

The following **side-effects** have been reported. If any of these cause you problems or if they **last for more than one week**, you should **contact your doctor**.

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

- loss of appetite, feeling sick (nausea), vomiting, abdominal pain, indigestion, inflammation and ulcers of the mouth and throat
- blood test showing raised liver enzymes.

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

- infections
- decrease in white blood cell count which increases the risk of infection, decrease in red cells which can cause anaemia and decrease in platelets which can cause bleeding
- headache, dizziness, tiredness and drowsiness
- inflammation of the lungs (pneumonia) with dry cough, shortness of breath and fever
- eating disorders (anorexia)
- diarrhoea
- mild, red itchy skin rash.

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

- lymphoma (lump in neck, groin or armpits with associated backache, weight loss or night sweats)
- severe allergic reactions
- diabetes

- depression
- dizziness, confusion, seizures
- lung damage
- ulcers and bleeding in the digestive tract
- liver diseases, reduced content of blood proteins
- nettle rash, brown discoloration of the skin, hair loss, increased number of rheumatic nodules, shingles, painful psoriasis, slow wound healing

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

- chickenpox (herpes zoster)
- production of very large red blood cells which leads to tiredness, muscle weakness, weight loss, feeling sick, fast heart beat and tingling or numbness in the hands and feet
- severe vision problems
- mood swings
- inflammation of the heart sac, accumulation of fluid in the heart sac
- weakness and loss of movement, sometimes on one side of the body
- low blood pressure, high blood pressure, blood clots that can lead to strokes
- swelling at the back of the throat, swollen and bleeding gums, swollen tongue, ulcers and bleeding from the bowel, inflamed pancreas
- fatty liver, hepatitis, cirrhosis of the liver, jaundice and serious liver disorders
- tonsillitis, stopping breathing, asthma

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

- viral, fungal or bacterial systemic infections
- serious disorder of bone marrow (anaemia), swollen glands
- hepatitis
- an immune disorder that reduces antibodies that fight infection. Symptoms include pain, unable to sleep, tiredness and feeling depressed and anxious.
- insomnia
- pain, muscle weakness, changes in the sense of taste (metallic taste), inflammation of the membrane lining the brain resulting in paralysis or vomiting, sensation of numbness or tingling/having less sensitivity to stimulation than normal
- mixing words up when speaking and impaired thinking, loss of contact with reality (psychosis), feeling sleepy or tired, tingly sensations in the head, pain in the head caused by swelling, ringing in the ears

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

- pathological change of the white matter of the brain (leukoencephalopathy)
- wide spread cold sores and infections
- haemorrhages and bleeding problems
- bleeding from the lungs (has been reported for methotrexate used in patients with underlying rheumatologic disease)

Methotrexate can reduce the number of white blood cells and therefore weaken your immune defences. If you notice any symptoms of an infection such as fever or a marked worsening in your general state of health or fever with local signs of an infection such as sore throat/inflammation of the throat or mouth or problems passing water, see your doctor immediately. A blood test will be done to check for reduction in the white blood cells (agranulocytosis). It is important to tell your doctor about all the medicines you take.

Methotrexate can cause serious (sometimes life-threatening) side effects. Your doctor will therefore do tests to check for any changes in your blood (such as a low white blood cell count, a low blood platelet count, lymphomas), kidneys or liver.

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

#### 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.

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

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

## 5. How to store Methotrexate Oral Solution

- Keep this medicine out of the sight and reach of children.
- Do not store above 25°C. Do not refrigerate. Store in the original carton in order to protect from light.
- Do not use 3 months after you first open it. Take it back to the pharmacy.
- Do not use this medicine after the expiry date (month, year) which is stated on the label after EXP. The expiry date refers to the last day of that month.
- Do not use methotrexate if you notice anything wrong with the medicine. Talk to your doctor or pharmacist.
- Any unused medicine should be disposed of in accordance with local requirements for cytotoxics.
- 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 to protect the environment.

## 6. Contents of the pack and other information

### What Methotrexate Oral Solution contains

- The active substance is methotrexate disodium. Each ml of oral solution contains 2mg of methotrexate.
- The other ingredients are sodium methyl parahydroxybenzoate (E219), sodium ethyl parahydroxybenzoate (E215), di-sodium hydrogen phosphate dihydrate, citric acid monohydrate (E330), sucralose (E955), raspberry flavour (containing propylene glycol and sulphites) and purified water.

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

Methotrexate is a clear yellow solution. It comes in a brown glass bottle holding 35ml or 65ml of solution with a 10 ml syringe and bottle adaptor.

### The Marketing Authorisation Holder and Manufacturer is

Rosemont Pharmaceuticals Ltd, Yorkdale Industrial Park, Braithwaite Street, Leeds, LS11 9XE, UK.

Tel: + 44 (0) 113 244 1400

This leaflet was last revised in 07/2024.



## Package leaflet: Information for the user

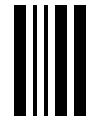
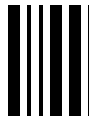
# Methotrexate 2mg/ml Oral Solution

**Read all of this leaflet carefully before you start taking 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, pharmacist or nurse.
- 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, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

### What is in this leaflet:

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



## 1. What Methotrexate Oral Solution is and what it is used for

The full name of your medicine is Methotrexate 2mg/ml Oral Solution. In this leaflet the shorter name methotrexate is used.

Methotrexate belongs to a group of medicines called 'cytotoxics' which are most commonly used to kill cancer cells and tumours. It is also known as an immunosuppressant which affects the reproduction of the body's cells and reduces the activity of the immune system. Methotrexate also has an anti-inflammatory effect.

Methotrexate can be given alone or in combination to treat:

- Severe active rheumatoid arthritis in adults.
- Polyarthritic forms (when five or more joints are affected) of active, severe juvenile idiopathic arthritis (JIA) in adolescents and children aged 3 years and over when the response to non-steroidal anti-inflammatory drugs (NSAIDs) has been inadequate.
- Acute Lymphocytic Leukaemia (ALL) in children over 3 years of age, adolescents and adults
- Malignant trophoblastic tumours
- Severe forms of psoriasis. It is usually used for patients who have tried other treatments but their condition has not improved.

You should consult your doctor if you are unsure why you have been given Methotrexate 2mg/ml Oral Solution.

## 2. What you need to know before you take Methotrexate Oral Solution

### Do not take methotrexate if:

- you are allergic to methotrexate or any of the other ingredients of this medicine (listed in section 6). The signs of an allergic reaction may include swelling of your face, lips, tongue or throat, difficulty breathing or swallowing, severe itching of your skin with raised lumps
- you have severe kidney problems, including conditions requiring kidney dialysis.
- you have severe liver problems
- you suffer from alcoholism or drink alcohol excessively
- you have an active infectious disease (e.g. HIV infection, tuberculosis, any condition causing fever, chills, joint pain)
- you have a medical condition or are receiving medication which lowers your resistance to infection
- you have any serious blood problems including bone marrow disorders, serious anaemia and clotting problems
- swelling or ulcers of the gums and mouth or ulcers in the digestive tract (stomach or gut)
- you are breast-feeding and additionally, for non-oncologic indications (for non-cancer treatment) if you are pregnant (see section 'Pregnancy, breast-feeding and fertility')
- you have been given or are going to be given a live vaccine.

Do not take this medicine if any of the above apply to you. If you are not sure, talk to your doctor or pharmacist before taking methotrexate.

### Warnings and precautions

#### Important warning about the dose of methotrexate:

**This oral solution contains 2 mg methotrexate in 1 ml solution and the scaling of the dosing syringe is in ml and not mg.** Take methotrexate **only once a week** for the treatment of rheumatic or skin diseases (RA, JIA and psoriasis or psoriatic arthritis). Taking too much of methotrexate may be fatal. Please read section 3 of this leaflet very carefully. If you have any questions, please talk to your doctor or pharmacist before you take this medicine.

Methotrexate temporarily affects sperm and egg production. Methotrexate can cause miscarriage and severe birth defects. You should avoid having a baby if you are being given methotrexate at the time and for at least 6 months after the end of your treatment with methotrexate 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".

Talk to your doctor, pharmacist or nurse before taking methotrexate if:

- you have any kidney, lung or liver problems
- you have diabetes
- you are particularly overweight
- you have any blood disorders or anaemia
- you have diarrhoea or have been vomiting as you may be dehydrated which can affect how you react to methotrexate
- you have gastro-intestinal (digestive) problems
- you have or have ever suffered from mental illness
- you have received or you are receiving radiotherapy (x-ray treatment)
- you have received any vaccinations recently or you are due to have any, as methotrexate can reduce their effect
- you have any symptoms or signs of infection or have a weak immune system
- you have excess fluid, between the lungs and chest wall (pleural effusions) or abdominal swelling caused by excess fluid (ascites)
- you have herpes zoster (chicken pox), HIV infection, tuberculosis (TB) or hepatitis B or C.

Methotrexate may make your skin more sensitive to sunlight. Avoid intense sun and do not use sun-beds or a sun-lamp without medical advice. To protect your skin from intense sun, wear adequate clothing or use a sunscreen with a high protection factor. If you had skin problems after radiotherapy (radiation dermatitis) or sunburn, these reactions can recur after methotrexate therapy (recall reaction).

Enlarged lymph nodes (lymphoma) may occur in patients receiving low dose methotrexate and if this is the case, therapy must be stopped.

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.

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

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

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

Psoriasis skin changes can become worse during treatment with methotrexate if you are under UV light.

If any of the above apply to you (or you are not sure), talk to your doctor or pharmacist before taking methotrexate.

### 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 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 tests 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.

#### Children and adolescents

Children and adolescents treated with methotrexate should have particularly careful medical monitoring in order to detect important side effects quickly.

This medicine is not recommended in children under 3 years of age as there is insufficient experience in this age group.

#### Other medicines and Methotrexate

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

This includes medicines obtained without a prescription and herbal medicines. This is because methotrexate can affect the way some other medicines work. Also, some other medicines can affect the way methotrexate works.

In particular tell your doctor or pharmacist if you are taking any of the following:

- live vaccinations
- medicines for pain or inflammation such as aspirin, diclofenac, ibuprofen, indometacin, amidopyrine, pyrazole, phenylbutazone
- metamizole (synonyms novaminsulfon and dipyrone) (medicine against severe pain and/or fever)
- medicines used to treat bacterial infections (antibiotics) such as chloramphenicol, glycopeptides, ciprofloxacin, cefalotin, sulphonamides, co-trimoxazole, trimethoprim/sulfamethoxazole and tetracyclines
- penicillins may reduce the excretion of methotrexate causing a potential increase in side effects
- diuretics, that reduce fluid retention such as bendroflumethiazide or triamterene
- medicines for lowering blood sugar levels such as metformin
- p-aminobenzoic acid and retinoids (such as acitretin), used to treat psoriasis or skin disorders
- adrenocortical steroids, used to treat cutaneous herpes zoster
- medicines used to treat epilepsy such as diphenylhydantoin (phenytoin) and barbiturates such as phenobarbital
- medicines used to treat gout such as probenecid and sulfinpyrazone
- vitamin preparations containing folic acid or similar products
- nitrous oxide (a gas used in general anaesthesia)
- medicines that help you sleep (tranquillisers)
- medicines to treat cancer such as doxorubicin, 5-fluorouracil, cisplatin, l-asparaginase or procarbazine
- blood transfusions
- pyrimethamine, used to treat malaria
- leflunomide, used to treat rheumatoid arthritis
- medicines used to suppress the immune system such as azathioprine, mercaptopurine and ciclosporin
- proton pump inhibitors (such as omeprazole or pantoprazole), used to treat excess stomach acid
- theophylline, used to treat lung problems such as asthma and COPD
- cholestyramine, used to lower cholesterol levels
- sulfasalazine, used to treat ulcerative colitis or rheumatoid arthritis
- oral contraceptive pill, used for contraception.

If any of the above apply to you (or you are not sure), talk to your doctor or pharmacist before taking Methotrexate

#### Taking Methotrexate Oral Solution with food, drink and alcohol

Alcohol should be avoided while receiving methotrexate and you should avoid drinking excessive amounts of coffee, caffeinated drinks and black leaf tea. Ensure that you drink a lot of fluids during treatment with methotrexate because dehydration (the reduction of body water) can increase the side effects of methotrexate.

Methotrexate can be taken with or without food.

When you have taken your dose, drink some water and swallow it to ensure you have taken your full dose and there is no methotrexate left in your mouth.

#### Pregnancy, breast-feeding and fertility

##### Pregnancy

Do not use methotrexate during pregnancy except if your doctor has prescribed it for oncology treatment. 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. It is therefore very important that methotrexate is not given to pregnant women or to women who are planning to become pregnant unless used for oncology treatment.

For non-oncological indications, in women of child-bearing age the possibility of a pregnancy must be ruled out, e.g. by pregnancy tests, before treatment is started.

Do not use methotrexate if you are trying to become pregnant. You must avoid becoming pregnant during treatment with methotrexate and for at least 6 months after the end of treatment. Therefore, you must ensure that you are taking effective contraception for the whole of this period (see also section "Warnings and precautions").

If you become pregnant during treatment or suspect you might be pregnant, speak to your doctor as soon as possible. If you do become pregnant during treatment, you should be offered advice regarding the risk of harmful effects on the child through treatment.

If you want to become pregnant, you should speak with your doctor, who may refer you for specialist advice before the planned start of treatment.

##### Breast-feeding

Methotrexate is excreted in human milk. Because of the potential for serious adverse reactions in infants, breast-feeding must be discontinued before starting treatment.

##### Fertility

- It may affect women's periods; they may become less frequent or stop completely.
- Methotrexate can affect sperm and egg production with the potential to cause birth defects.

##### 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 and there is no information regarding higher methotrexate doses. Methotrexate can have a genotoxic effect. This means that the medicine can cause genetic mutations. Methotrexate can affect the production of sperm, which is associated with the possibility of birth defects.

You should avoid fathering a child or to donate semen during treatment with methotrexate and for at least

3 months after the end of treatment. As treatment with methotrexate at higher doses commonly used in cancer treatment can cause infertility and genetic mutations, it may be advisable for male patients treated with methotrexate doses higher than 30 mg/week to consider sperm preservation before the beginning of treatment (see also section "Warnings and precautions").

#### Driving and using machines

Do not drive, cycle or use any tools or machines until you know how this medicine affects you. This is because you may feel drowsy, you may have a loss of co-ordination and you may get blurred vision. If you feel tired or dizzy, you should not drive a vehicle or use machines. If you are in doubt about whether you can do a particular activity, talk to your doctor or pharmacist.

#### Methotrexate contains sodium methyl parahydroxybenzoate, sodium ethyl parahydroxybenzoate, propylene glycol and sulphites

- Sodium methyl (E219) and ethyl parahydroxybenzoates (E215) - may cause allergic reactions (possibly delayed)
- Propylene Glycol (E1520) - this medicine contains 1.93mg propylene glycol in each 1ml dose
- Sulphites (from the flavour) - these may rarely cause a severe allergic reaction and difficulty breathing
- This medicine contains less than 1 mmol sodium (23mg) per 1ml dose, that is to say essentially 'sodium-free'.

### 3. How to take Methotrexate Oral Solution

#### Important warning about the dose of methotrexate:

Use methotrexate **only once a week** for the treatment of arthritis (including juvenile idiopathic arthritis or JIA) and psoriasis. Using too much of methotrexate may be fatal. Please read section 3 of this leaflet very carefully. If you have any questions, please talk to your doctor or pharmacist before you take this medicine.

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

Methotrexate should be prescribed only by doctors who are familiar with the properties of the medicine and how it works.

The duration of treatment is determined by your doctor. Treatment of rheumatoid arthritis, severe juvenile idiopathic arthritis, severe psoriasis and severe psoriatic arthritis with methotrexate is long-term treatment.

If methotrexate comes into contact with skin, eyes or nose, you should wash the affected area with water and soap.

#### Taking this medicine

- This medicine contains 2 milligram (mg) of Methotrexate in each 1 millilitre (ml) of solution.
- Take this medicine by mouth.
- Patients with rheumatoid arthritis or psoriasis and children with juvenile idiopathic arthritis (JIA) will usually take their medicine orally once a week on the same day each week. Daily administration in non-oncological indications can lead to serious toxic effects.
- Do not take more medicine more often than your doctor has told you to.
- Always use the syringe supplied with the pack, or as directed by your doctor, nurse or pharmacist.
- Methotrexate can be taken with or without food. When you have taken your dose, drink some water and swallow it to ensure you have taken your full dose and there is no methotrexate left in your mouth.
- If you are a parent or care giver administering the medicine, wash your hands before and after administering a dose. Wipe up spillages immediately. To decrease the risk of exposure disposable gloves should be used when handling methotrexate
- Women who are pregnant, planning to be or breastfeeding should not handle methotrexate
- Parents / care givers and patients should be advised to keep methotrexate out of the reach and sight of children, preferably in a locked cupboard. Accidental ingestion can be lethal for children.

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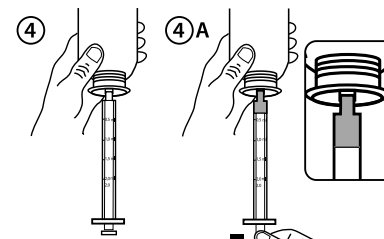
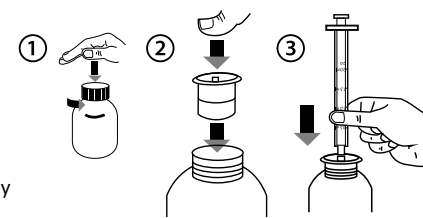
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- Keep the bottle tightly closed to protect the integrity of the product and minimise the risk of accidental spillage.

#### Measuring your dose

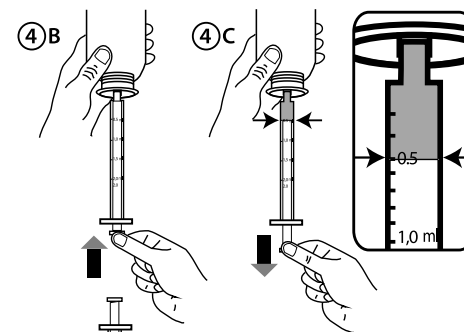
##### Instructions for use

- Open the bottle: press the cap and turn it anticlockwise (Figure 1).
- Separate the syringe adaptor from the syringe and insert the adaptor securely into the bottle neck (Figure 2).
- Take the syringe and put it in the adaptor opening (Figure 3).
- Turn the bottle upside down (Figure 4).
- Fill the syringe with a small amount of solution by pulling the plunger down (Figure 4A). Then push the plunger upward in order to remove any possible bubbles (Figure 4B).



Finally, pull the plunger down to the graduation mark corresponding to the quantity in millilitres (ml) prescribed by your doctor. The top flat edge of the plunger should be in line with the graduation mark you are measuring to (Figure 4C).

- Turn the bottle the right way up (Figure 5A).
- Remove the syringe from the adaptor (Figure 5B).
- Put the end of the syringe into your mouth and push the plunger slowly back in to take the medicine.
- Close the bottle with the plastic screw cap - leave the syringe adaptor in the bottle.
- Wash the syringe with warm 'soapy' water and rinse well. Hold the syringe under water and move the plunger up and down several times to make sure the inside of the syringe is clean. Let the syringe dry completely before you use that syringe again for dosing. Store the syringe in a hygienic place with the medicine (Figure 6).



WASH YOUR HANDS THOROUGHLY with soap and warm water.

#### How much to take

##### Recommended dose:

##### Dose in rheumatoid arthritis

Take methotrexate **only once a week.**

##### Adults

- The usual dose is 7.5mg to 15mg (3.75 - 7.5ml), once a week on the same day each week.
- Your doctor may adjust the dose to suit you according to your response to treatment and side effects.
- If you are elderly, your doctor may give you lower doses.

##### Dose in polyarthritic forms of juvenile idiopathic arthritis

Use methotrexate **once a week.**

##### Children and adolescents:

The doctor will calculate the dose required from the child's body surface area (m<sup>2</sup>), and the dose is expressed as mg/m<sup>2</sup>.

##### Dose in psoriasis

Take methotrexate **only once a week.**

##### Adults and the Elderly

- The usual dose is 10mg to 25mg (5ml - 12.5ml), once a week on the same day each week.
- Your doctor may adjust the dose to suit you according to your response to treatment and side effects.

##### Children and adolescents:

Not recommended for use in children and adolescents.

#### Dosage for treatment of cancer:

##### Adults, the Elderly and Children

- Your doctor should give you a test dose of 5 to 10mg by injection one week before starting treatment.
- The doctor will calculate the dosage required from your body surface area (m<sup>2</sup>), and the dose is expressed as mg/m<sup>2</sup>.
- Methotrexate Oral Solution is usually given as a single dose
  - For malignant tumours, the usual dose is 15mg/m<sup>2</sup> for 5 days
  - For Acute Lymphoblastic Leukaemia the usual dose is 20 - 40mg/m<sup>2</sup>
- A rest period of at least two weeks is advised between treatments, to allow recovery from any side effects.
- Doses in excess of 100mg are usually given by injection by a doctor.
- Doses of more than 70mg/m<sup>2</sup> should not be administered without leucovorin rescue (folinic acid rescue) or blood levels of methotrexate being checked 24 to 48 hours after taking your medicine.
- These doses may be reduced if you are receiving other medication. Your doctor will decide the correct dose for you, if you want more information you should ask your doctor.

#### If you take more Methotrexate than you should

- If you take more methotrexate than you should, talk to your doctor or go to the nearest hospital straight away. Take the medicine pack with you.
- Taking the wrong dose, resulting in overdose, can sometimes lead to death.
- The symptoms of an overdose can include bleeding, an unusual feeling of weakness, ulcers in the mouth, feeling sick, vomiting, black or bloody stools, coughing up blood or vomiting blood with a coffee grounds appearance and reduced urine. See also section 4 "Possible side effects".

#### If you forget to take Methotrexate

- If you forget a dose, skip the missed dose. Then wait until the next dose is due.
- Do not take a double dose to make up for a forgotten dose.

#### If you stop taking Methotrexate

Keep taking this medicine until your doctor tells you to stop. Do not stop taking this medicine just because you feel better.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

### 4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. The following side effects may happen with this medicine:

#### Stop taking methotrexate and see a doctor or go to a hospital straight away if you notice the following serious side effect - you may need urgent medical treatment:

- allergic reaction - the signs may include swelling of your face, lips, tongue or throat, difficulty breathing or swallowing, severe itching of your skin with raised lumps.
- the first signs of life-threatening complications can be: fever, sore throat, mouth ulcers, flu-like symptoms, severe fatigue, nose bleeds and bruising.
- serious heart problems where fluid is filling around the heart affecting the heartbeat
- sepsis, whole body inflammation that can be life-threatening.

#### Tell your doctor straight away if you have any of the following side effects:

- a severe skin rash with blisters and peeling skin, particularly around the mouth, nose, eyes and genitals (Stevens Johnson Syndrome) and a more severe form causing severe skin peeling (Toxic Epidermal Necrolysis). Your doctor will stop your treatment in these cases. This is an uncommon side effect.
- persistent dry irritating cough, pain or difficulty breathing or becoming breathless as methotrexate can cause inflammation of the lungs. Symptoms can also include a general feeling of illness, chest pain or fever.
- spitting or coughing blood (has been reported for methotrexate used in patients with underlying rheumatological disease).
- unusual bleeding (including vomiting blood), black or tarry stools, blood in the urine, bruising or nose bleeds
- skin rash, red or purple spots on the skin, fever and swollen glands, particularly in the first two months of treatment, as these may be signs of a hypersensitivity reaction.
- nausea, vomiting, abdominal discomfort or severe diarrhoea
- pain or difficulty passing urine
- thirst and/or frequent urination
- blurred or restricted vision
- loss of coordination, loss of ability to speak or understand speech, weakness and inability to move one side of the body, or the whole body, severe fatigue (tiredness), unconsciousness, convulsions or fits.
- swelling of the hands, ankles or feet, which may be a sign of kidney damage
- yellowing of the skin and whites of the eye, a sign of liver damage
- rapid expansion of the large intestines (toxic megacolon). Symptoms may come on suddenly and may include: abdominal pain, bloating of the abdomen, abdominal tenderness, fever, rapid heart rate, shock, bloody diarrhoea. This is a very rare side effect.

Continued overleaf