

**Package leaflet: Information for the user**

**Calcium Folate 10 mg/ml,  
solution for injection  
calcium folinate**

**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.
- 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 Calcium Folate is and what it is used for
2. What you need to know before you are given Calcium Folate
3. How you are given Calcium Folate
4. Possible side effects
5. How to store Calcium Folate
6. Contents of the pack and other information

**1 What Calcium Folate is and what it is used for**

Calcium Folate is an antidote. Antidotes prevent the damage caused by other substances. Calcium Folate is administered as an injection or infusion by your doctor. Calcium Folate is used to help prevent the side effects of treatment or overdose with the medicine methotrexate, when used in high doses. Calcium Folate is being administered a few hours after methotrexate, to allow methotrexate to have its effect first.

Calcium Folate is also used in combination with the medicine 5-fluorouracil for the treatment of certain forms of colon cancer (metastatic colorectal carcinoma). This therapy should only be applied when supervised by a doctor with experience in the use of cancer chemotherapeutics. Finally Calcium Folate is also used to prevent or treat a folate deficiency, only when it is impossible to administer folic acid tablets.

**Use**

- to diminish the harmfulness and effect of certain medicines (like methotrexate) in children and adults.
- in combination with the medicine 5-fluorouracil, for the treatment of certain forms of cancer.

**2 What you need to know before you are given Calcium Folate**

**Do not use Calcium Folate:**

- if you are allergic to calcium folinate or any of the other ingredients of this medicine (listed in section 6). An allergic reaction may include rash, itching, difficulty breathing or swelling of the face, lips, throat or tongue.
- if you suffer from anaemia which is due to a shortage of vitamin B<sub>12</sub> (for example pernicious anaemia).

You should not be given Calcium Folate together with certain anticancer drugs if you are pregnant or breastfeeding (your doctor will know which these are).

**Warnings and precautions**

**Calcium Folate should only be given by intramuscular or intravenous injection and must not be administered intrathecally.**

Talk to your doctor or pharmacist before you are given Calcium Folate

- if diarrhoea or mucositis occur during the use of Calcium Folate in combination with the medicine 5-fluorouracil (see also "Possible side effects"). Your doctor can decide to decrease the 5-fluorouracil dose or stop the treatment. Elderly and weak patients are more susceptible to these side effects.
- if you are simultaneously being treated with methotrexate; Calcium Folate should not be administered together with methotrexate, because Calcium Folate is able to counteract the effects of methotrexate totally. Therefore, Calcium Folate should always be administered several hours **after** the treatment with methotrexate (see also section 3. "How to use Calcium Folate").
- if you have been treated with radiotherapy before, and you receive Calcium Folate in combination with the medicine 5-fluorouracil; your doctor will reduce the dosage of 5-fluorouracil.
- if you receive Calcium Folate in combination with the medicine 5-fluorouracil and your doctor notices that the amount of calcium in your blood has decreased; your doctor will prescribe extra calcium.
- if you take certain anti-epileptics; epileptic seizures may occur more frequently (see also the paragraph "Other medicines and Calcium Folate" and the section "Possible side effects").
- if you take/are given certain medicines for the treatment of cancer, like hydroxycarbamide, cytarabine, mercaptopurine

and thioguanine. These medicines may cause a blood disorder (macrocytosis) that should not be treated with Calcium Folate.

- if your kidneys do not function well and Calcium Folate is given in combination with methotrexate; your doctor may decide to increase the Calcium Folate dosage or to prescribe longer use of it.

Inform your doctor if one of these warnings applies to you, or has applied in the past.

**Other medicines and Calcium Folate**

Tell your doctor or pharmacist if you are taking/using, have recently taken/used or might take/use any other medicines.

Please note that the name of the medicines mentioned below might be familiar to you under a different name, e.g. the brand name. In this paragraph only the name of the active substance is used and not the brand name. Therefore, you should check the package and patient information leaflet for the active substance of the medicines you already take or have taken in the recent past.

Sometimes (medicinal) products that are given/taken concomitantly can influence each other's effect and/or side effect. This is called an interaction. An interaction can occur during concomitant use of the solution for injection and:

- 5-fluorouracil (a medicine against certain forms of cancer). The effect and side effects of 5-fluorouracil are increased. Calcium Folate and 5-fluorouracil are often given in combination intentionally. However, also the undesirable side effects are enhanced.
- folic acid antagonists like cotrimoxazole (an antibiotic), pyrimethamine (a treatment for malaria) or methotrexate. The effect of the folic acid antagonist may either be reduced or completely neutralised. Calcium Folate and methotrexate are often given in combination intentionally.
- phenobarbital, primidone, phenytoin and succinimides (medicines against epilepsy). The effect of these medicines may be diminished, which can cause epileptic seizures.

**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 using this medicine.

The effects of Calcium Folate on the unborn child are unknown. Calcium Folate may only be administered during pregnancy when clearly needed. This will be decided by your doctor.

This advice is also applicable when Calcium Folate is administered in combination with methotrexate. The administration of Calcium Folate in combination with 5-fluorouracil during pregnancy is not allowed because of the harmful effects of 5-fluorouracil.

It is not known whether Calcium Folate is excreted in breast milk. Calcium Folate should only be administered to breast-feeding mothers when clearly needed. This will be decided by your doctor. In combination with 5-fluorouracil, the administration of Calcium Folate during breastfeeding is not advised because of the harmful effects of 5-fluorouracil.

**Driving and using machines**

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

**Calcium Folate contains sodium**

**5 ml vials:**

This medicine contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially 'sodium-free'.

**10 ml vials:**

This medicine contains 32.2 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 1.6 % of the recommended maximum daily dietary intake of sodium for an adult.

**20 ml vials:**

This medicine contains 64.4 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 3.2 % of the recommended maximum daily dietary intake of sodium for an adult.

**30 ml vials:**

This medicine contains 96.6 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 4.8 % of the recommended maximum daily dietary intake of sodium for an adult.

**50 ml vials:**

This medicine contains 161 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 8.1 % of the recommended maximum daily dietary intake of sodium for an adult.

**3 How you are given Calcium Folate**

Calcium Folate will only be given by a doctor or nurse under the supervision of a doctor who has experience in the use of chemotherapy. Calcium Folate may be given by injection or infusion into a vein, or as an injection into a muscle.

The dosage can vary from patient to patient since the dose will be calculated by your body surface area (based on your height and weight). Your doctor will decide what dosage is best for you.

The recommended dose is



#### **After one cycle of moderate- to high-dose methotrexate:**

##### **Adults, elderly patients and children**

As a rule, the first dose of Calcium Folate is 15 mg (6-12 mg/per square metre of your body surface area) to be given 12-24 hours (at the latest 24 hours) after starting the methotrexate infusion. Over a period of 72 hours, the same dose is repeated every 6 hours. After administration of a few injections or infusions, it is possible to switch to tablets.

##### **In combination with 5-fluorouracil for the treatment of certain forms of colon cancer (metastatic colorectal carcinoma):**

##### **Adults and elderly patients**

- Bimonthly regimen: on two consecutive days, every two weeks: 200 mg of Calcium Folate per square metre of your body surface area as an infusion over a period of two hours, followed by an injection of 400 mg of 5-fluorouracil per square metre of your body surface area and 600 mg of 5-fluorouracil per square metre of your body surface area as an infusion over a period of 22 hours.
- Weekly regimen: 20 mg of Calcium Folate per square metre of your body surface area as a single injection, or 200 to 500 mg of Calcium Folate per square metre of your body surface area as an infusion over a period of two hours plus 500 mg of 5-fluorouracil per square metre of your body surface area as an intravenous injection in the middle or at the end of the Calcium Folate infusion.
- Monthly regimen: once a month during five consecutive days: 20 mg of Calcium Folate per square metre of your body surface area as a single injection, or 200 to 500 mg of Calcium Folate per square metre of your body surface area as an infusion over a period of two hours, immediately followed by 425 or 370 mg of 5-fluorouracil per square metre of your body surface area as a single injection.

##### **To counteract the harmful effects of trimetrexate, trimethoprim, and pyrimethamine:**

**Harmful effects of trimetrexate (a medicine used to treat certain forms of pneumonia, especially in patients with AIDS):**  
To prevent toxicity caused by trimetrexate, you will receive Calcium Folate every day during treatment with trimetrexate, and until 72 hours after the last dose of trimetrexate. Your doctor will administer Calcium Folate by infusion for 5-10 minutes in a dose of 20 mg per square metre of your body surface area. This will be repeated every 6 hours, resulting in a total daily dose of 80 mg per square metre of your body surface area. Tablets are an alternative to infusion. Four times a day you will receive a dosage of 20 mg per square metre of your body surface area, equally divided over the day. Your doctor may decide to give you another dose. In case of overdosage of trimetrexate, your doctor will administer Calcium Folate after stopping trimetrexate. Calcium Folate will be administered in a vein every 6 hours for 3 days, in a dosage of 40 mg per square metre of your body surface area.

##### **Harmful effects of trimethoprim (an antibiotic used to treat certain infections):**

After stopping treatment with trimethoprim, you will receive 3-10 mg Calcium Folate daily. Your doctor will decide on the duration of this treatment.

##### **Harmful effects of pyrimethamine (a medicine that is used for the treatment of malaria and for an infection called toxoplasmosis, caused by a parasite):**

If you receive a high dose of pyrimethamine or if pyrimethamine is taken for a long period, you will receive 5-50 mg Calcium Folate per day simultaneously.

##### **If you use more Calcium Folate than you should**

If more Calcium Folate is given than recommended, the doctor will treat you as appropriate. If you suspect a serious overdose, talk to a doctor or pharmacist immediately. In case of a high dose, the effects as described in the section "possible side effects" can occur. If Calcium Folate is given in combination with methotrexate, too much Calcium Folate can diminish the effect of methotrexate.

##### **If you forget to use Calcium Folate**

When a dose is forgotten and Calcium Folate is given in combination with methotrexate, the toxic effects of methotrexate can occur (see Patient Information Leaflet of methotrexate). Consult your doctor when you have any doubt.

##### **If you stop using Calcium Folate**

When Calcium Folate is given in combination with methotrexate and treatment is stopped abruptly, the side effects of methotrexate, which were counteracted before by Calcium Folate, can appear. Therefore it is not advised to stop Calcium Folate abruptly.

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 notice any of the following symptoms:**

- sudden wheeziness, difficulty in breathing, swelling of the eyelids, face or lips, rash or itching (especially affecting your whole body)

- diarrhoea
- mucositis

Above mentioned reactions can be serious side effects. Your doctor can decide to discontinue the treatment.

#### **The following side effects have been reported:**

**Uncommon: may affect up to 1 in 100 people**  
Fever

**Rare: may affect up to 1 in 1,000 people**

Sleeplessness, agitation, depression and gastrointestinal disturbances after administration of high doses. In combination with certain anti-epileptics, the frequency of seizures is rarely increased (see also the paragraphs "Warning and precautions" and "Other medicines and Calcium Folate" in section 2).

**Very rare: may affect up to 1 in 10,000 people**

Severe allergic reactions, including a sudden feeling of illness, feeling of fear, chills, itching, paleness or redness, sweating, uncommon breathlessness, fast heart beat and shock (anaphylactic or anaphylactoid reaction) skin rash with intense itching (urticaria) and swelling of hands, feet ankles, face, lips mouth or throat (which may cause difficulty in swallowing or breathing).

#### **When given in combination with the medicine**

**5-fluorouracil the following side effects may also occur:**

**Very common: may affect more than 1 in 10 people**

- Diarrhoea (possibly severe and leading to drying out), vomiting and nausea
- 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 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 Yellow Card Scheme Website: [www.mhra.gov.uk/yellowcard](http://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 Calcium Folate**

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 package after EXP. The expiry date refers to the last day of that month.

Store in a refrigerator (2 °C-8 °C) in the original package.

Do not throw away any medicines via wastewater. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

#### **6 Contents of the pack and other information**

##### **Pharmaceutical form and content**

Calcium Folate is a solution for injection and contains calcium folinate corresponding to 10 mg of folinic acid per ml, which equals 50 mg folinic acid for the 5 ml vial, 100 mg for the 10 ml vial, 200 mg for the 20 ml vial, 300 mg for the 30 ml vial, and 500 mg for the 50 ml vial.

##### **What Calcium Folate contains**

- The active substance is calcium folinate corresponding to 50 mg (5 ml), 100 mg (10 ml), 200 mg (20 ml), 300 mg (30 ml), and 500 mg (50 ml) of folinic acid, respectively. Each ml solution for injection contains 10.8 mg of calcium folinate, equivalent to 10.0 mg of folinic acid.
- The other ingredients are sodium chloride, sodium hydroxide, hydrochloric acid, water for injections.

##### **What Calcium Folate looks like and contents of the pack**

Solution for injection.  
Calcium Folate 10 mg/ml, solution for injection is a clear, yellow, particle-free solution.

Calcium Folate is packed in clear, colourless Type I glass vials with chlorobutyl rubber stoppers, with aluminium crimping caps.

The vials contain 5 ml, 10 ml, 20 ml, 30 ml or 50 ml solution for injection.

Package size: 1 vial per carton.

##### **Marketing Authorisation Holder**

Teva UK Limited, Ridings Point, Whistler Drive, Castleford, WF10 5HX, United Kingdom

##### **Manufacturer**

Pharmachemie B.V, Swensweg 5, 2031 GA Haarlem, The Netherlands

**This leaflet was last revised November 2023.**

PL 00289/0851

135728\_s1

93.131.319-F