Patient Information Leaflet (PIL)

Vyxeos Liposomal 44 mg / 100 mg,
Powder for Concentrate for Solution for Infusion
Daunorubicin and Cytarabine

▼ **This medicine is subject to further examination and monitoring, which will allow you to quickly identify the new safety information. You can help by reporting any side effects that you may feel. See Section 6 to find out how to report side effects.**

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, pharmacist, or nurse.
- If you suffer from any side effects, inform a doctor, pharmacist, or nurse. This includes any potential side effects that are not contained in this leaflet (See Section 4).

What is in this leaflet:

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", which are used in treating cancer. The medicine contains two active substances, Daunorubicin and Cytarabine, in the form of tiny particles known as "Liposomes".
The two active substances kill cancer cells in different manners by preventing them from growing and dividing. Packaging these two active substances in the liposomes prolongs their effect on the body and helps them enter and then kill the cancer cells.

What Vyxeos Liposomal is used for
Vyxeos liposomal is used to treat patients with newly diagnosed Acute Myeloid Leukemia "AML" (white blood cell cancer). The medicine is administered when leukemia is caused by previous treatments (known as Acute Myeloid Leukemia "AML" treatment) or when there are certain changes in the bone marrow (known as Acute Myeloid Leukemia with Myelodysplasia-Related Changes "AML-MRC").

2. What you need to know before you take Vyxeos Liposomal

Do not take Vyxeos Liposomal:
- If you are allergic to the two active substances (Daunorubicin and Cytarabine) or any other component in this medicine (listed in Section 6).

Warnings and Precautions
Your doctor will monitor your condition while receiving the treatment. Talk to your doctor, pharmacist, or nurse before you are given Vyxeos Liposomal:

- If you have low platelet count, and low red or white blood cells count (you will undergo a blood test before starting the treatment). If this applies to you:
  - Your doctor may also give you a medication to help prevent infection.
  - Your doctor will also examine you to check for any infection during treatment.
- If you have previously had a heart problem or heart attack, or if you have previously taken "Anthracyclines" for cancer treatment. If this applies to you, your doctor may check your heart before and during treatment.
- If you think you are pregnant. You should use an effective contraception method to avoid pregnancy (you or your partner) during treatment, and for a period of 6 months after the last dose.
- If you have any allergic reactions (hypersensitivity). Your doctor may temporarily or completely stop the treatment, or slow down the intravenous infusion rate, in the event of any hypersensitivity reaction.
- If you have suffered from kidney or liver problems, your doctor will monitor you while taking the treatment.
- If you have suffered from a condition known as Wilson's disease or other disorders associated with copper accumulation in the body, as Vyxeos Liposomal contains a component known as Copper Gluconate.
- If you will receive a vaccine.

Your doctor will monitor your overall health while receiving the treatment, and he may also give you other medicines to support your treatment, whether before or while receiving the Vyxeos Liposomal treatment. If any of the above applies 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 children and adolescents under the age of 18 years old.

Other Medicines and Vyxeos Liposomal
Tell your doctor, nurse, or pharmacist if you are using, have recently used, or may be using any other medicines. This is because Vyxeos Liposomal may affect how some other medicines work. In addition, some other medicines may affect how Vyxeos Liposomal works.

Tell your doctor, nurse, or pharmacist if you are taking any of the following medicines, especially:

- Cancer medicines that may affect your heart, such as Doxorubicin.
- Medicines that may affect the liver.

Pregnancy, Breastfeeding, and Fertility
You should not use Vyxeos Liposomal during pregnancy because it may be harmful to the fetus. Use an effective contraception method during treatment and for a period of 6 months after treatment. Tell your doctor immediately if you become pregnant during the treatment.

You should not breastfeed while being treated with Vyxeos Liposomal, as it can be harmful to the baby.

If you are pregnant or breastfeeding, think you are pregnant or planning to have a baby, consult your doctor before he gives you this medicine.

Contraception in males
Use an effective method of contraception during and for 6 months after treatment with Vyxeos liposomal.

Driving and Using Machines
You may feel drowsy or dizzy after taking Vyxeos Liposomal. If this occurs, do not drive or use any tools or machines.

3. How to take Vyxeos Liposomal

Vyxeos Liposomal must be given to you by a doctor or nurse who is experienced in the AML treatment.
- It is given to you as a drip (infusion) into a vein.
- The intravenous infusion will be given over an hour and a half (90 minutes).

Your doctor, nurse, or pharmacist will determine the medicine's dosage based on your weight and height. Your treatment will be provided in the form of "treatment courses". Each course is given in the form of a separate intravenous infusion, and each course may be given weeks apart.

You will receive the first treatment course, and your doctor will decide whether you will receive further treatment courses based on your response to the treatment and the side effects you develop. Your doctor will assess your response to the treatment after each treatment course.

- During the first treatment course - you will receive an infusion on days 1, 3 and 5.
- In other treatment courses - you will receive an infusion on days 1 and 3. This can be repeated if necessary.

While being treated with Vyxeos Liposomal, your doctor will perform regular blood tests to assess your response to treatment and ensure that it is well-tolerated. Your doctor may also check your heart because Vyxeos Liposomal may affect it.

If you are given more Vyxeos Liposomal doses than you should
You will be given this medicine at the hospital by your doctor or nurse; so, it is unlikely that you will be given more doses than you should; however, tell your doctor or nurse if you have any concerns.

If you miss the medicine dose
Call your doctor or nurse as soon as possible.

If you have any other questions about using 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.

Serious Side effects may appear in more than 1 in 10 people (Very Common)
Vyxeos Liposomal may reduce the white blood cells count that fight infection, along with reducing the blood cells count that help blood to clot (platelets) thus resulting in bleeding disorders, such as nosebleeds and bruises. Vyxeos Liposomal may also cause heart problems and heart muscle damage.

Therefore, you **must tell your doctor immediately** if you experience any of the following symptoms:
- Fever, chills, sore throat, cough, mouth ulcers or any other symptoms of infection.
- Bleeding or bruising without an injury.
- Chest pain or leg pain.
- Shortness of breath.

Tell your doctor immediately if you develop any of the side effects mentioned above.

Other Side Effects

Very Common Side Effects (may affect more than 1 in 10 people):
- A decline in the platelet count (cells that help blood to clot), which may cause bruising or bleeding.
- Fever, often accompanied by other signs of infection, due to a very low white blood cell count (Febrile Neutropenia).
- Slow, fast, or irregular heartbeat, and chest pain (which may be a sign of infection).
- Vision problems, and blurred vision.
- Pain or swelling of the tissues lining the digestive tract (Mucositis), abdominal pain (abdomen), constipation, loss of appetite, diarrhea, nausea (feeling sick) or vomiting.
- Skin redness, rashes, muscle pain, headaches, bone pain, joint pain, fatigue, and general body swelling, including the swelling of the arms and legs.
- Headache, dizziness, confusion, difficulty sleeping, and anxiety.
- Kidney failure.
- Shortness of breath, cough, and fluids in the lungs.
- Itching.
- Bleeding.
- High blood pressure (Hypertension) or low blood pressure (Hypotension).
- Chills, low body temperature, or high body temperature.
- Excessive sweating.

Common Side Effects (may affect up to 1 in 10 people):
- Low red blood cells count (anemia) leading to fatigue and weakness.
- Kidney failure and abnormal blood tests due to the massive death of cancer cells (Tumor 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 Erythrodysesthesia Syndrome).

Reporting of Side Effects
If you have any side effects, talk to your doctor, pharmacist, nurse. This includes any potential side effects that are not included in this leaflet.

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 package and 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 package to protect it from light.
- Store in an upright position.
- After the medicine's reconstitution, the vials must be stored in the refrigerator (2°C to 8°C) for up to 4 hours in an upright position.
- After dilution, store the solution in intravenous infusion bags in the refrigerator (2 to 8°C) for up to 4 hours. The maximum combined storage period for both the reconstituted product in a vial stored in an upright position and the reconstituted product after its dilution in the infusion bag should not exceed 4 hours. The duration of the intravenous infusion is 90 minutes; in addition to a storage time of 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. Further Information

What the Contents of Vyxeos Liposomal are
- The two active substances are Daunorubicin and Cytarabine. Each 50 ml vial contains 44 mg Daunorubicin and 100 mg Cytarabine.
- After reconstitution, the solution contains 2.2 mg/ml Daunorubicin and 5 mg/ml Cytarabine encapsulated in liposomes.
- The other components are Distearoylphosphatidylcholine (DSPC), Distearoyl Phosphatidylglycerol, Cholesterol, Copper Gluconate, Trolamine, and Sucrose.

What Vyxeos Liposomal looks like and the 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 Authorization Holder and Manufacturer:

Marketing Authorization Holder and Final Batch Releaser:

Jazz Pharmaceuticals Ireland Ltd
5th Floor
Waterloo Exchange
Waterloo Road
Dublin
D04 E5W7
Ireland
Tel: +44 8450305089
E-mail: medinfo-int@jazzpharma.com

Bulk Manufacturer:
Baxter Oncology GmbH
Kantstrasse 2
33790 Halle/Westfalen
Germany

For any information about this medicinal product, please contact the local representative of the Marketing Authorisation Holder:

In the Kingdom of Saudi Arabia (KSA):
Biologix, FZ Co, Hibatullah Al Ghaffari Street-Suliemaniah Kingdom of Saudi Arabia P.O.Box 991, Riyadh 11421.
Tel: +966 11 464 6955
Fax: +966 11 463 4362

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To report any side effects:

- **Kingdom of Saudi Arabia:**

-The National Pharmacovigilance Centre (NPC)
-Saudi Food & Drug Authority (SFDA) Call Center: 19999
-E-mail: npc.drug@sfda.gov.sa
-Website: https://ade.sfda.gov.sa/

- **Kuwait:**

Drug & Food Control, Ministry of Health, Kuwait
- Tel. No.: +965-24811532
- Fax No.: +965-24811507
- E-mail: Adr_reporting@moh.gov.kw

- **United Arab Emirates:**

Pharmacovigilance & Medical Device section
P.O.Box: 1853
Tel: 80011111
Email: pv@mohap.gov.ae
Drug Department
Ministry of Health & Prevention
Dubai, UAE

- **Iraq:**

- Iraqi Pharmacovigilance center, Ministry of Health, Iraq
- Mobile: 00964 7807820490
- Email: iraqiphvc@moh.gov.iq
- Website: www.tec-moh.com

- **Jordan:**

Jordan Food & Drug Administration JFDA, Jordan
Tel.: +962 06 563 2000
Website: www.jfda.jo
Mobile app: Jordan FDA
Reporting form: Yellow card

- **Other GCC Countries:**

- Please contact the relevant competent authority.

Council of Arab Health Ministers

This medicine:

- *This medicine is a product that affects your health, and its consumption contrary to instructions is dangerous for you.*
- *Strictly follow the doctor's prescription, the method of use, and the instructions of the pharmacist who sold you the medicine.*
- *The doctor and the pharmacist are experts in medicines, their benefits and risks.*
- *Do not stop your prescribed treatment period on your own.*
- *Do not repeat the same prescription without consulting your doctor.*
- *Keep all medicines out of reach of children.*

Council of Arab Health Ministers
Arab Pharmacists Union

This Patient Information Leaflet (PIL) is approved by the Saudi Food & Drug Authority and the GCC.

The following information is provided specifically for the healthcare professionals only:

Vyxeos Liposomal is a cytotoxic medical product. Special procedures must be followed for the handling and disposal of the medicine. The medical product is intended for single use only and does not contain any preservatives. Unused portions of the medicine should not be saved for later use.

Preparation Instructions:

- Determine the Vyxeos Liposomal dose and the number of its vials based on the Body Surface Area (BSA) for each patient as described in Section 4.2.
- Take the right number of Vyxeos Liposomal vials out of the fridge, then leave them for 30 minutes; in order to equilibrate at room temperature (15°C to 30°C).
- Afterwards, reconstitute each vial with 19 ml of sterile water for injection using a 20 ml syringe, and then immediately start a 5-minute timer.
- Carefully swirl the vial's contents for 5 minutes, and gently flip it every 30 seconds.
- Do not overheat, spin or shake the vial violently.
- After reconstitution, let the solution rest for 15 minutes.
- The reconstituted product must be an evenly-distributed opaque solution, purple in color, and mainly free of visible particles.
- If the reconstituted product is not immediately diluted in the infusion bag, store it in the refrigerator (2°C to 8°C) for up to 4 hours.
- After storing the reconstituted product in the vial for up to 4 hours at 2 to 8°C in an upright position, the reconstituted product should be immediately diluted in the infusion solution and used for 90 minutes at the time of infusion.
    - The reconstituted product in the vial and the reconstituted product that has been diluted in the infusion solution are stable for a combined storage period of up to 4 hours when stored at a temperature of 2°C to 8°C. The 4-hour stability period for the reconstituted product in the vial does not allow for an additional 4-hour stability period after the appropriate dose of the reconstituted vial is diluted in the infusion solution.
    - The 4-hour stability period when storing the reconstituted product that has been diluted in the infusion bag at 2°C to 8°C does not include the time required for reconstitution or the estimated 90-minute infusion time.
    - The diluted infusion solution must be injected immediately for a period of 90 minutes, i.e. the intravenous infusion time; and that is after the solution's stability period of up to 4 hours.
- Calculate the volume of the reconstituted Vyxeos Liposomal medicine using the following formula:
- [Required Volume (ml) = Daunorubicin Dose (mg/m^2) x Patient's Body Surface Area (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 flip each vial 5 times before drawing the concentrate for dilution.
- Using a sterile syringe, draw the calculated volume of the reconstituted Vyxeos Liposomal medicine in a sterile manner from the vial(s), 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 a portion of the medicine left in the vial. Discard the unused portion of the medicine.
- Gently flip the bag to mix the solution. The dilution of the reconstituted product results in a dark purple, transparent, and evenly-distributed solution.

- If the diluted infusion solution is not used immediately, store in the refrigerator (2°C to 8°C) for up to 4 hours.
- Gently flip the infusion bag to mix the solution after being cooled.

Medicine Administration Instructions

- Do not mix Vyxeos Liposomal or administer it as an infusion with other medical products.
- Administer Vyxeos Liposomal through a 90-minute continuous intravenous infusion through the infusion pump via a Central Venous Catheter or a Peripherally-Inserted Central Catheter (PICC). An internal membrane filter can be used for the intravenous infusion of Vyxeos Liposomal, provided that the filter's minimum pore diameter is greater than or equal to 15 µm.
- Wash the internal filter after administering the medicine using a sodium chloride 9 mg/ml (0.9%) solution for injection.

Medicine Disposal Method

This medical product can involve potential environmental risks as a result of cytotoxic and antibiotic activities, which can lead to potential reproductive effects. All substances used to dilute and administer the medicine must be disposed of according to the applicable local procedures in regard to the disposal methods for antineoplastic agents. Any unused medical product or wastes must be disposed of in accordance with the local requirements for the cytotoxic agents.