Package leaflet: Information for the user

Clofarabine 1 mg/ml concentrate for solution for infusion

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 Clofarabine is and what it is used for

Clofarabine contains the active substance clofarabine. Clofarabine is one of a family of medicines called anticancer medicines. It works by hindering the growth of abnormal white blood cells, and eventually kills them. It works best against cells which are multiplying quickly – such as cancer cells.

Clofarabine is used to treat children (≥ 1 year old), teenagers and young adults up to 21 years old with acute lymphoblastic leukaemia (ALL) when previous treatments have not worked or have stopped working. Acute lymphoblastic leukaemia is caused by abnormal growth of some types of white blood cells.

2. What you need to know before you use Clofarabine

Do not use Clofarabine:
- if you are allergic to clofarabine or any of the other ingredients of this medicine (listed in section 6);
- **if you are breast-feeding** (please read the section "*Pregnancy and breast-feeding*" below);
- **if you have severe kidney or liver problems.**

Tell your doctor if any of these conditions apply to you. If you are the parent of a child who is being treated with Clofarabine, **tell the doctor if any of them apply to your child.**

Warnings and precautions
Talk to your doctor or pharmacist before using Clofarabine.

Tell your doctor if any of these apply to you. Clofarabine may not be suitable for you:
- **if you have suffered a severe reaction** after previously using this medicine;
- **if you have kidney disease**, or used to have it;
- **if you have liver disease**, or used to have it;
- **if you have heart disease**, or used to have it.

Tell your doctor or carer immediately if you experience any of the following as you may need to stop treatment:

- if you get a fever or high temperature – because clofarabine reduces the number of blood cells made in the bone marrow, you may be more likely to catch infections;
- if you have breathing difficulties, rapid breathing, or breathlessness;
- if you feel a change in your heart rate;
- if you suffer from dizziness (light-headedness) or fainting – it may be a symptom of low blood pressure;
- if you feel sick or have diarrhoea (loose bowels);
- if your urine is darker than usual – it is important to drink plenty of water to avoid dehydration;
- if you get a rash with blisters or mouth ulcers;
- if you lose your appetite, have nausea (feeling sick), vomiting, diarrhoea, dark-coloured urine and light-coloured stools, stomach pain, jaundice (yellowing of the skin and eyes), or if you feel generally unwell, these could be symptoms of an inflammation of the liver (hepatitis), or liver damage (hepatic failure);
- if you pass little or no urine, or experience drowsiness, nausea, vomiting, breathlessness, loss of appetite and / or weakness (these may be signs of acute kidney failure / kidney failure).

If you are the parent of a child who is being treated with Clofarabine, **tell the doctor if any of the above conditions apply to your child.**

During treatment with Clofarabine your doctor will carry out regular blood tests and other tests to monitor your health. Because of the way this medicine works, it will affect your blood and other organs.

Talk to your doctor about contraception. Young men and women must use effective contraception during and after treatment. See the section *"Pregnancy and breast-feeding"* below. Clofarabine may harm both male and female reproductive organs. Ask your doctor to explain what can be done to protect you or allow you to have a family.

Other medicines and Clofarabine
Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines.

Tell your doctor if you are using or have recently used:
- medicines for heart disease;
- any medicine that changes your blood pressure;
- medicines that affect your liver or kidneys;
- any other medicines including those obtained without a prescription.

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.

Clofarabine should not be used during pregnancy unless clearly necessary.
Women who are able to get pregnant: you must use effective contraception during treatment with clofarabine. Clofarabine may cause harm to unborn babies when used by pregnant women. If you are pregnant or you become pregnant during treatment with clofarabine, **get medical advice immediately**.

Men must also use effective contraception while they or their partner are treated with clofarabine.

If you are breast-feeding, you must stop breast-feeding before starting the treatment, and must not breast-feed during your treatment and within 3 months after completion of your treatment.

Driving and using machines
Do not drive or use any tools or machines if you feel dizzy, light-headed or faint.

Clofarabine contains sodium
This medicine contains 70.77 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 3.54% of the recommended maximum daily dietary intake of sodium for an adult. This is equivalent to 3.08 mmol of sodium. The recommended maximum level of intake of 2 g/day sodium in adults should be adjusted downward based on the energy requirements of children relative to those of adults.

3. How to use Clofarabine

Your treatment with Clofarabine has been prescribed by a qualified doctor experienced in treating leukaemia.

Your doctor will work out the dose that is right for you depending on your height, weight and how well you are. Before Clofarabine is given to you, it will be diluted in a sodium chloride solution (salt and water). Tell your doctor if you are on a controlled sodium diet as it could affect how you will be given your medicine.

Your doctor will give you Clofarabine once every day for 5 days. It will be given to you as an infusion through a long thin tube which goes into a vein (a drip), or into a small medical appliance that is inserted under the skin (port-a-cath) if you (or your child) have one implanted. The infusion will be given over 2 hours. If you (or your child) weigh less than 20 kg, the infusion time may be longer.

Your doctor will monitor your health and may change your dose depending on your response to the treatment. It is important to drink plenty of water to avoid dehydration.

If you use more Clofarabine than you should
If you think you may have been given too much medicine, tell your doctor straight away.

If you forget to use Clofarabine
Your doctor will tell you when you need to be given this medicine. If you think that you have missed a dose, tell your doctor straight away.

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 common (may affect more than 1 in 10 people):
- anxiety, headache, fever, tiredness;
- feeling and being sick, diarrhoea (loose bowels);
- flushing, itching and inflamed skin, inflammation of mucus (moist) linings such as the mouth and other areas;
- you may have more infections than normal because Clofarabine can lower the number of certain types of blood cells in your body;
- skin rashes which may be itchy, red, painful or peeling skin including palms of the hands and soles of the feet, or small reddish or purple spots underneath the skin.

Common (may affect up to 1 in 10 people):
- infections of the blood, pneumonia, shingles, implant infections, infections of the mouth such as thrush and cold sores;
- changes in blood chemistry, changes in white blood cells;
- allergic reactions;

- feeling thirsty and producing darker or less urine than normal, decreased or loss of appetite, weight loss;
- agitation, irritability, or restlessness;
- feeling numb or weak in the arms and legs, numbness of the skin, sleepiness, dizziness, tremor;
- hearing problems;
- water collecting around the heart, fast heartbeat;
- low blood pressure, lump due to bad bruising;
- leaking from tiny blood vessels, rapid breathing, nosebleeds, breathing difficulties, breathlessness, cough;
- vomiting blood, stomach ache, pain in the bottom;
- bleeding inside the head, stomach, intestine or lungs, mouth or gums, mouth ulcers, inflamed mouth lining;
- yellowing of the skin and eyes (also called jaundice), or other liver disorders;
- bruising, hair loss, changes to skin colour, increased sweating, dry skin, or other skin problems;
- pain in the chest wall or bones, neck or back pain, pain in limbs, muscles, or joints;
- blood in urine;
- failure of organs, pain, increased muscle tension, water retention and swelling in parts of the body, including the arms and legs, changes in mental state, feeling hot, cold or abnormal;
- clofarabine may affect the levels of certain substances in the blood. Your doctor will carry out regular blood tests to check whether your body is working properly;
- liver damage (liver failure);
- little or no urine, drowsiness, nausea, vomiting, breathlessness, loss of appetite and /or weakness (possible signs of acute kidney failure or kidney failure).

Uncommon side effects (may affect up to 1 in 100 people):
- inflammation of the liver (hepatitis).

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 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 Clofarabine

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 label and carton after EXP. The expiry date refers to the last day of that month.

This medicine does not require any special storage conditions.

Once prepared and diluted, Clofarabine should be used straight away or within 24 hours if stored in a refrigerator (at 2°C to 8°C).

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 Clofarabine contains

- The active substance is clofarabine. Each ml contains 1 mg of clofarabine. Each 20 ml vial contains 20 mg of clofarabine.
- The other ingredients are sodium chloride and water for injections

What Clofarabine looks like and contents of the pack
A clear, colourless solution, free from visible particles, filled in 20 ml glass (type I) vial with grey bromobutyl rubber stopper and aluminium flip off dark blue seal.

Each pack contains 1 single use vial.

Marketing Authorisation Holder
Neon Healthcare Ltd
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This leaflet was last revised in 08/2023.

Clofarabine contains the same active substance and works in the same way as a "reference medicine" already authorised in the EU. The reference medicine for Clofarabine has been authorised under "exceptional circumstances". This means that because of the rarity of this disease it has been impossible to get complete Information on the reference medicine. The European Medicines Agency will review any new information on the reference medicine every year and any updates for the reference medicine will also be included as appropriate in the information for Clofarabine, such as this leaflet.

The following information is intended for healthcare professionals only:

Special precautions for administration

Clofarabine 1 mg/ml concentrate for solution for infusion must be diluted prior to administration. It should be filtered through a sterile 0.2 micrometre syringe filter and then diluted with sodium chloride 9 mg/ml (0.9%) intravenous infusion to produce a total volume according to the examples given in the table below. However, the final dilution volume may vary depending on the patient's clinical status and physician discretion. (If the use of a 0.2 micrometre syringe filter is not feasible, the concentrate should be pre-filtered with a 5 micrometre filter, diluted and then administered through a 0.22 micrometre inline filter.)

Suggested dilution schedule based on the recommended dosage of 52 mg/m^2/day clofarabine		
Body surface area (m^2)	**Concentrate (ml)***	**Total diluted volume**
≤ 1.44	≤ 74.9	100 ml
1.45 to 2.40	75.4 to 124.8	150 ml
2.41 to 2.50	125.3 to 130.0	200 ml
*Each ml of concentrate contains 1 mg of clofarabine. Each 20 ml vial contains 20 mg of clofarabine. Therefore, for patients with a body surface area ≤ 0.38 m^2, the partial contents of a single vial will be required to produce the recommended daily dosage of clofarabine. However, for patients with a body surface area > 0.38 m^2, the contents of between 1 to 7 vials will be required to produce the recommended daily dosage of clofarabine.		

The diluted concentrate should be a clear, colourless solution. It should be visually inspected for particulate matter and discolouration prior to administration.

The diluted concentrate is chemically and physically stable for 3 days at 2°C to 8°C and at room temperature (up to 25°C). From a microbiological point of view, it 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 to 8°C unless dilution has taken place under controlled and validated aseptic conditions. Do not freeze.

Instructions for handling

Procedures for proper handling of antineoplastic agents should be observed. Cytotoxic medicinal products should be handled with caution.

The use of disposable gloves and protective garments is recommended when handling Clofarabine. If the product comes into contact with eyes, skin or mucous membranes, rinse immediately with copious amounts of water.
Clofarabine should not be handled by pregnant women.

Disposal

Clofarabine is for single use only. Any unused medicinal product or waste material should be disposed of in accordance with local requirements