Vyxeos® Liposomal

44 mg/100 mg Powder for concentrate for solution for infusion

daunorubicin / cytarabine

is indicated for the treatment of adults with

newly diagnosed ***t-AML*** **or** ***AML-MRC***[1]

t-AML and AML-MRC are distinct subgroups with

HIGH-RISK *FEATURES*[2–5]

and up to 1 in 3* patients with newly diagnosed AML may fall into these high-risk categories[3,6]

t-AML

PREVIOUSLY UNTREATED AML with a history of prior **cytotoxic treatment** or **radiation therapy**[4,7]

AML-MRC

≥20% blood or marrow blasts[4] **AND** any of the following:[4,8]

AML arising from previous **MDS** or **MPN**

AML with **MDS-related cytogenetic abnormality**

AML with **multilineage dysplasia****

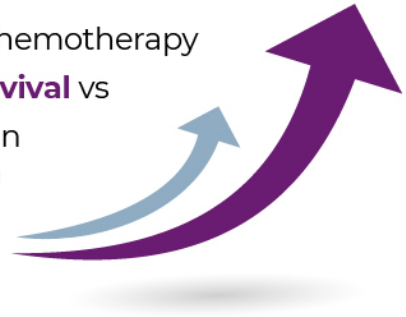
Up to 1 in 3*

newly diagnosed patients

with AML may fall into these high-risk categories[3,6] and could be

ELIGIBLE FOR TREATMENT WITH VYXEOS LIPOSOMAL[1,9]

Vyxeos Liposomal is the first chemotherapy in over 40 years to **improve survival** vs **conventional chemotherapy**† in patients with high-risk‡ AML[5,10,11]



*t-AML: ~7% OF AML CASES[3], AML-MRC: ~25% OF AML CASES[6]

**In the absence of mutations of NPM1 or biallelic mutation of CEBPA[4]

†Comparator arm conventional chemotherapy is 7+3 in induction, 5+2 in second induction and consolidation where given

‡High-risk AML is defined as therapy-related acute myeloid leukaemia (t-AML) or AML with myelodysplasia-related changes (AML-MRC)

MDS, myelodysplastic syndrome; MPN, myeloproliferative neoplasm

International Core Prescribing Information
Vyxeos® Liposomal 44mg/100mg powder for concentrate for solution for infusion
(Daunorubicin and cytarabine)
Please refer to the Summary of Product Characteristics before prescribing.

Presentation: Purple lyophilised cake of powder for concentrate for solution for infusion. Each 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 in a fixed combination in a 1:5 molar ratio. **Indication:** For the treatment of adults with newly diagnosed, therapy-related acute myeloid leukaemia (t-AML) or AML with myelodysplasiarelated changes (AML-MRC). **Dosage and administration:** For intravenous infusion use only. An in-line membrane filter may be used provided the minimum pore diameter of the filter is greater than or equal to 15 µm. It must not be administered via an intramuscular, intrathecal, or subcutaneous route. *Refer to the full SmPC for detailed information on preparation of solution for infusion.* Treatment should be initiated and monitored under the supervision of a physician experienced in the use of chemotherapeutic medicinal products. *Recommended dosing schedule for induction of remission:* 44 mg/100 mg/m2, administered intravenously over 90 minutes on days 1, 3, and 5 as the first course of induction therapy; then on days 1 and 3 as subsequent course of induction therapy, if needed. *Recommended dosing schedule for consolidation:* The first consolidation cycle should be administered 5 to 8 weeks after the start of the last induction. The recommended dosing schedule is 29 mg/65 mg/m2, administered intravenously over 90 minutes on days 1 and 3 as subsequent courses of consolidation therapy, if needed. Dose adjustments during treatment may be required in hypersensitivity symptoms and cardiotoxicity. Assessment of cardiac function prior to start of treatment is recommended. *Renal impairment:* Dose adjustment is not required for patients with mild (creatinine clearance [CrCL] 60 mL/min to 89 mL/min by Cockcroft Gault equation [C-G]) or moderate (CrCL 30 mL/min to 59 mL/min) renal impairment. There is no experience in patients with severe renal impairment (CrCL 15 mL/min to 29 mL/min) or end-stage renal disease. It should only be used in patients with severe renal impairment if the benefits outweigh the risks. *Hepatic impairment:* Dose adjustment is not required for patients with a bilirubin level less than or equal to 50 µmol/L. There is no experience in patients with hepatic impairment resulting in a bilirubin level greater than 50 µmol/L. It should only be used in patients with severe hepatic impairment if the benefits outweigh the risks. *Elderly population (≥65 years):* No dose adjustment is required. *Paediatric population:* The safety and efficacy in children aged 0–18 years has not yet been established. C**ontraindications:** Hypersensitivity to the active substance or to any of the excipients. **Warnings, precautions and interactions:** Do not substitute or interchange with other daunorubicin and/or cytarabine-containing products. Severe myelosuppression and serious or fatal haemorrhagic events have been reported. Due to the long plasma half-life of Vyxeos liposomal, time to recovery of ANC and platelets may be prolonged and require additional monitoring. Prophylactic anti-infectives may be administered during the period of profound neutropenia until ANC returns to 500/µL or greater. If myelosuppressive complications occur, appropriate supportive measures should be used. Blood counts should be regularly monitored until recovery. As cardiotoxicity is a known risk prior therapy with anthracyclines, pre-existing cardiac disease, previous radiotherapy of the mediastinum, or concomitant use of cardiotoxic products may increase the risk. Hepatotoxic medicinal products may impair liver function and increase toxicity. Evaluation of hepatic and renal function is recommended prior to administration and periodically during treatment. Blood uric acid levels should be monitored and appropriate therapy initiated if hyperuricemia develops. Each vial of Vyxeos liposomal contains 100 mg of copper gluconate. It should only be used in patients with a history of Wilson's disease or other copper-related disorder if the benefits outweigh the risks. To avoid local tissue necrosis care should be taken to ensure that there is no extravasation of Vyxeos liposomal during administration. Administration of live or live-attenuated vaccines should be avoided. Killed or inactivated vaccines may be administered; however, the response to such vaccines may be diminished. The absorption of oral accompanying medicinal products may be considerably influenced by gastrointestinal mucositis and/or diarrhoea frequently occurring in association with intensive chemotherapy. **Pregnancy, lactation and fertility:** There are no data on use in pregnant women. It should not be used during pregnancy unless the benefit of treatment outweighs the risk. It is not known if Vyxeos liposomal is excreted in human milk therefore mothers should be advised to discontinue breastfeeding during therapy. Patients should be advised to avoid becoming pregnant while receiving Vyxeos liposomal. Male patients and women of childbearing potential must use an effective method of contraception during treatment and for 6 months following the last dose. Male fertility may be compromised by treatment. **Undesirable effects: *Please refer to the full SmPC for the complete list of undesirable effects.*** The most frequently occurring adverse reactions were hypersensitivity, febrile neutropenia, oedema, diarrhoea/colitis, mucositis, fatigue, musculoskeletal pain, abdominal pain, decreased appetite, cough, headache, chills, arrhythmia, pyrexia, sleep disorders, and hypotension. The most serious and frequently occurring ADRs were infection, cardiotoxicity and haemorrhage. **Overdose:** There is no specific antidote for overdose and treatment should be symptomatic. **Storage and Handling:** Store in a refrigerator (2°C - 8°C). Shelf life of unopened vials: 2 years. Keep vial in the original carton to protect from light and store in an upright position. Vyxeos liposomal is a cytotoxic medicinal product intended for single use only. Any unused medicinal product or waste material should be disposed of in accordance with local requirements for cytotoxic agents.

Legal category: POM. **Marketing authorisation number:** EU/1/18/1308/001 **Package quantity and Cost:** carton containing 1 × 50 mL vial. Price differs across countries. Further information is available from the **Marketing Authorisation Holder:** Jazz Pharmaceuticals Ireland Ltd., 5th Floor, Waterloo Exchange, Waterloo Road, Dublin D04 E5W7, Ireland.

Date of preparation: November 2019. INT-VYX-1900009

Vyxeos® is a registered trade mark.
For country specific information please refer to your local SmPC or Product Monograph

Adverse events should be reported. Healthcare professionals are asked to report any suspected adverse events via their national reporting system. Adverse events should also be reported to Jazz Pharmaceuticals by email to aereporting@jazzpharma.com or by fax to +44 (0) 1865 598765

References

1. Vyxeos Liposomal – Summary of Product Characteristics, October 2019
2. Boddu PC *et al. Cancer* 2017; 123(16): 3050–3060
3. Granfeldt Østgård LS *et al. J Clin Oncol* 2015; 33(31): 3641–3649
4. Arber DA *et al. Blood* 2016; 127(20): 2391–2405
5. Lancet JE *et al. J Clin Oncol* 2018; 36(26): 2684–2692
6. Nagel G *et al. Ann Hematol* 2017; 96(12): 1993–2003
7. National Cancer Institute. Cancer Terms. Available from: www.cancer.gov/publications/dictionaries/cancer-terms/def/t-aml. Accessed June 2020
8. Weinburg OK *et al. Blood* 2009; 113(9): 1906–1908
9. Drummond MW. *Int J Hematol* 2019; 8(2): IJH16
10. Fernandez HF *et al. Hematology Am Soc Hematol Educ Program* 2010; 2010: 56–61
11. Mayer LD *et al. Int J Nanomedicine* 2019; 14: 3819–3830

Jazz Pharmaceuticals

INT-VYX-2000077 | June 2020