Package leaflet: Information for the patient

Amekrin 75 mg/1.5 ml concentrate and solvent for concentrate for solution for infusion

amsacrine

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

What is in this leaflet

1. What Amekrin is and what it is used for

Amekrin belongs to a group of medicines called cytostatics (medicine for the treatment of cancer).
It is used to treat acute myeloid leukaemia also known as AML. AML is a form of cancer of the blood and bone marrow.
Amekrin is used in adults, whose disease has not responded to other therapies or in case of relapse.

2. What you need to know before you use Amekrin

Do not use Amekrin:
- if you are allergic to amsacrine or acridine derivates or any of the other ingredients of this medicine (listed in section 6)
- if you are already receiving (or have recently received) other treatments for cancer
- if you are breast-feeding.

Talk to your doctor before you use this medicine if any of these conditions apply to you.

Warnings and precautions
Talk to your doctor, pharmacist or nurse before you are given Amekrin.
Your doctor will take special care if any of the following conditions apply to you.
- You have ever had kidney or liver disease
- You have any problem with your heart
- You have been told that the potassium level in your blood is too low
- You suffer from porphyria.

Talk to your doctor before you use this medicine if any of these conditions apply to you.

Children and adolescents
Amekrin should only be used by adults. Amekrin shall not be used by children or adolescents under the age of 18 years.

Regular examinations
Your doctor will be making regular medical examinations, e.g. blood tests to check your blood cell counts, your kidney and liver function as well as examination of your heart.

Other medicines and Amekrin
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.
A large numbers of medicines can interact with Amekrin which can significantly alter their effects. These medicines include:
- Influenza or pneumococcal vaccinations
- Live vaccines
- Other medicines used in the treatment of cancer
- Methotrexate used in the treatment of e.g. cancer or rheumathoid arthritis

If you are already taking any of these medicines, speak to your doctor before you receive Amekrin.

Pregnancy, breast-feeding and fertility
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.

Pregnancy
This medicine should only be given during pregnancy if absolutely necessary. The benefit of your treatment must be outweighed against the risk to your unborn baby.

Pregnancy precautions for men and women
Women of childbearing potential must use effective contraception during and up to 3 months after treatment. Men must use effective contraception during and up to 6 months after treatment.

Breast-feeding
Do not breast-feed during treatment with Amekrin.

Fertility
There is some evidence suggesting that Amekrin has a negative impact on the fertility in women. Some evidence suggest a reversible negative effect on male fertility.

Driving and using machines
Amekrin is not likely to affect your ability to drive or use machinery. However, if you experience side effects such as headache, dizziness following administration of the infusion be cautious when driving or using machines.

3. How to use Amekrin

You will normally be given Amekrin by a doctor or a nurse experienced in the use of cytostatics in a hospital.
Amekrin will be slowly injected as an infusion into a vein over 1-2 hours.
The dose will be calculated by your doctor according to your age and the surface area of your body (normally 300-650 mg per square metre per treatment period).

Initial treatment
You will be given one infusion a day for 3-7 days.

Further treatment
Following this initial dosing period, further doses will be given, depending on the number of your blood cells.
If Amekrin decreases the number of your blood cells too much, it may be necessary for your doctor to give you a blood transfusion.

If you have any further questions on the use of this medicinal product, ask your doctor.

If you use more Amekrin than you should
As the infusion will be administered under the supervision of a doctor, it is unlikely that you will be given more than necessary. However, if you have any concerns about the dose of your medicine discuss them with your doctor.

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.

All medicines can cause allergic reactions although serious allergic reactions are rare. Any sudden wheeziness, difficulty in breathing, swelling of the eyelids, face or lips, rash or itching (especially affecting your whole body) should be reported to a doctor immediately.

Very common (may affect more than 1 in 10 people)
- Minor bleeding of skin and mucous membranes
- Diarrhoea, stomach ache
- Low blood pressure
- Pain and swelling at the injection site due to inflammation of a blood vessel
- Increase in liver values
- Inflammation of the mouth
- Nausea, vomitting.

Common (may affect up to 1 in 10 people)
- Severe reduction in blood cells which can cause weakness, bruising or bleeding, or make infections more likely
- Bleeding
- Severe heart problems (e.g. heart failure causing breathlessness), irregular heart beat
- Fits
- Inflammation of the liver, jaundice (this causes yellowing of the skin and of the whites of yours eyes), impaired liver function
- Blood in your urine
- Loss of skin, inflammation of the skin
- Infection
- Fever
- Shortness of breath
- Low levels of potassium which can cause muscle weakness, twitching or abnormal heart rhythm
- Mood swings
- Hair loss
- Nettle rash, rash
- Irritation at the injection site.

Rare (may affect up to 1 in 1,000 people)
- Other severe heart problems (e.g. life-threatening irregular heart beat, racing heart beat, slow heart beat, ECG changes)
- Anaemia, a reduction in red blood cells which can make the skin pale and cause weakness or breathlessness
- Severe reduction in the number of white blood cells which makes infections more likely
- Severe allergic reaction, swelling due to excess fluid in the body, hypersensitivity,
- Impaired kidney function (e.g. absence of urine, kidney failure)
- Weight decreased, weight increased
- Lethargy (extreme fatigue or drowsiness), confusion
- Headache, dizziness
- Reduced sense of touch or sensation

- A disorder of the nerves which can cause weakness, tingling or numbness
- Visual disturbances
- Proteins in the urine
- Liver and kidney tests abnormal

Not known (frequency cannot be estimated from the available data)
- High levels of uric acid in the blood

Althoug the above list of possible side effects appears daunting, acute leukemia is a serious disease which requires aggressive treatment.

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 national reporting system listed in AppendixV*. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Amekrin

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

Do not store above 25°C.

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

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 Amekrin contains

- The active substance is amsacrine. Each ml of concentrate for solution for infusion contains 50 mg amsacrine. Each vial contains 75 mg amsacrine
- The other ingredients are N, N, dimethylacetamide, lactic acid and water for injection.

What Amekrin looks like and contents of the pack
Amekrin comes in sets with one clear glass vial of concentrate and one clear glass vial with solvent. The vials with concentrate contains the active ingredient amsacrine and N, N, dimethylacetamide in 1.5 ml clear bright orange/red liquid.
The vial with solvent contains 13.5 ml of a solution of lactic acid in water for injection as a clear solution.

Pack size
1 x 6 vials of concentrate for solution for infusion and 6 vials of solvent for solution for infusion.

Marketing Authorisation Holder and Manufacturer
Eurocept International BV
Trapgans 5
1244 RL Ankeveen
The Netherlands

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

Name of the Member state	Name of the medicinal product
Austria	Amsidyl 75 mg/1,5 ml Konzentrat und Lösungsmittel für ein Konzentrat zur Herstellung einer Infusionslösung
Belgium	Amsdine 75 mg/1,5 ml concentraat en oplosmiddel voor concentraat voor oplossing voor infusie
Czech Republic	Amsidyl 75 mg/1,5 ml koncentrát a rozpouštědlo koncentrátu pro infuzní roztok
Denmark	Amekrin 75 mg/1,5 ml koncentrat og fortyndermiddel til koncentrat til opløsning med henblik på infusion
Finland	Amekrin 75 mg/1,5 ml konsentraatti ja liuotin välikonsentraatiksi infuusionestettä varten, liuos
Germany	Amsidyl 75 mg/1,5 ml Konzentrat und Lösungsmittel für ein Konzentrat zur Herstellung einer Infusionslösung
Iceland	Amekrin 75 mg/1,5 ml þykkni og leysir fyrir innrennslisþykkni, lausn
Ireland	Amsidine 75 mg/1.5 ml Concentrate and Solvent for Concentrate for Solution for Infusion
Italy	Amsadina 75 mg/1,5 ml concentrato e solvente per concentrato per soluzione per infusione
Luxembourg	Amsidine 75 mg/1,5 ml solution à diluer et solvant pour solution à diluer pour perfusion
Malta	Amsidine 75 mg/1.5 ml Concentrate and Solvent for Concentrate for Solution for Infusion
The Netherlands	Amsidine 75 mg/1,5 ml concentraat en oplosmiddel voor concentraat voor oplossing voor infusie
Norway	Amekrin 75 mg/1,5 ml konsentrat og væske til konsentrat til infusjonsvæske, oppløsning
Poland	Amsidyl, 75 mg/1,5 ml, koncentrat i rozpuszczalnik do sporządzania roztworu do infuzji
Portugal	Amekrin 75 mg/1,5 ml concentrado e solvente para concentrado para solução para perfusão
Slovakia	Amsidyl 75 mg/1,5 ml koncentrát a rozpúšťadlo na infúzny koncentrát
Spain	Amekrin 75 mg/1,5 ml - Concentrado y disolvente para concentrado para solución para perfusión
Sweden	Amekrin 75 mg/1,5 ml koncentrat och vätska till koncentrat till infusionsvätska, lösning
United Kingdom	Amsidine 75 mg/1.5 ml Concentrate and Solvent for Concentrate for Solution for Infusion

This leaflet was last revised in 2021-03-25.

The following information is intended for healthcare professionals only:

Method of administration and handling
Cytostatics should be handled in accordance with national requirements.

Administration
Intravenous use.
Amekrin is administered as an intravenous infusion in a glucose solution over 1-2 hours.
At doses of 125 mg/m^2 or higher the duration of infusion should be at least 90 minutes.

Preparation of the medicinal product The concentrate for solution for infusion must be diluted with the enclosed solvent. The diluted solution is then added to at least 500 ml glucose 50 mg/ml. Solutions other than glucose may not be used. Amsacrine is incompatible with chloride ions. Sodium chloride solutions may not be used.

Only glass syringes may be used when removing and transferring the concentrated solutions. 1.5 ml of the concentrate for solution for infusion is transferred aseptically to the injection bottle containing the solvent and is gently shaken until a clear solution is obtained (concentration of the solution is 5 mg/ml amsacrine). 75, 90 and 120 mg amsacrine corresponds to 15, 18 and 24 ml diluted solution, respectively.

Note: the diluted solution may not be injected before it has been further diluted with at least 500 ml glucose solution 50 mg/ml.

Handling
In case the solution comes into contact with eyes or mucous membranes rinse with plenty of water and in contact with the skin immediately wash thoroughly with soap and water. If irritation persists after washing you must contact a doctor. In the case of extravasal administration rinse with a small amount of glucose solution 50 mg/ml after which the body part is immediately cooled down. The infusion is stopped and started in a different vessel.

Shelf life
Diluted solution (mixed concentrate and solvent, before further dilution):
The diluted solution should be used immediately for further dilution. However the chemical and physical in-use stability has been demonstrated for 48 hours when stored at 2° C – 25° C. If stored for 24-48 hours the diluted solution should be further diluted and used immediately.

Solution for infusion:
Chemical and physical in-use stability of the solution for infusions has been demonstrated for 48 hours at 2° C – 25° C. The chemical and physical in-use stability for the diluted solution from first dilution and the further diluted solution for infusion has not been demonstrated for more than a total of 48 hours.

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 reconstitution/dilution has taken place in controlled and validated aseptic conditions.

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