Package leaflet: Information for the patient

Vyxeos liposomal 44 mg/100 mg powder for concentrate for solution for infusion
daunorubicin and cytarabine

Read all of this leaflet carefully before you start taking 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 Vyxeos liposomal is and what it is used for
2. What you need to know before you are given Vyxeos liposomal
3. How you are given Vyxeos liposomal
4. Possible side effects
5. How to store Vyxeos liposomal
6. Contents of the pack and other information

1. What Vyxeos liposomal is and what it is used for

What Vyxeos liposomal is
Vyxeos liposomal belongs to a group of medicines called 'antineoplastics' used in cancer. It contains two active substances, called 'daunorubicin' and 'cytarabine', in the form of tiny particles known as 'liposomes'.
These active substances act in different ways to kill cancer cells by stopping them from growing and dividing. Packaging them in liposomes prolongs their action in the body and helps them to enter and kill the cancer cells.

What Vyxeos liposomal is used for
Vyxeos liposomal is used to treat patients with newly diagnosed acute myeloid leukaemia (a cancer of the white blood cells). It is given when the leukaemia was caused by previous treatments (known as therapy related acute myeloid leukaemia) or when there are certain changes in the bone marrow (known as acute myeloid leukaemia with "myelodysplasia-related changes").

2. What you need to know before you are given Vyxeos liposomal

You must not be given Vyxeos liposomal
- if you are allergic to the active substances (daunorubicin or cytarabine) or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Your doctor will monitor you during treatment. Talk to your doctor or nurse before you are given Vyxeos liposomal:
- if you have low numbers of platelets, red or white blood cells in your blood (you will have a blood test before starting treatment). If this applies to you:
  - your doctor may also give you a medicine to help stop you getting an infection.
  - your doctor will also check you for infections during treatment.
- if you have ever had a heart problem or heart attack, or you have previously taken 'anthracycline' cancer medicines. If this applies to you, your doctor may check your heart before starting, and during treatment.

- if you think you might be pregnant. You should use an effective method of contraception to avoid getting (you or your partner) pregnant during the treatment, and for the next 6 months after your last dose.
- if you have any allergic (hypersensitivity) reactions. Your doctor may pause or stop treatment, or slow the rate of your drip, if any hypersensitivity occurs.
- if you have had problems with your kidneys or liver. Your doctor will monitor you during treatment.
- if you have ever had a condition known as Wilson's disease or other copper-related disorder, as Vyxeos liposomal contains an ingredient known as 'copper gluconate'.
- if you are to be given a vaccine.

Your doctor will monitor you with regards to your general health during treatment and may also give you other medicines to support your treatment, either before or with Vyxeos liposomal. If any of the above apply to you (or you are not sure), talk to your doctor, pharmacist, or nurse before you are given Vyxeos liposomal.

Children and adolescents
Vyxeos liposomal is not recommended for use in children and adolescents under 18 years.

Other medicines and Vyxeos liposomal
Tell your doctor or nurse if you are using, have recently used or might use any other medicines. This is because Vyxeos liposomal may affect the way some other medicines work. Also, some other medicines may affect the way Vyxeos liposomal works.

In particular, tell your doctor or nurse if you are taking any of the following medicines:
- cancer medicines that can affect your heart, such as doxorubicin.
- medicines that can affect your liver.

Pregnancy and breast-feeding
You should not use Vyxeos liposomal during pregnancy as it may be harmful to the baby. Use an effective method of contraception during and for 6 months after treatment. Tell your doctor straight away if you become pregnant during treatment.

You should not breast-feed while you are receiving treatment with Vyxeos liposomal as it may be harmful to the baby.

If you are pregnant or breast-feeding, think you may be pregnant, or are planning to have a baby, ask your doctor for advice before you are given this medicine.

Driving and using machines
You may feel sleepy or dizzy after having Vyxeos liposomal. If this happens, do not drive or use any tools or machines.

3. How you are given Vyxeos liposomal

Vyxeos liposomal must be given to you by a doctor or nurse with experience in treating AML.
- It is given to you as a drip (infusion) into a vein.
- The infusion is given over one and a half hours (90 minutes).

Your doctor or nurse will work out your dose of the medicine based on your weight and height. Your treatment will be given in 'courses'. Each course is given as a separate infusion and can be given weeks apart.

You will receive a first course of treatment and your doctor will decide if you will receive further courses of treatment depending on how you respond to treatment and any side effects you get. Your doctor will assess how you respond to treatment after each course.

- During your first course - you will have an infusion on days 1, 3, and 5.
- On further courses - you will have an infusion on days 1 and 3. This can be repeated if necessary.

While you are receiving treatment with Vyxeos liposomal your doctor will perform regular blood tests to assess how you respond to the treatment and to check it is well tolerated. Your doctor may also check your heart as Vyxeos liposomal may affect it.

If you are given too much Vyxeos liposomal
This medicine will be given to you in a hospital by a doctor or nurse. It is unlikely that you will be given too much, however, tell your doctor or nurse if you have any concerns.

If you miss an appointment
Contact your doctor or nurse as soon as possible.

If you have any further questions on the use of this medicine, ask your doctor or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects which may affect more than 1 in 10 people (very common)
Vyxeos liposomal may reduce the number of white blood cells, which fight infection, and also the blood cells which help the blood to clot (platelets) leading to bleeding disorders such as nosebleeds and bruising. Vyxeos liposomal may also cause heart problems and damage to the heart muscle.

Therefore **you must tell your doctor immediately** if you experience:
- fever, chills, sore throat, cough, mouth ulcers or any other symptoms of infection
- bleeding or bruising without injury
- chest pain or leg pain
- feeling short of breath.

Tell your doctor immediately if you get any of the side effects listed above.

Other side effects

Very common side effects (may affect more than 1 in 10 people):
- a fall in the number of platelets (cells that help blood to clot) which may cause bruising or bleeding
- fever, often with other signs of infection, due to very low white blood cells (febrile neutropenia)
- slow, fast, or irregular heartbeat, chest pain (which may be a sign of infection)
- problems with your sight, blurred vision
- pain or swelling of the tissue lining the digestive system (mucositis), or pain in the abdomen (belly), constipation, loss of appetite, diarrhoea, nausea (feeling sick) or vomiting
- redness of skin, rashes, muscle aches, headache, bone pain, joint pain, tiredness, generalised swelling including swelling of your arms and legs
- headache, dizziness, confusion, difficulty sleeping, anxiety
- kidney failure
- shortness of breath, cough, fluid in the lungs
- itching
- bleeding
- increased blood pressure or a fall in blood pressure
- chills, low body temperature, or high body temperature

- increased sweating

Common side effects (may affect up to 1 in 10 people):
- a fall in the number of red blood cells (anaemia) leading to tiredness and weakness
- kidney failure and abnormal blood tests due to massive death of cancer cells (Tumour lysis syndrome).
- stomach cramps or excessive gas
- excessive sweating at night
- hair loss

Uncommon side effects (may affect up to 1 in 100 people):
- numbness and rash in the hands and feet (palmar-plantar erythrodysaesthesia syndrome).

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

5. How to store Vyxeos liposomal

- 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 carton and the vial 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.
- Store in an upright position.
- After reconstitution, the vials should be stored in a refrigerator (2°C to 8°C) for up to 4 hours in an upright position.
- After dilution, the solution in infusion bags should be stored in a refrigerator (2°C to 8°C) for up to 4 hours.
- Do not use this medicine if you notice any particles in the diluted solution.
- 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 Vyxeos liposomal contains
- The active substances are daunorubicin and cytarabine. Each 50 ml vial contains 44 mg of daunorubicin and 100 mg of cytarabine.
- After reconstitution the solution contains 2.2 mg/mL daunorubicin and 5 mg/mL cytarabine encapsulated in liposomes.
- The other ingredients are distearoylphosphatidylcholine, distearoylphosphatidylglycerol, cholesterol, copper gluconate, trolamine and sucrose.

What Vyxeos liposomal looks like and contents of the pack
Vyxeos liposomal is a purple powder for concentrate for solution for infusion supplied in a glass vial.

Each pack contains 1 vial, 2 vials or 5 vials. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Jazz Pharmaceuticals Ireland Ltd
5th Floor

Waterloo Exchange
Waterloo Road
Dublin
D04 E5W7
Ireland

Tel: +44 8450305089
Email: medinfo-int@jazzpharma.com

This leaflet was last revised in October 2019

Other sources of information

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.

This leaflet is available in all EU/EEA languages on the European Medicines Agency website.

The following information is intended for healthcare professionals only:

Vyxeos liposomal is a cytotoxic medicinal product. Applicable special handling and disposal procedures should be followed. The product is intended for single use only. It does not contain any preservatives. Unused portions should not be saved for later administration.

Preparation instructions

- Determine the dose and number of vials of Vyxeos liposomal based on the individual patient's BSA as outlined in section 4.2.
- Remove the appropriate number of vials of Vyxeos liposomal from the refrigerator and equilibrate to the room temperature (15°C to 30°C) for 30 minutes.
- Then, reconstitute each vial with 19 mL of sterile water for injections using a 20 mL syringe and immediately thereafter start a 5-minute timer.
- Carefully swirl the contents of the vial for 5 minutes while gently inverting the vial every 30 seconds.
- Do not heat, vortex, or shake vigorously.
- After reconstitution, let rest for 15 minutes.
- The reconstituted product should be an opaque, purple, homogeneous dispersion, essentially free from visual particulates.
- If the reconstituted product is not diluted into an infusion bag immediately, store in a refrigerator (2ºC to 8ºC) for up to 4 hours.
- Calculate the volume of reconstituted Vyxeos liposomal required using the following formula: [volume required (mL) = dose of daunorubicin (mg/m^2) x patient's BSA (m^2)/2.2 (mg/mL)]. The concentration of the reconstituted solution is 44 mg/20 mL (2.2 mg/mL) daunorubicin and 100 mg/20 mL (5 mg/mL) cytarabine.
- Gently invert each vial 5 times prior to withdrawing the concentrate for dilution.
- Aseptically withdraw the calculated volume of reconstituted Vyxeos liposomal from the vial(s) with a sterile syringe and transfer it to an infusion bag containing 500 mL of sodium chloride 9 mg/mL (0.9%) solution for injection, or 5% glucose. There may be residual product remaining in the vial. Discard unused portion.
- Gently invert the bag to mix the solution. The dilution of the reconstituted product results in a deep purple, translucent, homogeneous dispersion.
- If the diluted infusion solution is not used immediately, store in a refrigerator (2°C to 8°C) for up to 4 hours.
- Gently invert the bag to mix the solution after refrigeration

Administration instructions

- Do not mix Vyxeos liposomal with, or administer as an infusion with, other medicinal products.
- Administer Vyxeos liposomal by constant intravenous infusion over 90 minutes via an infusion pump through a central venous catheter or a peripherally inserted central catheter. An in-line membrane filter may be used for the intravenous infusion of Vyxeos liposomal, provided the minimum pore diameter of the filter is greater than or equal to 15 µm.
- Flush the line after administration with sodium chloride 9 mg/mL (0.9%) solution for injection.

Disposal

This medicinal product could have potential risk for the environment due to the cytotoxic and antimitotic activities, which could induce possible reproductive effects. All materials used for dilution and administration should be disposed of according to local procedures applicable to the discarding of antineoplastic agents. Any unused medicinal product or waste material should be disposed of in accordance with local requirements for cytotoxic agents.