Package leaflet: Information for the user

Jylamvo 2 mg/ml oral solution methotrexate

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 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 Jylamvo is and what it is used for

Jylamvo is a medicine that:
- suppresses the growth of certain cells in the body that multiply rapidly (an anticancer medicine)
- reduces unwanted reactions by the body's own defense mechanisms (an immunosuppressive agent)
- has an anti-inflammatory effect

Jylamvo is used in patients with:
- the following rheumatic and skin diseases:
  - active rheumatoid arthritis (RA) 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
  - severe, treatment-resistant, disabling psoriasis that does not respond sufficiently to other forms of treatment such as phototherapy, psoralen and ultraviolet A radiation (PUVA) therapy and retinoids, as well as in severe psoriasis that also affects the joints (psoriatic arthritis) in adult patients
- acute lymphoblastic leukaemia (ALL) in adults, adolescents and children aged 3 years and over

You must talk to a doctor if you do not feel better or if you feel worse

2. What you need to know before you take Jylamvo

Do not take Jylamvo
- if you are allergic to methotrexate or any of the other ingredients of this medicine (listed in section 6)
- if you have a severe kidney impairment (or your doctor classes the impairment as severe)
- if you have a liver impairment
- if you have blood disorders such as bone marrow hypoplasia, leukopenia, thrombocytopenia or significant anaemia
- if you drink alcohol excessively
- if you have a weakened immune system
- if you are suffering from a serious infection such as tuberculosis or HIV
- if you have ulcers in the stomach or in the intestines
- if you have an inflammation of the mucous membrane of the mouth or mouth ulcers
- if 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”)
- if you have had a live vaccine recently or are about to have one

Warnings and precautions

Important warning about the dose of Jylamvo (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 Jylamvo **only once a week** for the treatment of rheumatic or skin diseases (RA, JIA and psoriasis or psoriatic arthritis).
Taking too much of Jylamvo (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.

Talk to your doctor or pharmacist before taking Jylamvo:
- if you have diabetes mellitus treated with insulin
- if you are suffering from inactive, chronic infections (e.g. tuberculosis, hepatitis B or C, shingles [herpes zoster]) as they may flare up
- if you have ever had any liver or kidney disease
- if you have problems with your lung function
- if you are particularly overweight
- if you have an abnormal build-up of fluid in the abdomen (ascites) or around the lungs (pleural effusions)
- if you are dried out (dehydrated) or suffer from conditions that result in dehydration (vomiting, diarrhoea, constipation, inflammation of the mucous membrane of the mouth)

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 Jylamvo 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).

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.

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

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”.

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.

Children, adolescents and elderly
Children, adolescents and the elderly 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 Jylamvo
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription and herbal or natural medicinal products.
Remember to inform your doctor about the treatment with Jylamvo if you are prescribed another medicine during treatment.

It is especially important to tell your doctor if you are using:
- other medicines for rheumatoid arthritis or psoriasis, such as leflunomide, azathioprine (also used to prevent rejection after an organ transplant), sulfasalazine (also used for ulcerative colitis)
- ciclosporin (for supressing the immune system)
- non-steroidal anti-inflammatory drugs or salicylates (medicines against pain and/or inflammation such as acetylsalicylic acid, diclofenac and ibuprofen or pyrazole)
- live vaccines
- diuretics, that reduce fluid retention
- medicines for lowering blood sugar levels such as metformin
- retinoids (for the treatment of psoriasis and other skin diseases)
- antiepileptic medicines (prevention of seizures)
- barbiturates (sleeping medicines)
- sedatives
- oral contraceptives
- probenecid (for gout)
- antibiotics
- pyrimethamine (for the prevention and treatment of malaria)
- vitamin preparations containing folic acid
- proton pump inhibitors (for the treatment of heartburn, ulcers and some other stomach complaints)
- theophylline (for breathing problems)
- mercaptopurine (for the treatment of certain types of leukaemia)
- cancer treatments (such as doxorubicin and procarbazine during high-dose methotrexate therapy)
- metamizole (synonyms novaminsulfon and dipyrone) (medicine against severe pain and/or fever)
- valproate (for the treatment of epilepsy and bipolar disorders)

Jylamvo with food, drink and alcohol
This medicine 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. You should not drink alcohol during treatment with Jylamvo and should avoid drinking excessive amounts of coffee, caffeinated drinks and black leaf tea. Ensure that you drink a lot of fluids during treatment with Jylamvo because dehydration (the reduction of body water) can increase the side effects of methotrexate.

Pregnancy
Do not use Jylamvo 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 Jylamvo 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
Do not breast-feed during treatment as methotrexate passes into the breast milk. If your doctor considers that continuing treatment with methotrexate is essential, you must stop breast-feeding.

Male Fertility
The available evidence does not indicate an increased risk of malformations or miscarriage if the father takes methotrexate less than 30 mg (15 ml)/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 (15 ml)/week to consider sperm preservation before the beginning of treatment (see also section "Warnings and precautions").

Driving and using machines

Caution: This medicine can affect your capacity to react and your ability to drive.

Side effects affecting the central nervous system such as tiredness or dizziness can occur during treatment with Jylamvo. In some cases the ability to drive or use machines may be affected. If you feel tired or dizzy, you should not drive a vehicle or use machines.

Jylamvo contains ethyl parahydroxybenzoate and sodium methyl parahydroxybenzoate
Ethyl parahydroxybenzoate (E214) and sodium methyl parahydroxybenzoate (E219) may cause allergic reactions (possibly delayed).

3. How to take Jylamvo

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

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

Taking Jylamvo incorrectly can result in severe side effects and even death.

The duration of the treatment is determined by the treating physician. Treatment of rheumatoid arthritis, severe juvenile idiopathic arthritis, severe psoriasis and severe psoriatic arthritis with Jylamvo is a long-term treatment.

Recommended dose
Your doctor will decide what dose of Jylamvo you should take according to the condition you are being treated for, how severe it is and your general health. Keep to the dose exactly and follow your doctor’s instructions exactly on when to take the medicine.

Dose in rheumatic and skin diseases (RA, JIA and psoriasis or psoriatic arthritis)
Take Jylamvo **only once a week.** Decide with your doctor the most suitable day of the week to take the medicine.

Dosage in adult rheumatoid arthritis:
The usual initial dose is 7.5 mg (3.75 ml), once a week.

Dosage for psoriasis and psoriatic arthritis:
The usual initial dose is 7.5 mg (3.75 ml), once a week.

The doctor may increase the dose if the used dose is not effective but tolerated well.
Your doctor may adjust the dose to suit you according to your response to treatment and side effects.

Dose in acute lymphoblastic leukaemia (ALL)
Your doctor will tell you what dose you should take for your condition and when you should take the dose. Keep to this dose exactly.

Use in children and adolescents
The doctor will calculate the dose required from the child's body surface area (m^2), and the dose is expressed as mg/m^2.

Elderly
Because of the reduced liver and kidney function and the lower folate reserves in elderly patients, a relatively low dosage should be chosen for them.

How to take the medicine
Your pack of Jylamvo contains a bottle of medicine with a cap, a bottle adaptor and a white dosing syringe. Always use the syringe provided to take your medicine.

If you are a parent or caregiver giving the medicine, wash your hands before and after giving a dose. Wipe up spillages immediately. For protection, you should wear disposable gloves when handling Jylamvo.

Women who are pregnant, planning to be or breast-feeding should not handle methotrexate.

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

Jylamvo is for oral use and provided ready for use.

Please note that this oral solution contains 2 mg methotrexate in 1 ml solution and that the scaling of the dosing syringe is in ml and not mg.

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.

When you use the medicine follow the instructions below:
1. Put on disposable gloves before handling.
2. Shake the bottle.
3. Remove the bottle cap and push the adaptor firmly into the top of the bottle.
4. Push the tip of the dosing syringe into the hole in the adaptor.
5. Turn the bottle upside down.
6. Pull the syringe plunger back SLOWLY so that the medicine is drawn from the bottle into the syringe until the WIDEST part of the white syringe plunger is lined up to the black syringe marking of the dose required. DO NOT measure to the narrow tip of the plunger. If there are air bubbles in the syringe, repeat until bubbles are eliminated.
7. Turn the bottle back the right way up and carefully remove the syringe from the adaptor, holding the syringe by the barrel rather than the plunger.
8. Confirm that the dose in the syringe is correct.
9. Ensure that the patient is sitting up or standing before giving the medicine.
10. Gently place the tip of the syringe into the patient's mouth and direct it to the inside of the cheek.
11. Slowly and gently push the plunger down to gently squirt the medicine into the inside of the cheek. DO NOT push down the plunger too hard or squirt the medicine to the back of the mouth or throat as this may cause choking. The plunger should be pushed back gently to the seated position until it clicks into place.
12. Remove the syringe from the patient's mouth.
13. Ask the patient to swallow the medicine and then to drink some water, making sure no medicine is left in the mouth.
14. Put the cap back on the bottle with the adaptor left in place. Ensure that the cap is tightly closed.
15. Wash the syringe immediately after use with fresh warm, 'soapy' water and rinse well. The syringe should be held under water and the plunger drawn in and out several times until all traces of medicine are removed from inside the syringe including the tip. The plunger and barrel should then be separated and both washed thoroughly in the warm soapy water. They should then be rinsed thoroughly under COLD water and excess water shaken off before wiping dry with a clean paper towel. The plunger and barrel should be stored in a clean dry container with the medicine and reassembled before next use. All parts of the syringe should be completely dry before using it for the next dose.

Repeat the above instructions for each dose, as instructed by your doctor or pharmacist.

If you take more Jylamvo than you should
Follow your doctor's dose recommendations. Never change the dose on your own.

If you suspect that you (or someone else) have (has) taken too much Jylamvo, tell your doctor immediately or contact the nearest hospital casualty department. The doctor will decide whether any treatment is needed.

An overdose of methotrexate can cause serious reactions. 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 a reduced urine. See also section 4 "Possible side effects".

Take the medicine pack with you when you visit your doctor or the hospital.
The antidote in the event of an overdose is calcium folinate.

If you forget to take Jylamvo
Never take a double dose to make up for a forgotten dose but continue with the prescribed dose. Ask your doctor for advice.

If you stop taking Jylamvo
Do not interrupt or stop the treatment with Jylamvo without first discussing this with your doctor. If you suspect you have a severe side effect, talk to your doctor immediately.

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

4. Possible side effects

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

Tell your doctor immediately if you suddenly get wheeziness, difficulty in breathing, swelling of the eyelids, face or lips, rash or itching (especially affecting your whole body).

Contact your doctor immediately if you develop any of the side effects listed below:

- breathing problems (these include a general feeling of illness, dry, irritating cough, shortness of breath, difficulty in breathing, chest pain or fever)
- spitting or coughing blood*
- serious peeling or blistering of the skin
- unusual bleeding (including vomiting blood), bruising or nose bleeds
- nausea, vomiting, abdominal discomfort or severe diarrhoea
- mouth ulcers
- black or tarry stools
- blood in the urine or stool
- small red spots on the skin
- fever, sore throat, flu-like symptoms
- yellow colouring of the skin (jaundice) or dark urine
- pain or difficulties in passing urine
- thirst and/or frequent urination
- seizures (convulsions)
- unconsciousness
- blurred or restricted vision
- severe fatigue.
  * has been reported for methotrexate used in patients with underlying rheumatologic disease.

The following side effects have also been reported:

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
- reduced blood cell formation with a decrease in white and/or red blood cells and/or platelets (leucocytopenia, anaemia, thrombocytopenia)
- headache, tiredness, lightheadedness
- inflammation of the lungs (pneumonia) with dry cough, shortness of breath and fever
- diarrhoea
- skin rash, skin redness and itching.

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, sunburn-like reactions due to increased sensitivity of the skin to sunlight, brown discoloration of the skin, hair loss, increased number of rheumatic nodules, shingles, painful psoriasis, slow wound healing
- joint or muscle pain, osteoporosis (reduction in bone strength)
- kidney disease, inflammation or ulcers of the bladder (possibly also with blood in the urine), painful urination
- inflammation and ulcers of the vagina.

Rare (may affect up to 1 in 1,000 people):
- a blood disorder characterised by the appearance of very large red blood cells (megaloblastic anaemia)
- mood swings
- weakness in movements, also only limited to the left or right side of the body
- severe visual disorders
- inflammation of the heart sac, accumulation of fluid in the heart sac
- low blood pressure, blood clots
- tonsillitis, stopping breathing, asthma
- inflammation of the pancreas, inflammation of the digestive tract, bloody stools, inflamed gums, indigestion
- acute hepatitis (inflammation of the liver)
- discoloration of the nails, acne, red or purple spots due to bleeding from blood vessels
- worsening of psoriasis during treatment with UV therapy
- skin lesions resembling sunburn or dermatitis after radiotherapy
- bone fractures
- kidney failure, reduction or lack of urine production, abnormal levels of electrolytes in blood
- impaired sperm formation, menstrual disorders.

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
- lymphoproliferative disorders (excessive growth of white blood cells)
- 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
- impaired movement of the muscles used for speech production, difficulty in speaking, impairment of language, feeling sleepy or tired, feeling confused, having unusual sensations in the head, brain swelling, ringing in ears
- red eyes, damage to the retina of the eye
- accumulation of fluid in the lung, lung infections
- vomiting blood, severe complications in the digestive tract
- liver failure
- fingernail infections, detachment of the nail from the nail bed, boils, widening of small blood vessels, damage to the blood vessels of the skin, allergic inflammation of blood vessels
- protein in the urine
- loss of sex drive, erection problems, vaginal discharge, infertility, enlargement of the breasts in men (gynaecomastia)
- fever.

Not known (frequency cannot be estimated from the available data)
- pathological change of the white matter of the brain (leukoencephalopathy)
- haemorrhages
- bleeding from the lungs*
- redness and shedding of skin
- bone damage in the jaw (secondary to excessive growth of white blood cells)
- swelling.
  * 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.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed below.

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

United Kingdom
Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

5. How to store Jylamvo

Keep this medicine out of the sight and reach of children, preferably in a locked cupboard. Accidental ingestion can be lethal for children.

Do not use the medicine after the expiry date which is stated on the carton and label after 'Exp'. The expiry date refers to the last day of that month.

Do not store above 25°C.

Keep the bottle tightly closed to prevent spoilage of the medicine and reduce the risk of accidental spillage.

After first opening, throw away any unused medicine after 3 months.

Any unused medicine or waste material should be disposed of in accordance with local requirements for cytotoxic products - check with your pharmacist.

6. Contents of the pack and other information

What Jylamvo contains
The active substance is methotrexate. One ml of solution contains 2 mg of methotrexate.

The other ingredients are: macrogol 400, glycerol, orange flavour, sucralose, ethyl parahydroxybenzoate (E214), sodium methyl parahydroxybenzoate (E219), citric acid, tri-sodium citrate, purified water. See section 2 "Jylamvo contains ethyl parahydroxybenzoate and sodium methyl parahydroxybenzoate".

What Jylamvo looks like and contents of the pack
Jylamvo is a clear yellow solution. It is presented in a brown glass bottle containing 60 ml of solution and capped with a child-resistant closure. Each pack contains one bottle, a bottle adaptor and a white dosing syringe.

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