Preparation of VYXEOS[1]

Vyxeos® (daunorubicin and cytarabine) 44 mg/100 mg per vial liposome for injection

INDICATION

VYXEOS is indicated for the treatment of newly-diagnosed therapy-related acute myeloid leukemia (t-AML) or AML with myelodysplasia-related changes (AML-MRC) in adults and pediatric patients 1 year and older.

Calculate the number of vials of VYXEOS needed based on the daunorubicin dose and the patient's body surface area (BSA) using the equation at right[1]:

$$\frac{\text{Dose of daunorubicin (mg/m}^2\text{)} \times \text{patient's BSA (m}^2\text{)}}{\text{2.2 mg/mL}} = \text{mL volume required}$$

Each vial contains 20 mL of solution after reconstitution.

VYXEOS is a hazardous drug. Follow applicable special handling and disposal procedures[1]

Equilibrate the appropriate number of vials of VYXEOS to room temperature for 30 minutes[1]

Reconstitute and further dilute VYXEOS prior to intravenous infusion[1]

Reconstitute each vial with 19 mL of Sterile Water for Injection using a sterile syringe

- **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 visible particulates
- After reconstitution but before final dilution, each mL of VYXEOS will contain 2.2 mg of daunorubicin and 5 mg of cytarabine

Use the reconstituted solution immediately. If needed, store the reconstituted solution in the vial refrigerated at 2°C to 8°C (36°F to 46°F) for up to 4 hours. Note that the reconstituted product in the vial and the reconstituted product which has been diluted into an infusion solution are stable for a total of 4 hours (not 4 hours each) when stored at 2°C to 8°C

See next page for additional instructions

IMPORTANT SAFETY INFORMATION

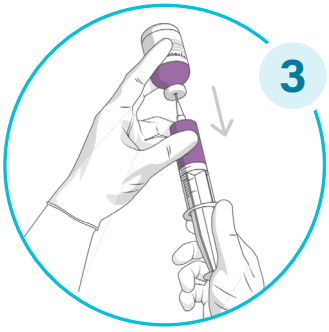
WARNING: DO NOT INTERCHANGE WITH OTHER DAUNORUBICIN AND/OR CYTARABINE-CONTAINING PRODUCTS

VYXEOS has different dosage recommendations than daunorubicin hydrochloride injection, cytarabine injection, daunorubicin citrate liposome injection, and cytarabine liposome injection. Verify drug name and dose prior to preparation and administration to avoid dosing errors.

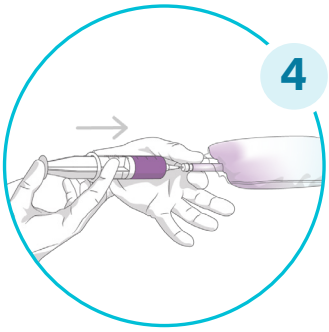
- VYXEOS is contraindicated in patients with a history of serious hypersensitivity reactions to cytarabine, daunorubicin, or any component of the formulation.
- Serious or fatal hemorrhage events, including fatal CNS hemorrhages, associated with prolonged severe thrombocytopenia, have occurred in patients treated with VYXEOS. Monitor blood counts regularly and administer platelet transfusion support as required.

Please see additional Important Safety Information on next page and full Prescribing Information, including BOXED Warning.

Preparation of VYXEOS,[1] continued



Gently invert each vial 5 times and aseptically withdraw the calculated volume of reconstituted product from the vial(s) using a sterile syringe



Transfer the calculated volume to an infusion bag containing 500 mL of 0.9% Sodium Chloride Injection, USP or 5% Dextrose Injection, USP

- Discard any unused portion or residual product remaining in the vial and do not save any unused portions for later administration

Gently invert the bag to mix the solution

- The dilution of the reconstituted product results in a deep purple, translucent, homogeneous dispersion, free from visible particulates
- Only solutions without visible particulates should be used

If the diluted infusion solution is not used immediately, store in a refrigerator at 2°C to 8°C (36°F to 46°F) for up to 4 hours. If the reconstituted solution in the vial was stored for 4 hours, the diluted infusion solution must be used immediately and cannot be stored for an additional 4 hours

Please see VYXEOS full Prescribing Information for complete preparation and handling instructions, including BOXED Warning.

IMPORTANT SAFETY INFORMATION, continued

- VYXEOS contains daunorubicin, which has a known risk of cardiotoxicity. Assess cardiac function before, during, and after treatment as clinically indicated. Discontinue in patients with impaired cardiac function unless the benefit of treatment outweighs the risk. VYXEOS treatment is not recommended in patients with cardiac function that is less than normal. Calculate the lifetime cumulative anthracycline exposure prior to each cycle of VYXEOS. VYXEOS is not recommended in patients who have reached the maximum lifetime anthracycline dose limit.
- If a severe or life-threatening hypersensitivity reaction occurs, discontinue VYXEOS permanently, treat according to the standard of care, and monitor until signs and symptoms resolve.
- VYXEOS contains copper and has the potential to cause copper overload in patients with Wilson's disease or other copper-related metabolic disorders. Monitor patients and use only if the benefits outweigh the risks. Discontinue in patients with signs or symptoms of acute copper toxicity.
- Daunorubicin has been associated with severe local tissue necrosis at the site of drug extravasation. Administer VYXEOS by the intravenous route only. Confirm patency of intravenous access before administration.
- VYXEOS can cause fetal harm. Advise females and males of reproductive potential of the potential risk to a fetus and to use effective contraception.
- The most common adverse reactions (incidence ≥25%) are hemorrhagic events (74%), febrile neutropenia (70%), rash (56%), edema (55%), nausea (49%), mucositis (48%), diarrhea (48%), constipation (42%), musculoskeletal pain (43%), fatigue (39%), abdominal pain (36%), dyspnea (36%), headache (35%), cough (35%), decreased appetite (33%), arrhythmia (31%), pneumonia (31%), bacteremia (29%), chills (27%), sleep disorders (26%), and vomiting (25%).

Please see additional Important Safety Information on previous page and full Prescribing Information, including BOXED Warning.

USP=United States Pharmacopeia.

Reference: 1. VYXEOS [package insert]. Palo Alto, CA: Jazz Pharmaceuticals.

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