

**PART III: CONSUMER INFORMATION**

**PrMETOJECT® SUBCUTANEOUS  
methotrexate injection**

**This leaflet is part III of a three-part "Product Monograph" published when METOJECT SUBCUTANEOUS was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about METOJECT SUBCUTANEOUS. Contact your doctor or pharmacist if you have any questions about the drug.**

**ABOUT THIS MEDICATION**

What the medication is used for:

METOJECT SUBCUTANEOUS belongs to a group of medicines known as immunosuppressants. It is used to treat psoriasis and rheumatoid arthritis.

What it does:

In rheumatoid arthritis, methotrexate acts on the inflammatory cells that cause joint swelling. METOJECT SUBCUTANEOUS therapy is used to control psoriasis and rheumatoid arthritis but it will not cure them. Some normal cells in the body may be affected as well.

Ask your doctor if you have any questions about why it has been prescribed for you.

When it should not be used:

**Do not take METOJECT SUBCUTANEOUS if you:**

- Are allergic to methotrexate or any component of the drug (see What the nonmedicinal ingredients are). Some of the symptoms of an allergic reaction to methotrexate may include rash, itching or hives on the skin, swelling of the face, lips, tongue or other parts of the body, shortness of breath, wheezing or troubled breathing.
- Have any blood disorders including:
  - bleeding from a lack of blood cells called platelets.
  - low iron in the blood (anemia).
- Have an immune system disorder such as AIDS (autoimmune deficiency syndrome) or HIV, the virus which causes AIDS.
- Have an infection.
- Have severe kidney problems.
- Have severe liver disorder.
- Suffer from alcoholism or alcoholic liver disease.
- Have a stomach ulcer.
- Have inflammation and bleeding from the rectum, with abdominal pain and diarrhea (ulcerative colitis).
- Are pregnant (see section "Pregnancy and Fertility").
- Are breastfeeding (see section "Pregnancy and Fertility").

- You are on dialysis
- You are going to receive a general anesthetic called nitrous oxide. It is also known as laughing gas.

What the medicinal ingredient is:

Methotrexate (meth-o-TREX-ate).

What the nonmedicinal ingredients are:

Sodium chloride, sodium hydroxide and water for injection.

What dosage forms it comes in:

METOJECT SUBCUTANEOUS (methotrexate injection) 50 mg/mL (as methotrexate sodium) is available in single-dose pre-filled syringes.

METOJECT SUBCUTANEOUS is available as follows;

- 1 mL syringe with 0.15 mL solution for injection, equivalent to 7.5 mg methotrexate
- 1 mL syringe with 0.2 mL solution for injection, equivalent to 10 mg methotrexate
- 1 mL syringe with 0.25 mL solution for injection, equivalent to 12.5 mg methotrexate
- 1 mL syringe with 0.3 mL solution for injection, equivalent to 15 mg methotrexate
- 1 mL syringe with 0.35 mL solution for injection, equivalent to 17.5 mg methotrexate
- 1 mL syringe with 0.4 mL solution for injection, equivalent to 20 mg methotrexate
- 1 mL syringe with 0.45 mL solution for injection, equivalent to 22.5 mg methotrexate
- 1 mL syringe with 0.5 mL solution for injection, equivalent to 25 mg methotrexate

**WARNINGS AND PRECAUTIONS**

**Serious Warnings and Precautions**

- \* You should not plan to have children while taking METOJECT SUBCUTANEOUS or for a while after stopping treatment. (Talk to your doctor for further details.)
- \* Use a reliable method of birth control to prevent pregnancy.

Before Using This Medicine

Before you begin treatment with METOJECT SUBCUTANEOUS, you should talk to your doctor about the good this medicine will do as well as the risks of using it.

In deciding to use a medicine, the risks of taking the medicine must be weighed against the good it will do. This is a decision you and your doctor will make. For METOJECT SUBCUTANEOUS, the following should be considered:

Allergies:

- Tell your doctor if you have ever had any unusual or allergic reaction to methotrexate.

Pregnancy and Fertility:

- Tell your doctor if you are pregnant or if you plan to have children. Do not use Metoject 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 whilst taking methotrexate from 6 months to one year after treatment is stopped by using reliable contraception throughout this time. 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. Tell your doctor right away if you think you have become pregnant while taking METOJECT SUBCUTANEOUS.
- If you wish to become pregnant you should consult your doctor, who may refer you for specialist advice before the planned start of treatment.
- Methotrexate temporarily affects sperm and egg production. Methotrexate can cause miscarriage and severe birth defects. You must avoid becoming pregnant when using methotrexate and for six months to one year after treatment has stopped.

Male Fertility

- 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 whilst taking methotrexate and from 6 months to one year after treatment is stopped.

Breast-feeding:

- Stop breast feeding prior to and during treatment with METOJECT SUBCUTANEOUS.

Children:

- METOJECT SUBCUTANEOUS is not for use in children.

Older adults:

- Side effects may be more likely to occur in the elderly, who are usually more sensitive to the effects of METOJECT SUBCUTANEOUS.

Other medicines:

- When you are taking METOJECT SUBCUTANEOUS, it is important that your doctor know if you are taking any other prescription or non-prescription medicine. They should also be told if you have ever been treated with x-rays or cancer medicines or if you drink alcohol.

Other medical problems:

The presence of other medical problems may affect the use of METOJECT SUBCUTANEOUS. Tell your doctor if you have any other medical problems, especially:

- Alcohol abuse (or history of)
- Chickenpox (including recent exposure) or Herpes zoster (shingles)
- Colitis
- Disease of the immune system
- Gout (or history of)
- Kidney stones (or history of)
- Infection
- Intestine blockage
- Kidney disease
- If you are dehydrated or have a lot of vomiting, diarrhea, or sweating.
- Liver disease, including hepatitis B and C infection
- Mouth sores or inflammation
- Stomach ulcer

Precautions while using this medicine

It is very important that your doctor check your progress at regular visits to make sure that this medicine is working properly and to check for unwanted effects.

Do not drink alcohol while taking METOJECT SUBCUTANEOUS. Alcohol can increase the chance of liver problems.

Some patients who take METOJECT SUBCUTANEOUS may become more sensitive to sunlight than they are normally. Avoid too much sun exposure and do not use a sunlamp until you see how you react to the sun, especially if you tend to burn easily.

You should not receive certain vaccinations while taking METOJECT SUBCUTANEOUS. Discuss this with your doctor. Avoid anyone who has had oral polio vaccine for at least six weeks. Do not get close to them or stay in the same room for very long. If this is not possible, wear a mask over your nose and mouth.

Some side effects such as dizziness and fatigue may affect the ability to drive or operate machinery. These activities should be avoided. If you have any concerns, please consult your doctor.

METOJECT SUBCUTANEOUS can lower the number of white blood cells in your blood temporarily, increasing the chance of getting an infection. It can also lower the number of platelets, which are necessary for proper blood clotting. If this happens, there are certain precautions you can take, especially when your blood count is low to reduce the risk of infection or bleeding:

- If you can, avoid people with infections. Check with your doctor immediately if you think you are getting an infection or if you get a fever or chills, cough or hoarseness, lower back or side pain, or painful or difficult urination.
- Check with your doctor immediately if you notice any unusual bleeding or bruising; black, tarry stools; blood in urine or stools; or pinpoint red spots on your skin.
- Be careful when using a regular toothbrush, dental floss, or toothpick. Check with your doctor before having any dental work done.
- Do not touch your eyes or the inside of your nose unless you have just washed your hands.
- Be careful not to cut yourself when you are using sharp objects such as scissors or a razor.
- Avoid contact sports or other situations where bruising or injury could occur.

Methotrexate can cause sudden bleeding in the lungs. This is called **Pulmonary alveolar haemorrhage**. If you suddenly spit or cough up blood you must go to the hospital right away. You will need emergency care. This occurs in patients with some existing health problems. Some examples are rheumatic disorder (such as pain in your joints) or vasculitis such as swelling in an artery or vein.

### INTERACTIONS WITH THIS MEDICATION

Do not take METOJECT SUBCUTANEOUS if you are going to receive a general anesthetic called nitrous oxide. It is also known as laughing gas. When used together, they can cause:

- Myelosuppression (a condition in which the bone marrow cannot make enough blood cells),
- Mouth sores,
- Inflammation of the mouth,
- Inflammation of the kidneys,
- Damage to the nervous system

Tell your doctor and pharmacist what prescription and non-prescription medications you are taking. METOJECT SUBCUTANEOUS may interact with other medicines such as:

- acetyl salicylic acid (ASA) and other pain killers or nonsteroidal anti-inflammatory drugs (NSAIDs)
- some antibiotics (including penicillins tetracycline, and sulfonamides, and medicines to prevent malaria – pyrimethamine)
- some epilepsy treatments
- some cancer treatments
- some vaccines
- some medicines used to lower your cholesterol (including cholestyramine)
- azathioprine (used to prevent transplant organ rejection)
- cytarabine (used to treat leukemia)
- leflunomide (used to treat rheumatoid arthritis)
- mercaptopurine (used to treat leukemia)
- nitrous oxide anaesthesia
- probenecid (used to treat gout)
- retinoid medicines (used to treat acne)
- sulfonyleureas (used to treat diabetes)
- sulfasalazine (used to treat Crohn's disease, rheumatoid arthritis and ulcerative colitis)
- theophylline (used to treat asthma)
- the vitamin folic acid
- phenytoins
- proton pump inhibitors (PPI). They are drugs used to treat acid related stomach problems. Some PPIs are omeprazole, esomeprazole, and pantoprazole.
- amiodarone (used to treat irregular heart beat)
- triamterene (diuretic or “water pill”)
- PUVA therapy (used to treat skin conditions)

It is very important to tell your doctor about all other medicines you are taking including those you buy without a prescription. You may need to receive different amounts of your medicine or you may need to receive different medicines.

Tell any doctor that is treating you that you are taking METOJECT SUBCUTANEOUS.

If you have not told your doctor or pharmacist about any of the above, tell them before you are given METOJECT SUBCUTANEOUS.

### PROPER USE OF THIS MEDICATION

Take METOJECT SUBCUTANEOUS only as directed by your doctor. Do not take more or less of it, and do not take it more often than your doctor ordered. The exact amount of medicine you need has been carefully worked out. Taking

too much may increase the chance of side effects, while taking too little may not improve your condition.

The dose is given **once a week** only. It is given by your health care professional.

Each METOJECT SUBCUTANEOUS syringe can be used only one time.

While you are using METOJECT SUBCUTANEOUS, your doctor may want you to drink extra fluids so that you will pass more urine. This will help the drug to pass from the body, and will prevent kidney problems and keep your kidneys working well.

METOJECT SUBCUTANEOUS commonly causes nausea and vomiting. Even if you begin to feel ill, do not stop using this medicine without first checking with your doctor. Ask your doctor for ways to lessen these effects.

Always keep the syringe out of the reach of children.

Usual adult dose:

The dose of METOJECT SUBCUTANEOUS will be different for different patients. The dose that is used may depend on a number of things, including what the medicine is being used for, the patient's size, and whether or not other medicines are also being taken. If you have any questions about the proper dose of METOJECT SUBCUTANEOUS, ask your doctor.

The doctor may decrease your dose if you have problems with your kidneys.

Overdose

In case of a drug overdose, contact a healthcare professional, hospital emergency department or regional poison control centre, even if there are no symptoms. Always take the labeled medicine with you, even if it is empty.

Missed Dose

- If you missed a scheduled dose, or have any doubts or concerns about missed doses, contact your doctor for instruction

**SIDE EFFECTS AND WHAT TO DO ABOUT THEM**

Along with their needed effects, medicines like METOJECT SUBCUTANEOUS can sometimes cause unwanted effects. Also, because of the way these medicines act on the body, there is a chance that they might cause other unwanted effects that may not occur until months or years after the medicine is used. These delayed effects may

include certain types of cancer, such as leukemia. Discuss these possible effects with your doctor.

The most common side effects include:

- Upset stomach, stomach pain, vomiting, nausea, loss of appetite, dizziness, chills and fever, diarrhea or sores on lips or mouth.
- A fall in the number of white blood cells. This may reduce your resistance to infection and increase your chances of cold sores, blood poisoning or swelling of blood vessels.

Less common side effects are:

- Headaches, hair loss, mood changes, confusion, ringing in the ears, sore eyes, skin rashes.
- A fall in the number of other blood cells. This may increase your chances of bruising, bleeding or tiredness.
- Damage to the lungs.
- Harm to the unborn baby.

Rarely and generally at higher doses for treatment of other diseases, METOJECT SUBCUTANEOUS can cause other side effects including:

- Liver damage, kidney damage, pain or difficulty urinating, lower back or side pain, blood in urine or stools, dark urine
- Fits, blurred vision, short term blindness
- Drowsiness, weakness
- Hoarseness
- Bloody vomit, black tarry stools or pin-point red spots on the skin
- Reddening or whitening of the skin, acne, boils, itching yellow skin or eyes
- Impotence or loss of interest in sex, decreased fertility, abortion
- Diabetes, thinning of the bones, painful muscles and joints

More rarely, it can cause:

- Skin rash and other skin disorders.
- Cancer of lymph glands, sudden death.
- Severe allergic reactions.
- Lymphoproliferative disorders (excessive growth of white blood cells).

Although the frequency is unknown, it can cause:

- Bone damage in the jaw (secondary to excessive growth of white blood cells).
- Bleeding from the lungs.

Methotrexate can cause abnormal test results. Your doctor will decide when to perform tests and will interpret the results. This includes blood and urine tests to check how your kidneys are working.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM				
Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and seek immediate medical help
		Only if severe	In all cases	
Common	Diarrhea or mouth ulcers		√	
	Sore throat, fever, chills, or swelling of glands		√	
	<b>Inflammation of the lungs:</b> Persistent dry, non-productive cough, shortness of breath and fever.		√	
Less common	Chest pain, cough, shortness of breath or fever		√	
	Unusual bleeding or bruising		√	
Rare	Signs of severe allergic reaction: Skin rash, itching, chest tightness, wheezing, dizziness, hives, faintness, rapid heartbeat, shortness of breath, and/or a swollen face, lips or tongue			√

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM				
Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and seek immediate medical help
		Only if severe	In all cases	
	Pain or difficulty urinating, lower back or side pain, blood in urine or stools, dark urine		√	
	<b>Renal Failure/ kidney damage (inability of the kidneys to work properly):</b> swelling of the hands, ankles or feet. Nausea, vomiting. Blood in the urine. Changes in frequency or amount of urine.			√
Unknown	<b>Pulmonary alveolar haemorrhage:</b> suddenly spit or cough up blood			√

*This is not a complete list of side effects. For any unexpected effects while taking METOJECT SUBCUTANEOUS, contact your doctor or pharmacist.*

#### HOW TO STORE IT

- Store METOJECT SUBCUTANEOUS between 15-25°C. Any unused solution should be discarded.
- Keep out of the reach and sight of children.
- Store it at room temperature and away from heat and direct light. Avoid freezing.
- Do not keep outdated medicine or medicine no longer needed. Be sure that any discarded medicine is out of the reach and sight of children.

### **Reporting Side Effects**

You can report any suspected side effects associated with the use of health products to

Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<http://www.hc-sc.gc.ca/dhpmps/medeff/report-declaration/index-eng.php>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

*NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.*

### **MORE INFORMATION**

This document plus the full product monograph, prepared for health professionals can be found by contacting the sponsor, Medexus Inc. at: 1-877-MEDEXUS

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