Package leaflet: Information for the user

Defitelio 80 mg/mL concentrate for solution for infusion
defibrotide

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

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

What is in this leaflet:

1. What Defitelio is and what it is used for

Defitelio is a medicine that contains the active substance defibrotide.

It is used to treat a condition called hepatic veno-occlusive disease, in which the blood vessels in the liver become damaged and obstructed by blood clots. This can be caused by medicines that are given prior to a stem cell transplantation.

Defibrotide works by protecting the cells of the blood vessels and preventing or breaking down the blood clots.

This medicine can be used in adults, and in adolescents, children and infants over one month of age.

2. What you need to know before you take Defitelio

Do not use Defitelio
- if you are allergic to defibrotide or any of the other ingredients of this medicine (listed in section 6)
- if you are using other medicines to break down blood clots such as tissue plasminogen activator

Warnings and precautions
Talk to your doctor before using Defitelio:
- if you are taking medicine that increases the risk of bleeding
- if you have heavy bleeding and need a blood transfusion
- if you are undergoing surgery
- if you have problems with blood circulation because your body cannot maintain a constant blood pressure.

Children and adolescents
Defitelio is not recommended in children less than 1 month of age.

Other medicines and Defitelio
Tell your doctor if you are taking medicines to prevent blood clotting such as acetylsalicylic acid, heparins, warfarin, dabigatran, rivaroxaban or apixaban or if you are taking anti-inflammatory medicines (e.g., ibuprofen, naproxen, diclofenac and other non-steroidal anti-inflammatory medicines).

Pregnancy and breast-feeding
Do not use Defitelio if you are pregnant unless your disease requires treatment with Defitelio.
If you are sexually active and you or your partner could become pregnant, you both must use effective contraception during treatment with Defitelio and for 1 week after stopping the treatment.

Driving and using machines
It is not expected that Defitelio will affect your ability to drive and operate machines.

Defitelio contains sodium
This medicine contains less than 23 mg of sodium, which means it is essentially "sodium-free".

3. How you will be given Defitelio

The treatment with Defitelio can be initiated and continuously supervised only by an experienced doctor in a hospital or in a specialised centre for stem cells transplantation.

It will be slowly injected (over a 2-hour period) into one of your veins. This is called an 'intravenous infusion' or drip.

You will receive this treatment four times a day for at least 21 days or until your symptoms resolve.
The recommended dose in children from one month to 18 years of age is the same as in adults.

If a dose of Defitelio has been forgotten
As you will be given this medicine by a doctor or a nurse it is unlikely that a dose will be missed. However, tell your doctor or healthcare professional if you think that a dose has been forgotten. You must not be given a double dose to make up for a missed dose.
If you have any further questions on the use of this medicine, ask your doctor, nurse or pharmacist.

4. Possible side effects

Like all medicines, Defitelio can cause side effects, although not everybody gets them. For patients treated with Defitelio the following side effects were reported.

If you experience any of these side effects, you should **contact your doctor immediately**.

Very Common (may affect more than 1 in 10 people)

- low blood pressure

Common (may affect up to 1 in 10 people)

- bleeding in general
- bleeding from the nose
- bleeding in the brain
- bleeding in the gut
- vomiting blood
- bleeding in the lungs
- bleeding from the infusion line
- blood in the urine

- bleeding from the mouth
- bleeding into the skin
- coagulopathy (disturbance of blood clotting)
- nausea
- vomiting
- diarrhoea
- rash
- itching
- fever

Uncommon (may affect up to 1 in 100 people)

- bleeding from the eye
- blood in the stool
- bleeding at the site of injection
- localized blood collection out of the vessel (hematoma) in the brain
- haemothorax (accumulation of blood in the area between the heart and the lung)
- bruising
- severe allergic reaction (you might experience swelling of the hands, face, lips, tongue or throat, difficulty in breathing).

Children and adolescents
Side effects in children (1 month to 18 years old) are expected to be similar in type, severity and frequency and no other special precautions are needed.

Reporting of side effects
If you get any side effects, talk to your doctor. 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 Defitelio

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

Do not use Defitelio after the expiry date which is stated on the carton and vial label after EXP. The expiry date refers to the last day of that month.

Do not freeze.

Once diluted for use the infusion storage should not exceed 24 hours at 2°C -8°C unless dilution has taken place in controlled and validated aseptic conditions.

Defitelio should not be used if the solution is cloudy or contains particles.

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

What Defitelio contains

- The active substance is defibrotide. Each 2.5 mL vial contains 200 mg defibrotide and each mL solution contains 80 mg defibrotide.
- The other ingredients are sodium citrate dihydrate, hydrochloric acid and sodium hydroxide (both for pH-adjustment) and water for injections (see section 2 ‘Defitelio contains Sodium’).

What Defitelio looks like and contents of the pack
Defitelio is a clear light yellow to brown concentrate for solution for infusion, free from particulate matter or turbidity.

One carton contains 10 glass vials with 2.5 mL of concentrate each.

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This medicine has been authorised under 'exceptional circumstances'. This means that because of the rarity of this disease and for ethical reasons it has been impossible perform a placebo-controlled clinical trials and to get complete information on this medicine.

The European Medicines Agency will review any new information on this medicine every year and this leaflet will be updated as necessary.

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu. There are also links to other websites about rare diseases and treatments.
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