PACKAGE LEAFLET: INFORMATION FOR THE USER

Fluorouracil Injection 50 mg/ml, solution for injection

Fluorouracil

Read all of this leaflet carefully before you start using this medicine.
- 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. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- 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.

In this leaflet:

1. WHAT FLUOROURACIL INJECTION 50 MG/ML IS AND WHAT IT IS USED FOR

Fluorouracil is an anti-cancer drug.

Fluorouracil Injection 50 mg/ml, solution for injection, is used to treat the symptoms of many common cancers, particularly cancers of the large bowel and breast. It may be used in combination with other anti-cancer drugs.

2. WHAT YOU NEED TO KNOW BEFORE YOU USE FLUOROURACIL INJECTION 50 MG/ML

Do not use Fluorouracil Injection 50 mg/ml
- if you are allergic (hypersensitive) to fluorouracil or any of the other ingredients of Fluorouracil injection (listed in section 6),
- if your bone marrow has been damaged by other treatments (including radiotherapy),
- if your tumour is non-malignant,
- if you have serious impaired liver function,
- if you have serious infections (e.g. Herpes zoster, chickenpox),
- if you have been seriously weakened by long illness or other treatments (including radiotherapy) for your cancer,
- if you are breast-feeding,
- if you know that you do not have any activity of the enzyme dihydropyrimidine dehydrogenase (DPD) (complete DPD deficiency),
- if you are being treated now or have been treated in the last 4 weeks with brivudine as part of herpes zoster (chickenpox or shingles) therapy.

Warnings and precautions
Talk to your doctor or pharmacist before you receive Fluorouracil Injection 50 mg/ml
- if the number of cells in your blood become too low (you will have blood tests to check this),

- if you have gastrointestinal side effects (stomatitis, diarrhoea, bleeding from the G.I. tract) or hemorrhage at any site,
- if you have suffered from angina (heart condition marked by sudden attacks of chest pain),
- if you have a history of heart disease,
- if you have ever experienced chest pain and if you experience any chest pain during treatment,
- if you know that you have a partial deficiency in the activity of the enzyme dihydropyrimidine dehydrogenase (DPD),
- if you have a family member who has partial or complete deficiency of the enzyme dihydropyrimidine dehydrogenase (DPD),
- if you are being treated now or have been treated in the last 4 weeks with brivudine,
- if you take phenytoin for epileptic fits,
- if you have any problems with your kidneys,
- if you have any problems with your liver including jaundice (yellowing of the skin),
- if you will have prolonged exposure to sunlight. Sunlight is not advisable because of the risk of photosensitivity,
- if you have had high-dose radiotherapy in the pelvic region,
- if you should be treated with life vaccines,
- if you are being treated or take folinic acid. Folinic acid may increase the risk for fluorouracil toxicity, especially if you are older or weak.

.
DPD deficiency: DPD deficiency is a genetic condition that is not usually associated with health problems unless you receive certain medicines. If you have DPD deficiency and take Fluorouracil Injection 50 mg/ml, you are at an increased risk of severe side effects (listed under section 4 Possible side effects). It is recommended to test you for DPD deficiency before start of treatment. If you have no activity of the enzyme you should not take Fluorouracil Injection 50 mg/ml. If you have a reduced enzyme activity (partial deficiency) your doctor might prescribe a reduced dose. If you have negative test results for DPD deficiency, severe and life-threatening side effects may still occur.

Contact your healthcare provider immediately, if you experience the following signs or symptoms: new onset of confusion, disorientation, or otherwise altered mental status, difficulty with balance or coordination, visual disturbances. These could be signs of encephalopathy which can lead to coma and death, if left untreated.

Your treatment will be first given to you in hospital. Before you are given fluorouracil you will have to have a blood test, and possibly other tests, so that your doctor can be sure that you can undergo fluorouracil treatment.

Other medicines and Fluorouracil Injection

Before starting treatment, tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This is extremely important, as taking more than one medicine at the same time can strengthen or weaken the effect of the medicines.

You must not take brivudine (an anti-viral medicine for the treatment of shingles or chickenpox) at the same time as Fluorouracil Injection 50 mg/ml treatment (including during any rest periods when you are not taking Fluorouracil Injection 50 mg/ml).
If you have taken brivudine you must wait for at least 4 weeks after stopping brivudine before starting to take Fluorouracil Injection 50 mg/ml. See also section "Do not use Fluorouracil Injection 50 mg/ml".

Fluorouracil is known to interact with the following medicines:
- allopurinol (used to treat high levels of uric acid),
- certain medicines used to treat malignant diseases,
- radiotherapy,

- leucovorin (also called folinic acid – used in cancer therapy and treatment of folic acid deficiency),
- phenytoin (used to treat epilepsy),
- cimetidine (used to treat heartburn and gastrointestinal ulcers),
- metronidazole (used to treat infections),
- interferon alpha 2a (used to treat cancer or hepatitis),
- thiazides (e.g. hydrochlorothiazide),
- cyclophosphamide (an anti-cancer medicine),
- methotrexate (used to treat cancer or autoimmune diseases),
- warfarin (used to prevent blood from clotting),
- levamisol (medicine used to treat worm infection),
- clozapine (used to treat schizophrenia),
- anthracyclines (anti-cancer medicine; e.g. epirubicin, doxorubicin, daunorubicin),
- tamoxifen (an anti-cancer medicine),
- vinorelbine (an anti-cancer medicine),
- life vaccines should be avoided,
- cisplatin (an anticancer medicine).

Pregnancy, breast-feeding and fertility

Pregnancy
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.
Fluorouracil should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus. If you are a woman of childbearing potential, you must not become pregnant during treatment and use an effective method of contraception while taking this drug and at least for 6 months afterwards.
If pregnancy occurs during your treatment you must inform your doctor and should use genetic counselling.

Breast-feeding
Since it is not known whether fluorouracil passes into breast milk, breast-feeding must be discontinued before treatment with Fluorouracil Injection 50 mg/ml.

Fertility
If you are a man you should avoid father a child during and for up to 3 months following end of treatment with Fluorouracil Injection 50 mg/ml. You are advised to seek conservation of sperm prior to treatment because of the possibility of irreversible infertility due to therapy with Fluorouracil Injection 50 mg/ml.

Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines
Do not drive or use machines because Fluorouracil may induce side effects such as nausea and vomiting. It can also produce adverse event on your nervous system and visual changes. If you experience any of this effect, do not drive or use any tools or machines, it may impair your ability to drive or use machines.

Sodium
10 ml vial
This medicine contains 82.37 mg sodium (main component of cooking/table salt) in each 10 ml vial.
This is equivalent to 4.12% of the recommended maximum daily dietary intake of sodium for an adult.

20 ml vial
This medicine contains 164.75 mg sodium (main component of cooking/table salt) in each 20 ml vial. This is equivalent to 8.24% of the recommended maximum daily dietary intake of sodium for an adult.

50 ml vial
The maximum recommended daily dose of this medicinal product contains 411.87 mg sodium (found in table salt). This is equivalent to 20.59% of the adult recommended maximum daily dietary intake for sodium.
Talk to your pharmacist or doctor if you need Fluorouracil Injection 50 mg/ml, solution for injection, on a daily basis for a prolonged period of time, especially if you have been advised to have a low salt diet.

100 ml vial
The maximum recommended daily dose of this medicinal product contains 823.75 mg sodium (found in table salt). This is equivalent to 41.19% of the adult recommended maximum daily dietary intake for sodium.
Talk to your pharmacist or doctor if you need Fluorouracil Injection 50 mg/ml, solution for injection, on a daily basis for a prolonged period of time, especially if you have been advised to have a low salt diet.

3. HOW TO USE FLUOROURACIL INJECTION 50 MG/ML

If you are using Fluorouracil Injection 50 mg/ml, solution for injection, at home, it is important to follow the instructions given to you by your doctor, nurse and pharmacist. If the container is damaged, and fluorouracil is spilt, you should contact your nurse or pharmacist. If fluorouracil comes into contact with your skin, wash the area with soap and water and contact your doctor, nurse or pharmacist. Do not clean up spilt fluorouracil without first contacting your nurse or pharmacist.

Fluorouracil is given by intravenous injection or infusion (drip or pump). If you are in hospital it may be given by intra-arterial infusion.

The dosage will depend on the condition being treated and whether or not other drugs are being administered. It will also depend on the results of your blood tests and the state of your health.
The usual fluorouracil dose is around 1 g (1000 mg) per day. Your treatment may be given daily or at weekly intervals initially. Further courses may be prescribed by your doctor according to your response to treatment.

If you take more Fluorouracil Injection 50 mg/ml
This medicine will be given to you by your doctor or nurse. It is unlikely that you will receive too much or too little of this medicine, however, inform your doctor or nurse if you have any concerns.

Symptoms
Nausea, vomiting, diarrhoea, severe mucositis and gastrointestinal ulceration and bleeding may occur if you have too much fluorouracil.

Treatment
You will need to have blood tests during and after treatment with Fluorouracil Injection to check the levels of cells in your blood. Treatment may have to be stopped if the level of white blood cells drops too low.

If you have any further question on the use of this product ask your doctor.

If you forget to take Fluorouracil Injection 50 mg/ml
If you miss a dose or if you are at home and have any trouble with your pump, contact your nurse or pharmacist as soon as possible.

If you stop using Fluorouracil Injection 50 mg/ml
When your course of fluorouracil is finished you may feel tired and experience some of the undesirable effects (see below) associated with fluorouracil treatment.

4. POSSIBLE SIDE EFFECTS

Like all medicines, this medicine can cause side effects, although not everybody gets them.
Prior to commencement of treatment, your doctor will inform you of the expected benefits and potential risks of the use of Fluorouracil Injection 50 mg/ml, solution for injection.

Tell your doctor immediately if any of the following happen:
- your mouth becomes very sore or develops ulcers
- you experience chest pain or quickening of heart beat
- you experience shortness of breath
- you recognise symptoms of blood circulation disorders of the brain (cerebral ischaemia e.g. numbness of the face or the limbs, confusion, troubles speaking or seeing) or blood circulation disorder of the intestines (intestinal ischaemia e.g. sudden abdominal pain, abdominal tenderness or abdominal cramps, blood in your stools, troubles with bowel movements)
- you experience an allergic reaction (you may experience itching, flushing of the face, swelling of the face, eyes or tongue, difficulty swallowing, nausea or vomiting, pain or tightness in the chest, shortness of breath, unconsciousness)
- you notice leg pain, tenderness of the thigh or calf and leg swelling, maybe accompanied by symptoms of difficulty to breathe and fast heart rate. These might be symptoms of blood clots deep in the veins (thromboembolism).
- you notice symptoms of liver damage (liver necrosis) e.g. yellowing of your skin and eyeballs, pain in your upper right abdomen, abdominal swelling, abrupt weakness, nausea and vomiting.

If severe stomatitis (sores in your mouth and/or throat), mucosal inflammation, diarrhoea, neutropenia (increased risk for infections), or neurotoxicity occurs during the first cycle of treatment a DPD deficiency may be involved (please see Section 2: Warning and precautions).

Other side effects are listed below starting with the most frequent:

Very common (may affect more than 1 in 10 people):
- infections
- changes in the components of the blood (decrease in the number of white blood cells, of neutrophils, of granulocytes, red blood cells and / or platelets [seen in tests]) you will need to have blood tests during and after treatment with fluorouracil.
- sharp drop in circulating granular white blood
- suppression of the immune system
- increase in uric acid in the blood
- ischemic ECG abnormalities (an insufficient supply of blood to an organ, usually due to a blocked artery)
- difficulty breathing because the airways have narrowed
- nosebleed
- inflammation of gastrointestinal tract (oesophagitis, pharyngitis, proctitis)
- loss of appetite
- watery diarrhoea
- nausea
- vomiting
-
- hair loss: the hair usually grows again when fluorouracil is stopped. Talk to your nurse if you are unhappy about this.

- hand-and-foot skin reaction (palms of the hands or soles of the feet tingle, become numb, painful, swollen or red)
- fever
- delayed wound healing
- tiredness
- malaise
- weakness

Diarrhoea and sickness are quite common, but your doctor may be able to give you medicine(s) to reduce this.

Common (may affect up to 1 in 10 people):
- low white blood cell count accompanied by fever
- inflammation of the eyes

Uncommon (may affect up to 1 in 100 people):
- severe infection (sepsis)
- dehydration
- euphoria
- uncontrollable and rhythmic eye movement
- headaches
- dizziness
- symptoms of Parkinson's disease (e.g. unsteady on feet, abnormal movements)
- symptoms affecting the neurological tract (pyramidal signs)
- sleepiness
- nerve damage (e.g. problems with sensation, motor function and inflammation of the eye nerves)
- excess tearing
- vision changes (e.g. blurred vision, eye movement disturbance, seeing double, decreased sharpness of vision, sensitivity to light)
- inflammation of the eyelid margins (blepharitis)
- eyelid turning outward (ectropion)
- narrowing or blockage of the tear ducts (dacryostenosis)
- irregular heartbeat, inflammation of the heart muscle wall, myocardial ischaemia (a loss of oxygen to the heart muscle), heart failure, heart attack, dilated disease of the heart muscle wall, shock of the heart
- hypotension
- ulcers and bleeding in the stomach and intestine
- liver cell damage
- inflammation, reddening and rash of the skin
- skin changes (e.g. dry skin, fissure erosion, redness, pruritic maculopapular rash (rash that had originated on the lower extremities and had progressed to the arms, and then to the chest)
- sensitivity of skin to the sun
- hyper- or hypopigmentation of skin
- streaky hyperpigmentation or depigmentation near the veins
- nail disorders (e.g. diffuse superficial blue pigmentation, hyperpigmentation, lack of growth, pain and thickening of the nail bed, inflammation of the tissue surrounding a fingernail (paronychia), detachment of nail)
- skin rash similar to severe sunburn which can occur on skin that has previously been exposed to radiotherapy (recall phenomenon of the skin)
- sperm or ovum production disorder

Rare (may affect up to 1 in 1,000 people):
- severe allergic (anaphylactic) reactions and shock
- increase of thyroid hormones (T3 and T4)
- confusion
- brain disturbance and peripheral nerve damage

- inflammation of veins (vasculitis)
- Raynaud's phenomenon
- pain or discoloration of the vein where this medicine is administered (vein tracking)
- inflammation of veins (thrombophlebitis)

Very rare (may affect up to 1 in 10,000 people):
- disorientation
- symptoms of brain diseases (leukoencephalopathy) like unsteady movements, speaking disturbance, confusion, disorientation, muscle weakness, loss of speech, convulsion (seizure), unconsciousness
- cardiac arrest (sudden cessation of heartbeat and cardiac function)
- sudden cardiac death (unexpected death due to heart problems)
- slow progressive destruction of the small bile ducts
- inflammation of the gall bladder
- kidney failure

Not known (frequency cannot be estimated from the available data):
- impairment of the brain due to an increase of ammonium (hyperammonaemic encephalopathy)
- inflammation of the sac surrounding the heart (pericarditis)
- inflammation of the skin causing red scaly patches and possibly occurring together with pain in the joints and fever (cutaneous lupus erythematosus [CLE])
- heart disease that presents with chest pain, shortness of breath, dizziness, fainting, irregular heartbeat (stress cardiomyopathy)
- air in the intestinal wall
- serious condition that presents with difficulty breathing, vomiting and abdominal pain with muscle cramps (lactic acidosis)
- condition characterised by headache, confusion, seizures and changes in vision (posterior reversible encephalopathy syndrome [PRES])
- serious complication with rapid break down of cancer cells causing high levels of uric acid, potassium and phosphate (tumour lysis syndrome)

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 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 FLUOROURACIL INJECTION 50 MG/ML

Do not store above 25 °C.
Do not refrigerate or freeze.
Keep the container in the outer carton.
Do not use Fluorouracil Injection 50 mg/ml after the expiry date which is stated on the carton.
Keep out of the sight and reach of children!

6. FURTHER INFORMATION

What Fluorouracil Injection 50 mg/ml contains
The active substance is fluorouracil. Each septum vial contains 10 ml (20 ml, 50 ml, 100 ml) of solution containing 500 mg (1000 mg, 2500 mg, 5000 mg) fluorouracil.
The other ingredients are: sodium hydroxide and water for injections.

What Fluorouracil Injection 50 mg/ml looks like and contents of the pack

Fluorouracil Injection 50 mg/ml, solution for injection, is a clear, colourless or almost colourless solution.
Fluorouracil Injection 50 mg/ml, solution for injection, is an aqueous solution for injection which is supplied in colourless glass vials.
Fluorouracil Injection 50 mg/ml, solution for injection vials are supplied in packs containing one vial or ten vials.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder
medac
Gesellschaft für klinische
Spezialpräparate mbH
Theaterstr. 6
22880 Wedel
Germany

Manufacturer
medac
Gesellschaft für klinische
Spezialpräparate mbH
Theaterstr. 6
22880 Wedel
Germany

This leaflet was last revised in 11/2021.

The following information is intended for medical or healthcare professionals only:

Instructions on how to store, handle, and dispose Fluorouracil Injection 50 mg/ml

Shelf life after preparing the solution for infusion ready for use
Chemical and physical in-use stability of the solution diluted with glucose 5 % or sodium chloride 0.9 % injection has been demonstrated for 24 hours at a temperature not exceeding 25 °C.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8 °C, unless dilution has taken place in controlled and validated aseptic conditions.

If a precipitate has formed as a result of exposure to low temperatures, redissolve by heating to 40 °C accompanied by vigorous shaking. Allow to cool to body temperature prior to use.

Handling and disposal
Preparation of solution for administration should be carried out in a designated handling area and working over a washable tray or disposable plastic-backed absorbent paper.
Suitable eye protection, disposable gloves, face mask and disposable apron should be worn. Syringes and infusion sets should be assembled carefully to avoid leakage (use of Luer lock fittings is recommended).
All materials that have been utilised for dilution and administration should be disposed of according to standard procedures (incineration).
Any solution remaining after first use should be discarded. Waste disposal procedures should take into account the cytotoxic nature of this substance.