

## PART III: CONSUMER INFORMATION

### **Pr**ACH-METHOTREXATE Methotrexate Tablets USP

Read this carefully before you start taking ACH-METHOTREXATE and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about ACH-METHOTREXATE.

### **ABOUT THIS MEDICATION**

#### **What the medication is used for:**

ACH-METHOTREXATE belongs to a group of medicines known as antimetabolites. It is used to treat certain types of cancers, severe psoriasis and severe rheumatoid arthritis.

#### **What it does:**

ACH-METHOTREXATE works by blocking an enzyme needed by body cells to live. This interferes with the growth of some cells, such as skin cells in psoriasis that are growing rapidly. In rheumatoid arthritis, ACH-METHOTREXATE acts on the inflammatory cells that cause joint swelling. ACH-METHOTREXATE therapy is used to control psoriasis and rheumatoid arthritis but it will not cure them. In cancer, ACH-METHOTREXATE works by blocking an enzyme process in cancer cells so that they cannot grow. Some normal cells in the body may be affected as well.

#### **When it should not be used:**

Do not take ACH-METHOTREXATE if you:

- Are allergic to any component of the drug.
- Have severe kidney problems.
- Are on dialysis.
- Are pregnant. ACH-METHOTREXATE can cause harm to your unborn baby. Women of childbearing potential should not be started on ACH-METHOTREXATE until pregnancy is excluded.
- Are breast feeding.
- Have psoriasis or rheumatoid arthritis and the following:
  - alcoholism (drink excessive alcohol)
  - chronic liver disease
  - immunodeficiency (resistance to infectious diseases is reduced)
  - blood disorders
- 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:**

- Tablets: Lactose Anhydrous, Magnesium Stearate and Pregelatinized Starch

#### **What dosage form it comes in:**

- Tablet: 2.5 mg methotrexate (as methotrexate disodium)

### **WARNINGS AND PRECAUTIONS**

#### **Serious Warnings and Precautions**

ACH-METHOTREXATE should be prescribed by a doctor who is experienced with the use of antimetabolite therapy.

- ACH-METHOTREXATE can cause serious toxic reactions which may result in death.
- ACH-METHOTREXATE can cause birth defect (deformed babies) or death of an unborn baby when used in pregnant women. Pregnant women with psoriasis or rheumatoid arthritis should not take methotrexate.

BEFORE you use ACH-METHOTREXATE, talk to your doctor or pharmacist if you have any of the following conditions:

- have or have had any unusual or allergic reaction to methotrexate
- are pregnant or planning to become pregnant. ACH-METHOTREXATE can cause birth defects (deformed babies) or death of an unborn baby. Both male and female patients must use effective birth control methods all the time while taking ACH-METHOTREXATE and a few months after the last dose of the drug. ACH-METHOTREXATE may cause sterility (infertility), which could be permanent. Be sure to discuss this with your doctor before taking ACH-METHOTREXATE. Tell your doctor right away if you think you have become pregnant while taking ACH-METHOTREXATE.
- are breast-feeding or plan to breastfeed. ACH-METHOTREXATE may cause serious side effects. Do not breastfeed while you are taking the drug
- have kidney disease
- have or have had liver problems, including hepatitis B or hepatitis C infection
- have lung problems
- have problem with your immune system, or infections
- have gastrointestinal problems such as vomiting, diarrhea, mouth sores or inflammation, ulcer, or colitis (ulcer of intestines)
- are dehydrated or have a lot of vomiting, diarrhea, or sweating.
- have a skin disease
- have a neurologic disorder
- drink alcohol

ACH-METHOTREXATE increases sensitivity to sunlight. Avoid sun exposure and do not use a sunlamp while taking this drug.

#### **Precautions While Using This Medicine**

## IMPORTANT: PLEASE READ

- Do not take ACH-METHOTREXATE more than the dose prescribed. ACH-METHOTREXATE can cause serious toxic reactions which may result in death.
- Do not drink alcohol.
- Do not drive a car or operate machinery until you know how ACH-METHOTREXATE affects you since the drug may cause dizziness and fatigue.
- Drink extra fluid to prevent kidney problems.
- Have regular blood tests to reduce the risk of infection or bleeding. ACH-METHOTREXATE can lower the number of white blood cells and there is an increased risk of infection or bleeding.
- Talk to your doctor if you need a vaccination. Live vaccines may cause severe infections. Live vaccines or contact with any individual who has had a live vaccination should be avoided, since your ability to fight an infection (immune system) is decreased while taking ACH-METHOTREXATE.

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

Talk to your healthcare professional about all the medicines you take or have recently taken, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

ACH-METHOTREXATE may interact with the following drugs:

Do not take ACH-METHOTREXATE 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.
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- non-steroidal anti-inflammatory drugs (NSAIDs) and salicylate (acetylsalicylic acid or ASA)
  - Disease Modifying Antirheumatic drugs (DMARDs), such as gold, penicillamine, hydroxychloroquine, or sulfasalazine
  - drugs that may cause harm to the liver (leflunomide, azathioprine, sulfasalazine, retinoid)
  - phenylbutazone
  - phenytoin (to treat seizures)

- probenecid
- amphotericin B (may cause harm to kidneys)
- certain antibiotics such as penicillins, tetracycline, vancomycin, nystatin, neomycin, trimethoprim/sulfamethoxazole, ciprofloxacin, pristinamycin, chloramphenicol
- theophylline
- mercaptopurine
- folic acid or folinic acid
- cytarabine and other chemotherapy agents
- radiotherapy
- L-asparaginase, a drug used to treat cancer
- Proton pump inhibitors (PPI). They are drugs used to treat acid-related stomach problems. Some PPIs are omeprazole, esomeprazole, and pantoprazole.
- Pyrimethamine, an anti-parasitic drug
- Nitrous oxide, an inhaled gas used to prevent pain during medical procedures
- Amiodarone, a drug used to treat abnormal heart rhythms
- Sulfonylureas, drugs used to lower blood sugar levels, aminobenzoic acid, sulfonamides, also known as “sulfa drugs”
- Packed red blood cells, used for blood transfusions
- PUVA therapy, a type of ultraviolet light treatment for severe skin conditions
- Triamterene, a drug used to reduce blood pressure and decrease swelling

The absorption of ACH-METHOTREXATE is reduced by food, particularly milk.

### PROPER USE OF THIS MEDICATION

Take ACH-METHOTREXATE 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. You should check with your doctor if you are not certain how to take the medication.

- **In most cases, ACH-METHOTREXATE is taken once weekly; the prescribed dose is taken on a single day of the week.**
- **In some cases, your healthcare professional may instruct you to take ACH-METHOTREXATE every 12 hours for 3 doses; you should only do this once a week, and should not take more than 3 doses each week.**
- **It should never be taken every day of the week when used to treat psoriasis or rheumatoid arthritis. As well, in most cases of cancer, ACH-METHOTREXATE should not be taken every day of the week.**
- **Taking ACH-METHOTREXATE daily, or in a dose larger than prescribed can result in serious**

**complications, often requiring hospitalization, and sometimes resulting in death. Taking even small doses of ACH-METHOTREXATE daily for less than a week can result in serious consequences, including death.**

- Select a day of the week when you are most likely to remember to take ACH-METHOTREXATE, and take it on that same day each week.
- Each time you refill your prescription, check to see whether the dose and/or the number of tablets you need to take have changed.

ACH-METHOTREXATE is often given together with certain other medicines. If you are using a combination of medicines, make sure that you take each one at the proper time and do not mix them. Ask your doctor or pharmacist to help you plan a way to remember to take your medicines at the right times.

While you are using ACH-METHOTREXATE, 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.

If you vomit shortly after taking a dose of ACH-METHOTREXATE, check with your doctor. You will be told whether to take the dose again or to wait until the next scheduled dose.

#### **Usual dose:**

The dose of ACH-METHOTREXATE 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. The doctor may decrease your dose if you have problems with your kidneys. If you are taking or receiving ACH-METHOTREXATE at home, follow your doctor's orders or the directions on the label. If you have any questions about the proper dose of ACH-METHOTREXATE, ask your doctor.

#### **Overdose:**

If you think you have taken too much ACH-METHOTREXATE, contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

- Do this even if you have no signs of discomfort.
- Always take the labelled medicine bottle with you, even if it is empty.

#### **Missed Dose:**

- If you missed a scheduled dose, contact your doctor for instruction.

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

Along with their needed effects, medicines like ACH-METHOTREXATE can 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.

Methotrexate disodium 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.

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.
- Tiredness (fatigue).

Less common side effects are:

- Headaches, hair loss, mood changes, confusion, ringing in the ears, sore eyes, skin rashes, increased sensitivity to sunlight or unexplained weight loss.
- 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.
- Convulsions.

Rarely, ACH-METHOTREXATE 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.
- Low blood pressure.
- Gastrointestinal ulcers.

More rarely, it can cause:

- Skin rash and other skin disorders
- Cancer of lymph glands, sudden death.
- Severe allergic reactions.
- Leukoencephalopathy.
- Damage to heart.

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 call your doctor or pharmacist
		Only if severe	In all cases	
Common	Diarrhea, vomiting, abdominal pain, 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			√
	Severe headaches			√
Rare	Signs of severe allergic reaction: Skin rash, itching, chest tightness, wheezing, dizziness, hives,			√

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 call your doctor or pharmacist
		Only if severe	In all cases	
	faintness, rapid heartbeat, shortness of breath, and/or a swollen face, lips, or tongue			
	Pain or difficulty urinating, lower back or side pain, blood in urine or stools, dark urine		√	
	Yellow colour of eyes or skin			√
	<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><u>Gastrointestinal Related:</u></b> Severe abdominal pain, tenderness, chills, fever, nausea, vomiting, extreme thirst, difficulty			√

**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 call your doctor or pharmacist
		Only if severe	In all cases	
	passing urine or bowel movement			
	<b><u>Central Nervous System Related:</u></b> Behaviour changes, decreased consciousness, headache, weakness, numbness, vision loss or double vision, seizures, vomiting, loss of memory			√
	<b><u>DRESS (allergic reactions):</u></b> Fever, rash, hives, swelling of eyes, lips or tongue			√
	<b><u>Pulmonary alveolar haemorrhage:</u></b> suddenly spit or cough up blood			√

*This is not a complete list of side effects. For any unexpected effects while taking ACH-METHOTREXATE contact your doctor or pharmacist.*

**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 (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html>) 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.*

**HOW TO STORE IT**

- Keep out of the reach and sight of children.
- Store ACH-METHOTREXATE between 15-30°C and away from heat and direct light. The product should be preserved in well-closed containers.
- 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.

**MORE INFORMATION**

If you want more information about ACH-METHOTREXATE:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Consumer Information by visiting the Health Canada website (<https://health-products.canada.ca/dpd-bdpp/index-eng.jsp>); or by calling the sponsor Accord Healthcare Inc. at 1-866-296-0354.

This leaflet was prepared by  
Accord Healthcare Inc.  
3535 boul. St. Charles suite 704  
Kirkland, QC, H9H 5B9  
Canada

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