Package leaflet: Information for the user

Kalciumfolinat STADA, 10 mg/ml, solution for injection
Folinic acid

Read all of this leaflet carefully before you start using 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 Kalciumfolinat STADA is and what it is used for

Kalciumfolinat STADA contains calcium folinate. It is a calcium salt of folinic acid, which is related to the vitamin folic acid.

Kalciumfolinat STADA is used to:
- reduce the harmful effects of anti-cancer medicines for instance methotrexate. This is known as “calcium folinate rescue”. Methotrexate fights cancer cells by working against folic acid. Kalciumfolinat STADA helps healthy cells to recover from the harmful (cytotoxic) effects of methotrexate.

- treat cancer of the large bowel (colorectal cancer) in combination with 5-fluorouracil (an anti-cancer medicine). 5-fluorouracil works better when it is given together with Kalciumfolinat STADA.

2. What you need to know before you use Kalciumfolinat STADA

DO NOT use Kalciumfolinat STADA
- if you are allergic to calcium folinate or any of the other ingredients of this medicine (listed in section 6).

- if you suffer from anaemia (not enough red blood cells) caused by a lack of vitamin B12, such as:
- pernicious anaemia (your immune systems fights your red blood cells)
- megaloblastic anaemia (your red blood cells are larger than normal)

Warnings and precautions
Talk to your doctor before using Kalciumfolinat STADA
- if you are being treated with 5-fluorouracil, especially if you are elderly or feel unwell, because Kalciumfolinat STADA can increase the harmful effects of 5-fluorouracil. This may

make you more prone to infections (due to not enough white blood cells). You may also develop a sore mouth or diarrhoea. Digestive tract problems are also more common and may be severe or even life-threatening (see section 4, “Possible side effects”).Your doctor may decide stop the treatment with 5-fluorouracil and Kalciumfolinat STADA.

- if you suffer from epilepsy and use anti-epileptic medicines (such as phenobarbital, phenytoin or primidone). Because there is a risk that your seizures (fits) may occur more often when you receive Kalciumfolinat STADA, your doctor will decide if the dose of your anti-epileptic medicine has to be changed.

- if you suffer from a macrocytosis (enlarged blood cells) due to treatment with anti-cancer medicines (such as hydroxycarbamide, cytarabine, mercaptopurine, thioguanine), because you should not be treated with Kalciumfolinat STADA for this disease.

Other medicines and Kalciumfolinat STADA
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, especially:

- medicines which block the action of folic acid (folic acid antagonists) like cotrimoxazole (an antibiotic) or pyrimethamine (to treat special infections like malaria).
  Kalciumfolinat STADA can reduce the effectiveness of these medicines.

- medicines to treat epilepsy like phenobarbital, phenytoin, primidone or succinimides (e.g. ethosuximide, phensuximide).
  Kalciumfolinat STADA lowers the concentrations of these drugs in your body. This can increase the frequency of your seizures (fits). Your doctor will examine your blood to monitor the drug concentrations. Your doctor will also decide if the dose of your anti-epileptic medicine has to be changed.

- 5-fluorouracil:
  Kalciumfolinat STADA given together with 5-fluorouracil increases not only the efficacy of 5-fluorouracil, but can also increase its poisonousness. Your doctor will decide if your 5-fluorouracil dose has to be changed.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Kalciumfolinat STADA can be used to reduce the harmful effects of methotrexate, if your doctor decides that treatment with methotrexate is required for your condition when you are pregnant or breast-feeding. However, methotrexate should not generally be used when you are pregnant or breast-feeding.

There are no adequate data for the use of calcium folinate and 5-fluorouracil or other anti-cancer drugs in pregnant or breast-feeding women. However, anti-cancer drugs should not generally be used when you are pregnant or breast-feeding.

Driving and using machines
Kalciumfolinat STADA alone will not affect your ability to drive or use machines.
If Kalciumfolinat STADA is used together with 5-fluorouracil, you may experience the side effects of 5-fluorouracil more strongly. These are dizziness, drowsiness, visual disturbances and nausea (feeling sick). If you are given this combination, you should not drive or use machines.

3. How to use Kalciumfolinat STADA

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

The combination of Kalciumfolinat STADA with anti-cancer medicines (methotrexate, 5-fluorouracil) should only be given under the supervision of an experienced doctor.

Your doctor will decide about the dose you will receive based on your condition.

The solution of the medicine may be prepared especially for you individually by specialist staff. It is given slowly into a vein (as an injection or infusion) or it may be injected into a muscle. Your doctor will also decide how many injections or infusions you will need and how often they should be given.

If you use more Kalciumfolinat STADA than you should
Overdose of calcium folinate alone does not cause any symptoms.
However, too much calcium folinate can reduce the efficacy of methotrexate.

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.

Very rare (may affect up to 1 in 10,000 people):
- severe allergic reaction - you may experience a sudden itchy rash (hives), swelling of the hands, feet, ankles, face, lips, mouth or throat (which may cause difficulty in swallowing or breathing), and you may feel you are going to faint.
  This is a serious side effect. You may need urgent medical attention.

Other side effects that may occur:

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

Rare (may affect up to 1 in 1,000 people):
- an increase in convulsions (fits) in patients with epilepsy
- depression
- agitation
- problems with the digestive system
- difficulty sleeping (insomnia)

If you receive Kalciumfolinat STADA in combination with an anticancer medicine containing fluoropyrimidines, it is more likely that you experience the following side effects of this other medicine:

Very common (may affect more than 1 in 10 people):
- nausea
- vomiting
- severe diarrhoea
- drying out which may be due to diarrhoea
- inflammation of the lining of the intestine and mouth (life-threatening conditions have occurred)
- reduction in the number of blood cells (including life-threatening conditions)

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

- 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 the available data):
- elevated ammonia level in the blood

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

5. How to store Kalciumfolinat STADA

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

Store in a refrigerator (2 °C – 8 °C). Keep the vial in the outer carton in order to protect from light.

Do not use this medicine after the expiry date which is stated on the vial and outer carton.

6. Contents of the pack and other information

What Kalciumfolinat STADA contains
The active substance is calcium folinate.

1 ml solution for injection contains 10.8 mg of calcium folinate, equivalent to 10 mg folinic acid.
1 vial of 10 ml contains 108 mg of calcium folinate equivalent to 100 mg folinic acid.
1 vial of 20 ml contains 216 mg of calcium folinate equivalent to 200 mg folinic acid.
1 vial of 50 ml contains 540 mg of calcium folinate equivalent to 500 mg folinic acid.
1 vial of 100 ml contains 1080 mg of calcium folinate equivalent to 1000 mg folinic acid.

The other ingredients are trometamol, hydrochloric acid and water for injections.

What Kalciumfolinat STADA looks like and contents of the pack

This medicine is a solution for injection. It is a clear, slightly yellow to yellow solution. It is filled in brown or clear glass vials with rubber stoppers and aluminium caps.

The packages contain either 1 or 5 vials of 10 ml, 20 ml, 50 ml or 100 ml, respectively.

Not all pack sizes may be marketed.

Marketing Authorisation Holder
STADA Arzneimittel AG
Stadastrasse 2-18
D-61118 Bad Vilbel
Germany

Manufacturer
STADA Arzneimittel AG
Stadastraße 2-18
61118 Bad Vilbel
Germany

This medicinal product is authorised in the Member States of the EEA under the following names:

Belgium	Folinate EG, oplossing voor injectie
Finland	Kalciumfolinat STADA 10 mg/ml injektioneste, liuos
Luxembourg	Folinate EG solution injectable
Sweden	Kalciumfolinat STADA 10 mg/ml injektionsvätska, lösning

This leaflet was last revised in
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The following information is intended for medical or healthcare professionals only:

Incompatibilities:
Incompatibilities have been reported between injectable forms of calcium folinate and injectable forms of droperidol, fluorouracil, foscarnet and methotrexate.

Droperidol
1. Droperidol 1.25 mg/0.5 ml with calcium folinate 5 mg/0.5 ml, immediate precipitation in direct admixture in syringe for 5 minutes at 25 °C followed by 8 minutes of centrifugation.
2. Droperidol 2.5 mg/0.5 ml with calcium folinate 10 mg/0.5 ml, immediate precipitation when the drugs were injected sequentially into a Y-site without flushing the Y-side arm between injections.

Fluorouracil
Calcium folinate must not be mixed in the same infusion as 5-fluorouracil because a precipitate may form. Fluorouracil 50 mg/ml with calcium folinate 20 mg/ml, with or without dextrose 5 % in water, has been shown to be incompatible when mixed in different amounts and stored at 4 °C, 23 °C, or 32 °C in polyvinyl chloride containers.

Foscarnet
Foscarnet 24 mg/ml with calcium folinate 20 mg/ml; formation of a cloudy yellow solution reported.

Handling:
For intravenous infusion, calcium folinate may be diluted with 0.9 % sodium chloride solution or 5 % glucose solution.

The medicinal product is for single use only. Any unused solution should be discarded.

The solution for injection should be inspected visually prior to use. Only clear solutions without particles should be used.

Shelf life:
After dilution of the Kalciumfolinat STADA solution in 5 % glucose solution or in 0.9 % sodium chloride solution, the chemical and physical in-use stability has been demonstrated for 72 hours at +2 °C to +8 °C and at +25 °C, when protected from light.

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 should normally not be longer than 24 hours at +2 to +8 °C, unless dilution has taken place under controlled and validated aseptic conditions.