

Package leaflet: Information for the user

ISOVORIN Solution for Injection 10 mg/ml

calcium levofolinate

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, please ask your doctor, pharmacist or nurse.
- If you get any side effects talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

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

1. What Isovorin Solution is and what it is used for

Isovorin Solution contains the active substance calcium levofolinate.

Isovorin Solution for Injection 10 mg/ml may be used in combination with other medicines to treat cancer. In particular it may be used to reduce the harmful effects of an anti-cancer drug called methotrexate.

Isovorin Solution can be used to increase the effect of another drug, 5-fluorouracil (5FU) in treating some types of cancer such as cancer of the colon or rectum.

2. What you need to know before you use Isovorin Solution

Do not use Isovorin Solution if:

- you are allergic to calcium levofolinate or any of the other ingredients of this medicine (listed in section 6)
- you have a blood disease called anaemia caused by too little Vitamin B₁₂
- you are pregnant, think you might be pregnant or are breast-feeding

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using Isovorin Solution if:

- you have anaemia (megaloblastic or pernicious) caused by vitamin B12 deficiency
- you have blood problems caused by anti-cancer medicines
- you are elderly or debilitated and being treated with 5-Fluorouracil
- you are suffering from diarrhoea or stomach upset and receiving treatment along with 5-Fluorouracil
- you have undergone preliminary radiotherapy
- you take an accidental overdose with methotrexate

- you have taken an excessive dose of this as the activity of methotrexate may be impaired especially in anti-tumour therapy
- you are resistant to methotrexate or folinic acid

Other medicines and Isovorin Solution

Tell your doctor, pharmacist or nurse if you are taking, have recently taken or might take other medicines. In particular, you should tell your doctor if you are using:

- medicines for the treatment of epilepsy (e.g. phenobarbital, phenytoin, primidone or succinimides) as your medicine may reduce their effects
- anti folate drugs (e.g cotrimoxazole, pyrimethamine).

Pregnancy and breast-feeding

Do not use Isovorin Solution if you are pregnant, think you might be pregnant or are breast-feeding. Levofolinate may be excreted in breast milk. If you are breast-feeding, ask your doctor or pharmacist for advice before taking this medicine.

Driving and using machines

There is no evidence that calcium levofolinate has an effect on the ability to drive or use machines.

Isovorin Solution contains sodium

Isovorin 25 mg/2.5 ml solution for injection contains 7.6 mg of sodium (main component of cooking/table salt) in 2.5 ml of solution. This is equivalent to 0.4% of the recommended maximum daily dietary intake of sodium for an adult.

Isovorin 50 mg/5 ml solution for injection contains 15.2 mg of sodium (main component of cooking/table salt) in 5 ml of solution. This is equivalent to 0.8% of the recommended maximum daily dietary intake of sodium for an adult.

Isovorin 175 mg/17.5 ml solution for injection contains 53.03 mg of sodium (main component of cooking/table salt) in each 17.5 ml of solution. This is equivalent to 2.65% of the recommended maximum daily dietary intake of sodium for an adult.

3. How to use Isovorin Solution

Your doctor will give you Isovorin Solution by injecting it into one of your veins or muscle.

Isovorin Solution should not be injected into your spine

When used to reduce the harmful effects of methotrexate, your treatment will usually start about 24 hours after your methotrexate treatment starts. The usual dose of Isovorin Solution is 7.5 mg every 6 hours for 10 doses. However, the doctor may decide to change this, depending on your condition and the dose of methotrexate you have already received. During your treatment your doctor may also wish to give you other fluids and to take blood samples from you.

When used in combination with other drugs such as 5FU, the higher dose of 175 mg in 17.5 ml of Isovorin Solution will be given to you.

If you use more Isovorin Solution than you should

As this medicine will be given to you whilst you are in hospital it is unlikely that you will be given too little or too much however if you have any concerns then tell your doctor.

If you miss a dose of Isovorin Solution

If you think you have not been given a dose of **Isovorin Solution**, tell your doctor immediately.

If you think that you have missed a dose or have been given too much medicine, tell your doctor/nurse immediately.

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.

If any of the following happen, tell your doctor immediately or go to your nearest hospital:

- Severe allergic reactions such as breathing difficulties, swelling of the lips, face, neck and throat, and low blood pressure
- Very severe skin reactions with reddening, blistering, severe inflammation and skin loss
- Severe diarrhoea
- Excessive bruising, shortness of breath, tiredness or repeated infections.

The side effects listed below are those that have been seen with the use of Isovorin Solution.

- **Rare:** may affect up to 1 in 1,000 people
Fits; fainting
- **Not known:** frequency cannot be estimated from available data.
Mild allergic reactions, such as skin rash and itching; fever

The side effects listed below are those that have also been seen when Isovorin Solution has been used in combination with 5FU.

- **Very common:** may affect more than 1 in 10 people
Feeling or being sick; diarrhoea, inflammation of the lining of the intestine and mouth (including life-threatening conditions); reduction in the number of blood cells (including life-threatening conditions)
- **Common:** redness and swelling of the palms of the hands or the soles of the feet which may cause the skin to peel (hand-foot syndrome)
- **Not known:** frequency cannot be estimated from available data.
Elevated levels of ammonia in the blood

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 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 Isovorin Solution

Keep this medicine out of the sight and reach of children.

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

Isovorin Solution for Injection 10 mg/ml should be kept in a refrigerator (2-8°C) in the original container to protect from light.

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 Isovorin Solution contains

- The active substance is calcium levofolinate. Each vial contains 10mg per ml of calcium levofolinate.
- The other ingredients are sodium chloride, water for injection, hydrochloric acid and sodium hydroxide. Excipients containing sodium (see section 2 'Isovorin solution contains sodium').

What Isovorin Solution looks like and contents of the pack

Isovorin Solution is a clear yellow solution. It is supplied in small amber glass bottles (called vials). Each vial contains 25 mg, 50 mg or 175 mg of the active ingredient calcium levofolinate in 2.5 ml, 5 ml and 17.5 ml respectively.

Isovorin Solution for Injection 10mg/ml is supplied in a carton containing one vial.
Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

The marketing authorisation holder is: Pfizer Limited, Ramsgate Road, Sandwich, Kent, CT13 9NJ, United Kingdom

The manufacturer of this medicine is: Wyeth Lederle S.p.A, Via Franco Gorgone, Zona Industriale, Catania, Italy

The information in this leaflet applies only to Isovorin Solution. If you would like more information about Isovorin Solution for Injection 10 mg/ml, have any questions or you are not sure about anything, you should ask your doctor.

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