Product Name: **LEUCOVORIN**	Territory: **IE**	Colour: ● **BLACK** ● **DIE CUT** ● **TEAR OF SECTION**	1. Draft 02.11. 2015 06.30 Uhr 1. Correction 02.11. 2015 12.30 Uhr 2. Correction 03.11. 2015 11.20 Uhr 3. Correction 10.12. 2015 06.23 Uhr		Variable Data: **Batch no** **Lot** **Use before** **EXP**
Type of Packaging: **PIL**	Dosage: **1x5ml**				
Material number: **MOxxxxx/xx IE**	2-D-Matrix Code **X**				
Pharma-Code (Laetus)	EAN Code:				
Dimension: **210 x 520 mm**	Font: Interstate Smallest Size: 9 Pt.		Operator: **Christian Nagy** +43(0) 34 52 72266-22		

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Package leaflet: Information for the user

Folinic acid (as calcium folinate) 10 mg/ml solution for injection or infusion

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

What is in this leaflet:

1. What Folinic acid is and what it is used for

Folinic acid (as calcium folinate) 10 mg/ml solution for injection or infusion contains Folinic acid, which is one of a group of medicine called detoxifying agents. It is a calcium salt of folinic acid, which is related to the vitamin folic acid.

Folinic acid is used to:
- reduce the harmful effects and treat overdose of certain types of anti-cancer medicines for instance methotrexate and other folic acid antagonists. This is known as “calcium folinate rescue”.
- treat cancer in combination with 5-fluorouracil (an anti-cancer medicine). 5-fluorouracil works better when it is given together with Folinic acid.

2. What you need to know before you take Folinic acid

Do not take Folinic acid
- if you are allergic to Folinic acid 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 B_{12}, such as:
  - pernicious anaemia (your immune systems fights your red blood cells)
  - megaloblastic anaemia (your red blood cells are larger than normal)

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

Warnings and precautions
Talk to your doctor or nurse before using Folinic acid.

Folinic acid should only be given by intramuscular injection or intravenous injection or infusion and must not be administered intrathecally.

Please tell your doctor if you have any of the following illnesses or medical conditions:
- if you are being treated with 5-fluorouracil, especially if you are elderly or feel unwell, because Folinic acid 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 Folinic acid.
- if you suffer from epilepsy and use anti-epileptic medicines (such as phenobarbital, phenytoin, primidone or succinimides). Because there is a risk that your seizures (fits) may occur more often when you receive Folinic acid, 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, mecaptopurine, thioguanine), because you should not be treated with Folinic acid for this disease.
- if you have kidney problems, as your doctor might need to change your dose of Folinic acid.

Other medicines and Folinic acid
Tell your doctor if you are taking or have recently taken any other medicines.

Please tell your doctor if you are taking or have recently taken any of the following medicines:
- medicines which block the action of folic acid (folic acid antagonists) like cotrimoxazole (an antibiotic) or pyrimethamine (to treat special infections like malaria). Folinic acid can reduce the effectiveness of these medicines.
- medicines to treat epilepsy like phenobarbital, phenytoin, primidone or succinimides (e.g. ethosuximide, phensuximide). Folinic acid 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:
  Folinic acid 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, breast-feeding and fertility

Pregnancy
Folinic acid 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.

Breast-feeding
There are no adequate data for the use of Folinic acid 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.

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.

Driving and using machines
There is no evidence that Folinic acid has an effect on the ability to drive or use machines.

Folinic acid contains sodium
This medicinal product contains 3.14 mg/ml to 3.20 mg/ml (0.14 mmol/ml) sodium. To be taken into consideration by patients on a controlled sodium diet.

3. How to take Folinic acid

The combination of Folinic acid 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 receive more Folinic acid than you should
Reports of patients receiving significantly more Folinic acid than recommended dosage have not resulted in any symptoms. However, too much Folinic acid can reduce the efficacy of methotrexate.

If you have any further questions on the use of this product, 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 straight away if you get any sudden wheeziness, difficulty in breathing, swelling of the eyelids, face or lips, rash or itching (especially affecting your whole body) these could be symptoms of an allergic reaction to this medicine.

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

Rare: may affect up to 1 in 1,000 people:
- trouble sleeping (after high doses)
- agitation (an inability to keep still, after high doses)
- depression (after high doses)
- digestive tract disorders (after high doses) (like vomiting, nausea, diarrhoea and dehydration)
- increased frequency of seizures (fits) in patients with epilepsy

Very rare: may affect up to 1 in 10,000 people:
- allergic reactions, including serious allergic reactions with difficulty in breathing or dizziness and hives

The side effects of the combination of Folinic acid and 5-fluorouracil may vary. This depends on how often (once a week or once a month) the medicines are given. Elderly or frail patients are more likely to have side effects. Possible side effects include:

Weekly dosing:

Very common: may affect more than 1 in 10 people:
- severe diarrhoea and dehydration

Tell your doctor immediately if these symptoms occur. They can be life-threatening and may have to be treated in a hospital. Your doctor will decide if your treatment with 5-fluorouracil needs to be stopped until you feel better.

Monthly dosing:

Very common: may affect more than 1 in 10 people:
- vomiting
- nausea (feeling sick)
- severe mouth sores with ulcers, redness and swelling

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2, Tel: +353 1 6764971; Fax: +353 1 6762517; Website: www.hpra.ie; E-mail: medsafety@hpra.ie

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

The following information is intended for healthcare professionals only:

Incompatibilities
Folinic acid must not be mixed with other medicinal products except those mentioned in section “Handling”. Incompatibilities have been reported between injectable forms of Folinic acid and injectable forms of droperidol, fluorouracil, foscarnet and methotrexate.

Handling
For intramuscular injection or intravenous injection or infusion.
Fatal if given by other routes. Do not administer Folinic acid intrathecally.

For intravenous infusion, Folinic acid 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.

In the case of intravenous administration, no more than 160 mg of Folinic acid should be injected per minute due to the Calcium content of the solution.

5. How to store Folinic acid

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 vial and carton after EXP. The expiry date refers to the last day of that month.
Store in a refrigerator (2°C to 8°C).

Keep the vial in the outer carton in order to protect from light.

After first opening: For Single Dose Use Only. Discard any unused solution immediately after initial use.

After dilution:
When diluted according to directions with 0.9% sodium chloride solution or 5% glucose solution, chemical and physical in-use stability has been demonstrated when protected from light.

Chemical and physical in-use stability after dilution to 1.5 mg/ml with either 0.9% sodium chloride solution or 5% glucose solution was demonstrated for up to 24 hours, at both room temperature (25°C) and 2°C -8°C, when protected from light.

Chemical and physical in-use stability after dilution to 0.2 mg/ml with 0.9% sodium chloride solution was demonstrated for up to 24 hours at 2°C - 8°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 would normally not be longer than 24 hours at 2°C -8°C, unless dilution has taken place in controlled and validated aseptic conditions.

If the solution appears discoloured or contains visible particles, it should be discarded.

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 protect the environment.

6. Contents of the pack and other information

What Folinic acid contains
- The active substance is Folinic acid. Each ml contains 10 mg of folinic acid provided as calcium folinate.

Each 5, 10, 20, 35, 50, 100 ml vial contains 50, 100, 200, 350, 500 and 1000 mg of folinic acid respectively (provided as calcium folinate).

The other ingredients are: Sodium chloride, sodium hydroxide (for pH-adjustment), hydrochloric acid (for pH-adjustment), and water for injections.

What Folinic acid looks like and contents of the pack

This medicine is a solution for injection or infusion. It is a clear, yellowish solution, free from visible particles. It is filled in amber coloured glass vial, with chlorobutyl rubber stopper and sealed with red, yellow, violet, white, brown and orange aluminium flip-off closure, containing 5 ml, 10 ml, 20 ml, 35 ml, 50 ml or 100 ml solution for injection or infusion, respectively.

Package sizes:

The packages contain either 1, 5 or 10 vials of 5 ml, 10 ml, 20 ml, 35 ml, 50 ml or 100 ml, respectively.

Not all pack sizes may be marketed.

Marketing Authorisation Holder
Fresenius Kabi Deutschland GmbH
Else-Kroener Strasse 1,
Bad Homburg v.d.H. 61352,
Germany

Manufacturer
Fresenius Kabi Austria GmbH
Hafnerstrasse 36, Graz
A-8055
Austria

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

Austria	Calciumfolinat Kabi 10 mg/ml Injektions-/ Infusionslösung
Belgium	Folikabi 10 mg/ml, oplossing voor injectie/ infusie
Czech Republic	Calcium Folinate Kabi 10 mg/ml, injekční/ infuzní roztok
Germany	Calciumfolinat Kabi 10 mg/ml Injektions-/ Infusionslösung
Denmark	Calciumfolinat Fresenius Kabi
Spain	Folinato cálcico Kabi 10 mg/ml solución inyectable o para perfusión EFG
Finland	Calciumfolinat Fresenius Kabi
Hungary	Calcium Folinate Kabi 10 mg/ml oldatos injekció vagy infúzió
Ireland	Folinic acid (as calcium folinate) 10 mg/ml solution for injection or infusion
Luxembourg	Calciumfolinat Kabi 10 mg/ml Injektions-/ Infusionslösung
Malta	Calcium Folinate 10 mg/ml, Solution for Injection or Infusion
The Netherlands	Folikabi 10 mg/ml, oplossing voor injectie/ infusie
Poland	Calcium Folinate Kabi
Portugal	Folinato de Cálcio Kabi
Romania	Calcium Folinate calciu Kabi 10 mg/ml soluție injectabilă / perfuzabilă
United Kingdom	Calcium Folinate 10 mg/ml, Solution for Injection or Infusion

This leaflet was last revised in Oct 2015

Shelf life
After first opening: For Single Dose Use Only. Discard any unused solution immediately after initial use.
After dilution:
When diluted according to directions with 0.9% sodium chloride solution or 5% glucose solution, chemical and physical in-use stability has been demonstrated when protected from light.

Chemical and physical in-use stability after dilution to 1.5 mg/ml with either 0.9% sodium chloride solution or 5% glucose solution was demonstrated for up to 24 hours, at both room temperature (25°C) and 2°C -8°C, when protected from light.

Chemical and physical in-use stability after dilution to 0.2 mg/ml with 0.9% sodium chloride solution was demonstrated for up to 24 hours at 2°C - 8°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 would normally not be longer than 24 hours at 2°C -8°C, unless dilution has taken place in controlled and validated aseptic conditions.

Disposal:
Any unused product or waste material should be disposed of in accordance with local requirements.