect of Methotrexate is too strong or too weak, talk to your doctor or pharmacist.

## 4. POSSIBLE SIDE EFFECTS

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

The frequency as well as the degree of severity of the side effects depends on the dosage level and the frequency of administration. As severe side effects may occur even at low dosage, it is important that you are monitored regularly by your doctor. Your doctor will do **tests to check for abnormalities** developing in the blood (such as low white blood cells, low platelets, lymphoma) and changes in the kidneys and the liver.

When receiving a new medicine or a new dose of medicine always check that it matches what your doctor has prescribed you. Before using the pen, your healthcare provider should show you or your caregiver how to use it correctly.

## Prepare for your injection

**1. Wash your hands and unpack your pen (Figure C)**

- Wash your hands with soap and water.
- Carefully take the pen out of the carton.

**Do not** remove the protective cap until you are ready to inject.

**Figure C**

**2. Check your pen before use (Figure D)**

Carefully check the name and dose on the pen and verify that you have the correct medication. If you are not able to see well enough, ask someone for assistance.

- Check the expiry date on the label of the pen.
- Do not use the pen if it has expired.
- Check the medicine through the inspection window by turning it upside down or gently shaking it. The medicine inside the pen should look clear and yellow.
  - Do not inject if the solution looks cloudy or discoloured or contains particles.
  - It is normal to see one or more air bubbles. Do not try to remove them.
  - You may see a scale in the window; you do not need to consider that.
- Check that the pen is not damaged and that the cap is firmly on. Do not use the pen if it looks damaged or if the cap has been removed or is not firmly attached.

**If the pen is expired, appears damaged, or does not look as expected, do not use it and contact your healthcare provider.**

Carefully place the pen on a clean flat surface, such as a table before performing the next steps.

**Figure D**

**Tell your doctor immediately** if you experience any of the following symptoms, as these may indicate a serious, potentially life-threatening side effect, which require urgent specific treatment:

- **persistent dry, non-productive cough, shortness of breath and fever;** these may be signs of an inflammation of the lungs [common]
- **spitting or coughing blood;** these might be signs of bleeding from the lungs [not known]
- **symptoms of liver damage such as yellowing of the skin and whites of the eyes;** methotrexate can cause chronic liver damage (liver cirrhosis), formation of scar tissue in the liver (liver fibrosis), fatty degeneration of the liver [all uncommon], inflammation of the liver (acute hepatitis) [rare] and liver failure [very rare]
- **allergy symptoms such as skin rash including red itchy skin, swelling of the hands, feet, ankles, face, lips, mouth or throat (which may cause difficulty in swallowing or breathing) and feeling you are going to faint;** these may be signs of severe allergic reactions or an anaphylactic shock [rare]
- **symptoms of kidney damage such as swelling of the hands, ankles or feet or changes in frequency of urination or decrease (oliguria) or absence of urine (anuria);** these may be signs of kidney failure [rare]
- **symptoms of infections, e.g. fever, chills, achiness, sore throat;** methotrexate can make you more susceptible to infections. Severe infections like a certain type of pneumonia (*Pneumocystis jirovecii pneumonia*) or blood poisoning (sepsis) may occur [rare]
- **symptoms such as weakness of one side of the body (stroke) or pain, swelling, redness and unusual warmth in one of your legs (deep vein thrombosis); this may happen when a dislodged blood clot causes a blockage of a blood vessel** (thromboembolic event) [rare]
- **fever and serious deterioration of your general condition, or sudden fever accompanied by a sore throat or mouth, or urinary problems;** methotrexate can cause a sharp fall in certain white blood cells (agranulocytosis) and severe bone marrow suppression [very rare]
- **unexpected bleeding, e.g. bleeding gums, blood in the urine, vomiting blood or bruising,** these can be signs of a severely reduced number of blood platelets caused by severe courses of bone marrow depression [very rare]
- **symptoms such as severe headache often in combination with fever, neck stiffness, feeling sick, vomiting, disorientation and sensitivity to light** may indicate an inflammation of the membranes of the brain (acute aseptic meningitis) [very rare]
- certain brain disorders (encephalopathy/leukoencephalopathy) have been reported in cancer patients receiving methotrexate. Such side effects cannot be excluded when methotrexate therapy is used to treat other diseases. Signs of this kind of brain disorders may be **altered mental state, movement disorders (ataxia), visual disturbances or disturbances of memory [not known]**
- **severe skin rash or blistering of the skin (this can also affect your mouth, eyes and genitals);** these may be signs of conditions called Stevens Johnson syndrome or burned skin syndrome (toxic epidermal necrolysis/Lyell's syndrome) [very rare]

In the following, please find the other side effects that may occur:

- Very common:** may affect more than 1 in 10 people
- Inflammation of the mouth lining, indigestion, feeling sick, loss of appetite, abdominal pain.
  - Abnormal liver function test (ASAT, ALAT, bilirubin, alkaline phosphatase).

**Common:** may affect up to 1 in 10 people

- Mouth ulcers, diarrhoea.
- Rash, reddening of the skin, itching.
- Headache, tiredness, drowsiness.
- Reduced blood cell formation with decrease in white and/or red blood cells and/or platelets.

**Uncommon:** may affect up to 1 in 100 people

- Throat inflammation.
- Inflammation of the bowels, vomiting, inflammation of pancreas, black or tarry stools, gastrointestinal ulcers and bleeding.
- Sunburn-like reactions due to increased sensitivity of the skin to sunlight, loss of hair, increased number of rheumatic nodules, skin ulcer, shingles, inflammation of blood vessels, herpes-like skin rash, hives.
- Onset of diabetes mellitus.
- Dizziness, confusion, depression.
- Decrease in serum albumin.
- Decrease in the number of all blood cells and platelets.
- Inflammation and ulcer of the urinary bladder or vagina, reduced kidney function, disturbed urination.
- Joint pain, muscle pain, reduction of bone mass.

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

- Inflammation of gum tissue.
- Increased skin pigmentation, acne, blue spots on the skin due to vessel bleeding (ecchymosis, petechiae), allergic inflammation of blood vessels.
- Decreased number of anti-bodies in the blood.
- Infection (incl. reactivation of inactive chronic infection), red eyes (conjunctivitis).
- Mood swings (mood alterations).
- Visual disturbances.
- Inflammation of the sac around the heart, accumulation of fluid in the sac around the heart, obstruction of cardiac filling due to fluid in the sac around the heart.
- Low blood pressure.
- Formation of scar tissue in the lung (pulmonary fibrosis), shortness of breath and bronchial asthma, accumulation of fluid in the sac around the lung.
- Stress fracture.
- Electrolyte disturbances.
- Fever, wound-healing impairment.

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

- Acute toxic dilatation of the gut (toxic megacolon).
- Increased pigmentation of the nails, inflammation of the cuticles (acute paronychia), deep infection of hair follicles (furunculosis), visible enlargement of small blood vessels.
- Pain, loss of strength or sensation of numbness or tingling / having less sensitivity to stimulation than normal, changes in taste (metallic taste), convulsions, paralysis, meningism.
- Impaired vision, non-inflammatory eye disorder (retinopathy).
- Loss of sexual drive, impotence, male breast enlargement, defective sperm formation (oligospermia), menstrual disorder, vaginal discharge.
- Enlargement of lymphatic nodes (lymphoma).
- Lymphoproliferative disorders (excessive growth of white blood cells).

**Not known:** frequency cannot be estimated from the available data

- Increased number of certain white blood cells.
- Nosebleed.
- Proteins in urine.
- Feeling of weakness.
- Bone damage in the jaw (secondary to excessive growth of white blood cells).
- Tissue destruction at injection site.
- Redness and shedding of skin.
- Swelling.

Subcutaneous application of methotrexate is locally well tolerated. Only mild local skin reactions (such as burning sensations, erythema, swelling, discolouration, severe itching, pain) were observed, decreasing during therapy.

**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 Yellow Card Scheme at: [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard) or search for MHRA Yellow Card in the **Google Play** or **Apple App Store**.

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

## 5. HOW TO STORE METHOTREXATE

- Keep out of the sight and reach of children.
- Do not store above 25°C. Do not freeze.
- Keep the pre-filled pen in the outer carton in order to protect from light.
- Do not use Methotrexate after the expiry date which is stated on the pre-filled pen and carton after EXP. The expiry date refers to the last day of that month.
- If your medicine becomes discoloured or if your Methotrexate shows any sign of deterioration or doesn't work properly, take it back to your pharmacist.
- Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

## 6. CONTENTS OF THE PACK AND OTHER INFORMATION

**What Methotrexate contains**

1 pre-filled pen with 0.15 ml solution contains 7.5 mg methotrexate.

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

**What Methotrexate looks like and contents of the pack**

Methotrexate is a pre-filled pen containing a clear, yellow-brown solution.

Methotrexate pre-filled pen is a two-step auto-injector with a translucent protective cap and a blue needle cover

Methotrexate is available in packs of 1 pre-filled pen.

Manufactured by medac Gesellschaft für klinische Spezialpräparate mbH, Theaterstr. 6, 22880 Wedel, Germany.

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Leaflet dated 28<sup>th</sup> May 2025

Leaflet coded xxxxxxxxxx

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### 3. Choose your injection site (Figure E)

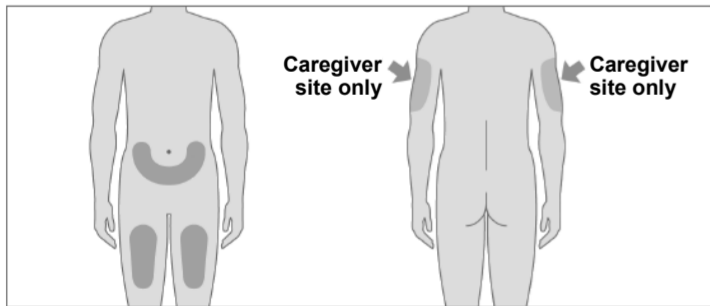


Figure E

- You can inject yourself into your:
  - upper thighs,
  - lower part of the abdomen except within 5 cm around the belly button.
- If a caregiver administers the injection for you, the person may also use the area at the back of the upper arm.
- Use a different site than for your last injection.

When selecting an injection site:

**Do not** inject into other parts of the body.  
**Do not** inject into skin that is bruised, tender, scaly, red or hard.  
**Do not** inject into moles, scars or stretch marks.  
**Do not** inject through clothing.

### 4. Clean your injection site (Figure F)

- Clean your injection site with alcohol disinfection; if not available you may use water and soap.
- Allow the skin to air dry.

**Do not** fan or blow on the clean area.

**Do not** touch your injection site again until you have finished your injection.



Figure F

### Inject your dose

#### 5. Remove the cap (Figure G)

Only remove the protective cap when you are ready to inject.

**Do not** try to put the cap back on the pen once it is removed.

- Hold the pen with the cap pointing upwards and firmly pull the cap straight off.

**Do not** bend or twist the cap while pulling off.

- Dispose of the cap right away.
- You may notice small droplets of the medicine. This is normal.
- Perform your injection immediately after removing the cap.

**Do not** touch the blue needle cover with your fingers. Touching the blue needle cover may accidentally trigger the injection and cause injury.

#### 6. Position your pen (Figure H)

- Position the uncapped blue needle cover at a 90 degree angle against the skin with the inspection window facing towards you so you can see it.
- You may feel more comfortable when grabbing a skin pinch by gently squeezing the area around the injection site with your thumb and forefingers before injecting, but this is not necessary for this pen.

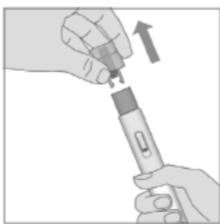


Figure G

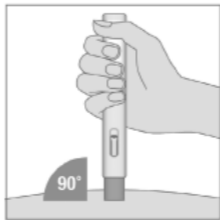


Figure H

#### 7. Start your injection (Figure I)

- To start your injection, push the pen down all the way. This will slide the blue needle cover up into the pen and the injection will start automatically.
- A first "click" hereby indicates the start of the injection. The blue plunger rod will move down.
- Keep holding the pen against the skin until all of the medicine is injected.

**Do not** change the position of the pen once the injection has started.

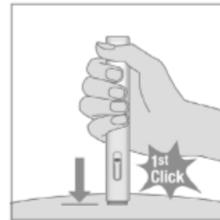


Figure I

#### 8. Hold the pen in place to complete your injection (Figure J)

- Continue holding the pen down against your skin.
- Your injection is complete when either:
  - you hear a second "click", shortly after the first
  - or: the blue plunger rod has stopped moving and fills the inspection window
  - or: 5 seconds have passed.

**Do not** remove the pen until at least 5 seconds have passed.

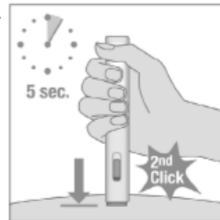


Figure J

#### 9. Finishing your injection (Figure K)

- Remove the pen by pulling it straight up from the injection site.
- The blue needle cover automatically moves into place over the needle. The blue needle cover is then locked.
- Check the inspection window for any leftover yellow medicine inside.

If you still see yellow medicine inside the window you may not have received the full dose. If this happens or if you have any other concerns, contact your healthcare provider.

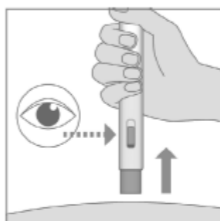


Figure K

**Do not** touch the blue needle cover after injection. This may cause injury.

### After your injection

#### 10. Treat your injection site (Figure L)

- You may notice a small drop of blood at the injection site. This is normal. Press a cotton ball or gauze on the area, if necessary.
- If needed, cover the injection site with a small bandage.

**Do not** rub your injection site.



Figure L

#### 11. Dispose of your pen (Figure M)

Each pen can only be used once.

**Do not** recap the pen.

**Keep your used pen and protective cap out of the sight and reach of children.**

- Dispose of the cap and your pen right away after use.

The manner of throwing away the medicine and the pre-filled pen must be in accordance with local requirements.

- Throw away the used supplies in your household trash. The paper carton can be recycled.

**Safely dispose of Methotrexate pre-filled pens that are expired, no longer needed, or otherwise unusable.**

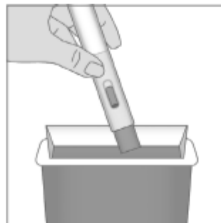


Figure M