

- **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.
- Increased sensitivity to light, 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 pens in the outer carton in order to protect from light.
- Do not use this medicine after the expiry date stated on the carton and pre-filled pen after EXP. The expiry date refers to the last day of that month.
- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.
- If your pre-filled pen shows any signs of deterioration, consult your doctor or pharmacist who will tell you what to do.

#### 6. Contents of the pack and other information

##### What Metoject PEN contains

- The active substance is methotrexate. 1 pre-filled pen with 0.25 ml solution contains 12.5 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

One pre-filled pen containing a clear, yellow-brown solution in pre-filled glass syringe with chlorobutyl rubber plunger stopper and embedded injection needle.

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

##### Product Licence holder

Procured from within the EU and repackaged by the Product Licence holder: S&M Medical Ltd., Chemilines House, Alperton Lane, Wembley, HA0 1DX.

##### Manufacturer

This product is manufactured by medac Gesellschaft für klinische Spezialpräparate mbH, Theaterstr. 6, 22880 Wedel, Germany.

**POM** PL: 19488/1798

Leaflet revision date: **04 September 2025**

## Blind or partially sighted? Is this leaflet hard to see or read? Call 02087997607 to obtain the leaflet in large print, tape, CD or Braille.

*Metoject® is a registered trade mark of medac Gesellschaft für klinische Spezialpräparate mbH, Germany.*

S1798 Leaflet Metoject Pen 12.5mg 20250904

S1798 Leaflet Metoject Pen 12.5mg 20250904

### Package leaflet: Information for the user Metoject® PEN 12.5 mg solution for injection in pre-filled pen (methotrexate)

Your medicine is known as above names but will be referred to as Metoject PEN throughout the following patient information leaflet.

Please note that Metoject PEN is also available in other strengths than those listed above.

#### 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.

#### 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.

#### Instructions for Use

##### Recommendations

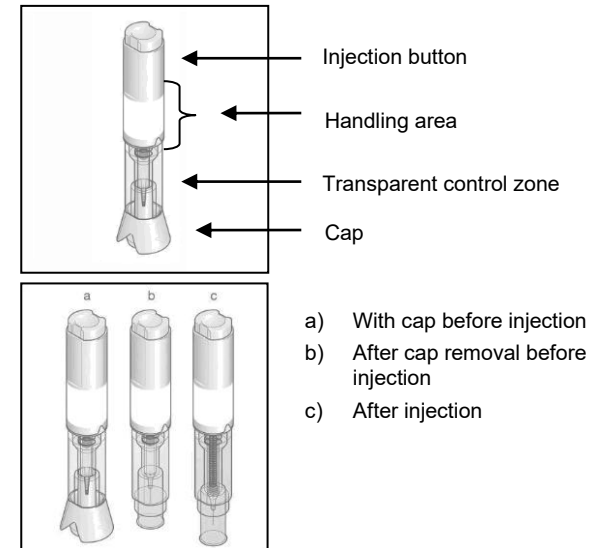
- Carefully read the instructions below before starting your injection.
- Always use the injection technique advised by your doctor, pharmacist or nurse.

##### 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.

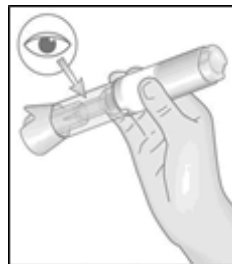
Methotrexate should not come into contact with the surface of the skin or mucosa. In the event of contamination, the affected area must be rinsed immediately with plenty of water.

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



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:



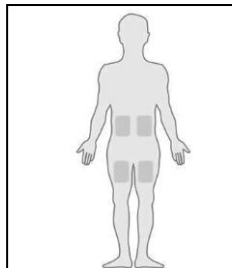
If the Metoject PEN pre-filled pen appears to be damaged **do not use it**. Use another one and contact your doctor, pharmacist or nurse.

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



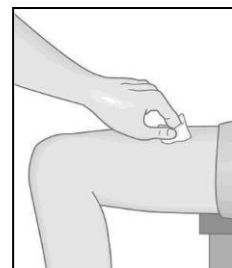
The most appropriate zones for your injection are:

- 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.

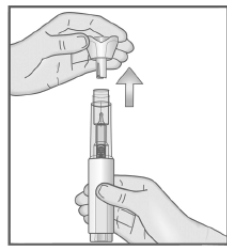
- Change the injection area with each injection. This will minimise any reactions at the injection site.

- Never inject into areas where the skin is tender, bruised, red or hard or where you have 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.

##### How to prepare the injection



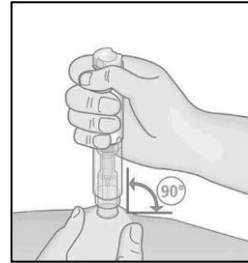
5. Choose an injection site and clean the area of and around the chosen injection site.



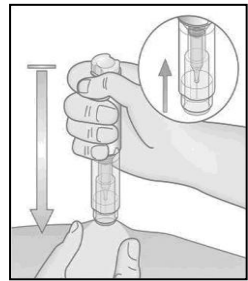
- Do not remove the cap before you are ready to administer the injection.
- Hold the pen with one hand in the handling area with the cap pointing upwards. Use your other hand to gently pull the cap straight off (do not bend or twist the cap). The cap has a small needle shield that should come off with 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.**

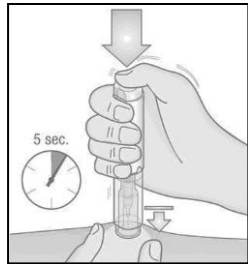


- With your free hand, build a skin fold by gently squeezing the area of the cleaned skin at the injection site.
  - The fold must be held pinched until the Metoject PEN pre-filled pen is removed from the skin after the injection.



- Position the uncapped transparent end of Metoject PEN pre-filled pen perpendicular to the fold of skin.
- 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:



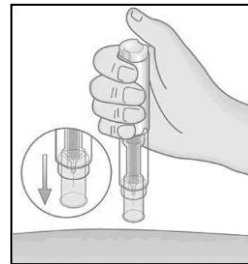
- While holding the Metoject PEN pre-filled pen firmly against the skin, **now press the button** with your thumb.
- You will hear a click which indicates the start of the injection. Keep holding the pen against the raised skin until all of the medicine is injected. This can take up to **5 seconds**.

#### 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.



- Remove the Metoject PEN pre-filled pen from the injection site, perpendicular to the skin (pull up).
- The protective shield automatically moves into place over the needle. The protective shield is then locked and the needle is protected.
- 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.

#### Product Licence holder

Procured from within the EU and repackaged by the Product Licence holder: S&M Medical Ltd., Chemilines House, Alperton Lane, Wembley, HA0 1DX.

Leaflet revision date: 04 September 2025

**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.**

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 ceftalotin (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).
- 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-sulphamethoxazole (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.

#### 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.
- Increased sensitivity to light, 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 Metex PEN

- **KEEP OUT OF THE SIGHT AND REACH OF CHILDREN.**
- Do not store above 25°C.
- Keep the pre-filled pens in the outer carton in order to protect from light.
- Do not use this medicine after the expiry date stated on the carton and pre-filled pen after EXP. The expiry date refers to the last day of that month.
- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.
- If your pre-filled pen shows any signs of deterioration, consult your doctor or pharmacist who will tell you what to do.

#### 6. Contents of the pack and other information

##### What Metex PEN contains

- The active substance is methotrexate. 1 pre-filled pen with 0.25 ml solution contains 12.5 mg methotrexate.
- The other ingredients are sodium chloride, sodium hydroxide and hydrochloric acid for pH adjustment and water for injections.

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

One pre-filled pen containing a clear, yellow-brown solution in pre-filled glass syringe with chlorobutyl rubber plunger stopper and embedded injection needle.

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

##### Product Licence holder

Procured from within the EU and repackaged by the Product Licence holder: S&M Medical Ltd., Chemilines House, Alperton Lane, Wembley, HA0 1DX.

##### Manufacturer

This product is manufactured by medac Gesellschaft für klinische Spezialpräparate mbH, Theaterstr. 6, 22880 Wedel, Germany.

**POM**

PL: 19488/1798 Metex<sup>®</sup> PEN 12.5 mg solution for injection in pre-filled pen

Leaflet revision date: 04 September 2025

## Blind or partially sighted? Is this leaflet hard to see or read? Call 02087997607 to obtain the leaflet in large print, tape, CD or Braille.

*Metex<sup>®</sup> is a registered trade mark of medac Gesellschaft für klinische Spezialpräparate mbH, Germany.*

S1798 Leaflet Metex Pen 12.5mg 20250904

S1798 Leaflet Metex Pen 12.5mg 20250904

#### Package leaflet: Information for the user

### Metex<sup>®</sup> PEN 12.5 mg solution for injection in pre-filled pen (methotrexate)

Your medicine is known as above names but will be referred to as Metex PEN throughout the following patient information leaflet.

Please note that Metex PEN is also available in other strengths than those listed above.

#### 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.

#### What is in this leaflet

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

#### 1. What Metex PEN is and what it is used for

Metex 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.

Metex 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 Metex PEN

##### Do not use Metex 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 Metex 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.

#### Instructions for Use

##### Recommendations

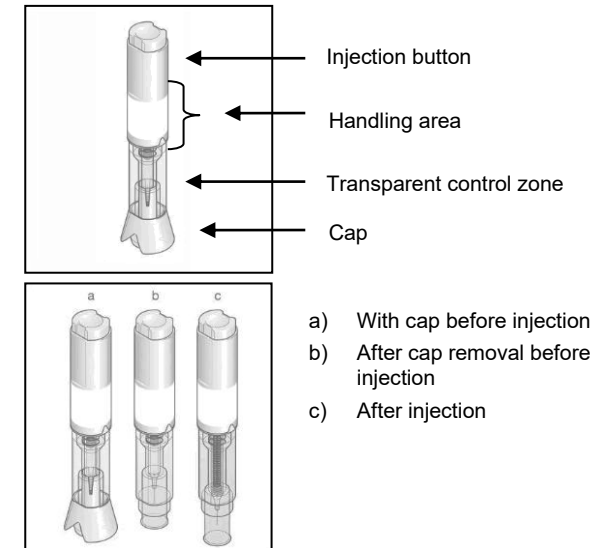
- Carefully read the instructions below before starting your injection.
- Always use the injection technique advised by your doctor, pharmacist or nurse.

##### 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 Metex PEN.

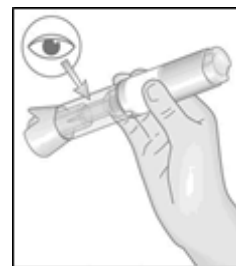
Methotrexate should not come into contact with the surface of the skin or mucosa. In the event of contamination, the affected area must be rinsed immediately with plenty of water.

##### Metex PEN pre-filled pen components:



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 Metex PEN pre-filled pen before using it:



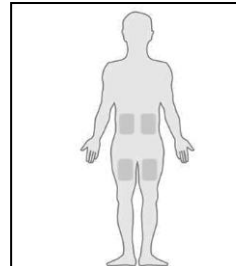
If the Metex PEN pre-filled pen appears to be damaged **do not use** it. Use another one and contact your doctor, pharmacist or nurse.

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 Metex PEN pre-filled pen on a clean flat surface (such as a table).

##### Where you should administer the injection



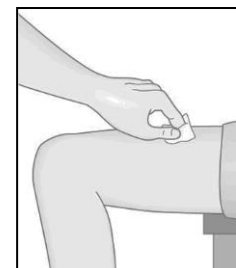
The most appropriate zones for your injection are:

- 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.

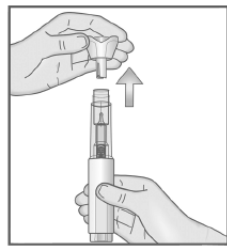
- Change the injection area with each injection. This will minimise any reactions at the injection site.

- Never inject into areas where the skin is tender, bruised, red or hard or where you have 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.

##### How to prepare the injection



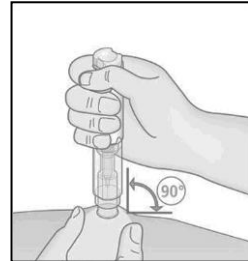
5. Choose an injection site and clean the area of and around the chosen injection site.



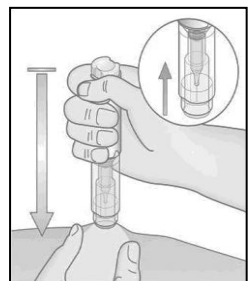
- Do not remove the cap before you are ready to administer the injection.
- Hold the pen with one hand in the handling area with the cap pointing upwards. Use your other hand to gently pull the cap straight off (do not bend or twist the cap). The cap has a small needle shield that should come off with 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.**

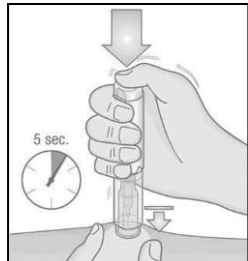


- With your free hand, build a skin fold by gently squeezing the area of the cleaned skin at the injection site.
  - The fold must be held pinched until the Metex PEN pre-filled pen is removed from the skin after the injection.



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

#### How to administer the injection:



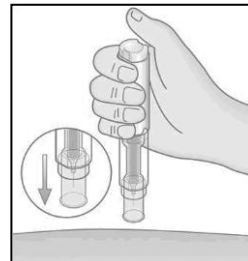
- While holding the Metex PEN pre-filled pen firmly against the skin, **now press the button** with your thumb.
- You will hear a click which indicates the start of the injection. Keep holding the pen against the raised skin until all of the medicine is injected. This can take up to **5 seconds**.

#### Note:

Do not remove the Metex 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 Metex 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 Metex PEN pre-filled pen from the injection site.



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

Before throwing away the Metex 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 Metex PEN pre-filled pen.

#### Product Licence holder

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Leaflet revision date: **04 September 2025**

#### Special precautionary measures for treatment with Metex 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 Metex PEN you must not be vaccinated with live vaccines.**

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 Metex 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 Metex 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 Metex 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).

- 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-sulphamethoxazole (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.**

#### Metex 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 Metex PEN.

#### Pregnancy, breast-feeding and fertility

##### Pregnancy

Do not use Metex 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 Metex 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 Metex 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.

#### Metex 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 Metex PEN

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

Use Metex 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 Metex 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.

Metex 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.

**Metex 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

Metex 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 Metex PEN is a long-term treatment.

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

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

#### If you forget to use Metex PEN

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

#### If you stop using Metex PEN

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

If you have the impression that the effect of Metex 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]