1. What Methotrexate 25 mg/ml is and what it is used for

Methotrexate has a cytostatic that inhibits cell growth. Methotrexate 25 mg/ml solution for injection is a cytostatic that inhibits cell growth.

Methotrexate has its greatest effect on cells which increase frequently like cancer cells, bone marrow cells and skin cells. Methotrexate 25 mg/ml is used in the treatment of the following types of cancer:
- acute lymphatic leukemia,
- prophylaxis of meningeval leukemia,
- non-Hodgkin’s lymphomas,
- osteogenic sarcoma,
- and in advanced disease of breast cancer,
- metastatic ovarian cancer and head and neck cancer,
- choriocarcinoma and similar trophoblastic diseases,
- advanced cancer of urinary bladder.

2. What you need to know before you take Methotrexate 25 mg/ml

Do not take Methotrexate 25 mg/ml:
- if you are allergic to methotrexate or any of the other ingredients of this medicine (listed in section 6).
- if you have significant liver disease (Your doctor decides the severity of your disease).
- if you have significant kidney disease (Your doctor decides the severity of your disease).
- if you have disorders of the blood-forming system.
- if you have severe or existing infection such as tuberculosis and HIV.
- if you have ulcers in the mouth and throat or ulcers in the stomach and gut.
- if you are pregnant or breastfeeding (see section Pregnancy, breast-feeding and fertility).
- if you have increased alcohol consumption.

You should not be given live vaccines during treatment with Methotrexate, as treatment with Methotrexate of both male and female can affect the foetus. How long you and your partner should wait before you/your partner try to get pregnant after completing treatment is not known. The recommendations vary from three months to one year. Methotrexate is excreted in breast milk in such quantities that there are risks of affecting the baby. Breast-feeding should therefore be suspended during treatment with Methotrexate.

Driving and using machines

Undesirable effects such as tiredness and dizziness may occur. If you feel tired or dizzy you do not drive and use machines.

Methotrexate 25 mg/ml contains 345.59 mg (15.033 mmol) of sodium per maximum daily dose (1800 mg).

To be taken into consideration by patients on a controlled sodium diet.

3. How to take Methotrexate 25 mg/ml

Methotrexate 25 mg/ml is given by health care professionals.

The dose you receive and how often you receive the dose, depend on the disease you are being treated for your state of health and your age, weight and body surface. Methotrexate 25 mg/ml can be given:
- in the mouth (if in a vial) in an artery (intra-arterially) or in the spine (intradurally).

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. Methotrexate 25 mg/ml can have undesirable effects which may be dangerous or life-threatening. During the treatment you should be alert to the signs of undesirable effects and report them to your doctor.

A doctor immediately if you notice any of the following undesirable effects. You may need immediate medical care:
- Unexplained breathlessness, dry cough or wheezing (symptoms of lung problems)
- Sudden itching, skin rash (urticaria), swollen hands, feet, ankles, face, lips, mouth or throat (which can make it hard to breathe and swallow).
- Headache, tiredness, drowsiness

Hair loss, herpes zoster, painful lesions of scaly patches

Brittle bones (osteoporosis), arthralgia, myalgia

Increase of rheumatic nodules (lumps of tissues)

Effects on the blood e.g. anaemia, leukocytopenia, thrombocytopenia

Inflammation in the so-called arachnoid membrane in the brain

Convulsions, encephalopathy

Anaphylactoid reactions and allergic vasculitis

Dry cough, shortness of breath, chest pain, fever

Headache, Tiredness, drowsiness

Dilation of colon (Toxic megacolon)

Thrombosis (cerebral, deep vein and retinal vein)

Pulmonary fibrosis

Convulsions, encephalopathy

Anaphylactoid reactions and allergic vasculitis

Fever, impaired wound healing

Discharge from the vagina

• Abnormal sensations, changes in sense of taste (metallic taste)
• Brittle bones (osteoporosis), arthralgia, myalgia
• Increase of rheumatic nodules (lumps of tissues)
• Effects on the blood e.g. anaemia, leukocytopenia, thrombocytopenia
• Inflammation in the so-called arachnoid membrane in the brain
• Convulsions, encephalopathy
• Anaphylactoid reactions and allergic vasculitis
• Dry cough, shortness of breath, chest pain, fever
• Headache, Tiredness, drowsiness
• Dilation of colon (Toxic megacolon)
• Thrombosis (cerebral, deep vein and retinal vein)
• Pulmonary fibrosis
• Convulsions, encephalopathy
• Anaphylactoid reactions and allergic vasculitis
• Fever, impaired wound healing
• Discharge from the vagina
• Abnormal sensations, changes in sense of taste (metallic taste)
A list of undesirable effects that have been reported in treatment with Methotrexate are set out below according to how common they are.

Very common (may affect more than 1 in 10 people):
- Loss of appetite, nausea, vomiting, abdominal pain, impaired digestion, diarrhoea
- Hyperrheumatoid arthritis

Common (may affect up to 1 in 10 people):
- Nausea, vomiting, diarrhoea, dry cough
- Diarrhoea
- Rash, redness, itching

Uncommon (may affect up to 1 in 100 people):
- Faint (symptoms of a severe allergic reaction).
- Fever
- Proteinuria

Rare (may affect up to 1 in 1000 people):
- Numbness of hands/feet
- Blood in the faeces
- Uncontrolled bleeding
- Black, tar-like faeces
- Inflammation and ulceration of vagina
- Stevens-Johnson syndrome
- Hyperuricemia

Not known (frequency cannot be estimated from the available data):
- Hyperkalaemia
- Thrombocytopenia
- Anaphylactoid reactions and allergic vasculitis
- Myelopathy
- Reduced blood pressure
- Tachycardia
- Convulsions
- Dilation of colon (toxic megacolon)
- Anaphylactic reactions to the drug

Epilepsy (phenytoin)
- Cancer (cisplatin, cytarabine, mercaptopurine)
- Pain and inflammation (so called NSAIDs and salicylates)

Hydrochlorothiazide and other diuretics
- Sodium diet.
- Water (e.g. water containing a diuretic agent) can increase the toxicity of Methotrexate 25 mg/ml.

Cimetidine
- In the event of contamination, the affected area must be irrigated immediately with copious quantities of water for at least ten minutes.

Pregnant healthcare personnel should not handle and/or administer Methotrexate.

Hydrochlorothiazide or other diuretics
- It should be avoided if the foetus is at risk of congenital malformations. Pregnancy should be avoided if you are planning to use Methotrexate 25 mg/ml.

Methotrexate has been reported to cause foetal death and/or congenital malformations. Pregnancy should be avoided if you are planning to use Methotrexate 25 mg/ml.