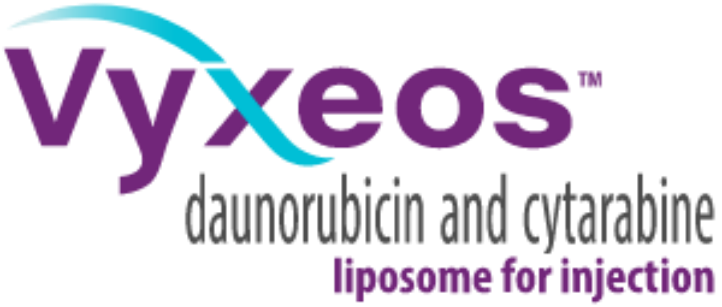
Vyxeos (daunorubicin/cytarabine)



NEW PRODUCT SLIDESHOW

MPR

Introduction

- **Brand name:** Vyxeos
- **Generic name:** Daunorubicin and cytarabine
- **Pharmacological class:** Anthracycline + antimetabolite
- **Strength and Formulation:** 44mg/100mg; per vial; lyophilized cake for IV infusion after reconstitution; contains copper; preservative-free
- **Manufacturer:** Jazz Pharmaceuticals
- **How supplied:** Single-dose vials—2,5
- **Legal Classification:** Rx

Indications

- Treatment of newly-diagnosed therapy-related acute myeloid leukemia (t-AML) or AML with myelodysplasia-related changes (AML-MRC)

Dosage & Administration

- Calculate the prior cumulative anthracycycline exposure before initiating each cycle
- Give prophylactic antiemetics
- Administer by IV infusion over 90mins

Dosage & Administration

- **First induction:** daunorubicin 44mg/m^2 and cytarabine 100mg/m^2 on Days 1, 3, and 5
- **Second induction** (may give after 2–5 weeks if remission not achieved and no unacceptable toxicity): daunorubicin 44mg/m^2 and cytarabine 100mg/m^2 on Days 1 and 3

Dosage & Administration

- **Consolidation** (give 5–8 weeks after last induction): daunorubicin 29mg/m^2 and cytarabine 65mg/m^2 on Days 1 and 3
- May give second consolidation 5–8 weeks after if no disease progression or unacceptable toxicity

Dosage & Administration

- **Do not** initiate consolidtion until ANC recovers to >0.5Gi/L and platelet count >50Gi/L in the absence of unacceptable toxicity

Considerations for Special Populations

- **Pregnancy:** Exclude status prior to initiation
- **Nursing mothers:** Not recommended during and for ≥2 weeks after last dose
- **Pediatric:** Not established
- **Elderly:** No overall differences in safety or efficacy were observed
- **Hepatic or severe renal impairment:** Not studied

Warnings/Precautions

- **Do not** interchange with other daunorubicin and/or cytarabine containing products
- Prior anthracycline therapy, pre-existing cardiac disease, or radiotherapy to mediastinum: increased risk of cardiotoxicity
- Assess CBCs, cardiac, liver, and renal function prior to initiation

Warnings/Precautions

- **Discontinue** if impaired cardiac function unless benefit outweighs risk
- If LVEF below normal or max lifetime cumulative anthracycline exposure limit reached: not recommended
- Monitor for hypersensitivity reactions; interrupt and reduce infusion rate if mild or moderate symptoms; permanently discontinue if severe/life-threatening reactions occur

Warnings/Precautions

- **Wilson's disease:** use only if benefit outweighs risk
- Monitor copper levels and serial neuropsychological exam; discontinue if signs/symptoms of acute copper toxicity develops
- Avoid extravasation

Warnings/Precautions

- Embryo-fetal toxicity
- Females of reproductive potential and males (with female partners) should **use effective contraception** during and for ≥6 months after last dose

Interactions

- **Increased toxicity** with concomitant cardiotoxic or hepatotoxic agents; monitor more frequently

Adverse Reactions

- Hemorrhagic events
- Febrile neutropenia
- Rash
- Edema
- Nausea
- Mucositis
- Diarrhea
- Constipation
- Musculoskeletal pain
- Fatigue
- Abdominal pain

Adverse Reactions

- Dyspnea
- Headache
- Cough
- Decreased appetite
- Arrhythmia
- Pneumonia
- Bacteremia
- Chills
- Sleep disorders
- Vomiting
- Cardiotoxicity
- Copper overload
- Tissue necrosis

Mechanism of Action

- **Daunorubicin** has antimitotic and cytotoxic activity, which is achieved by forming complexes with DNA, inhibiting topoisomerase II and DNA polymerase activity, affecting regulation of gene expression, and producing DNA-damaging free radicals
- **Cytarabine** is a cell cycle phase-specific antineoplastic agent, acting primarily through inhibition of DNA polymerase

Clinical Studies

- Vyxeos was evaluated in a randomized, multicenter, open-label, active-controlled clinical trial (Study 1) which compared Vyxeos to a standard combination of cytarabine and daunorubicin (7+3) in patients 60–75 years of age with newly diagnosed t-AML or AML-MRC

Clinical Studies

- Patients were randomized 1:1 and stratified by age and AML subtype to receive Vyxeos (n=153) or 7+3 (n=156) for induction and consolidation
- Efficacy was determined by **overall survival** from the date of randomization to death from any cause

Clinical Studies

- The **median survival time** was 9.6 months in the Vyxeos group vs. 5.9 months in the 7+3 group (hazard ratio 0.69, 95% CI: 0.52, 0.90; *P*=0.005)
- **Complete response** was seen in 38% of patients in the Vyxeos group vs. 26% of patients in the 7+3 group (*P*=0.036)

Clinical Studies

- Vyxeos demonstrated superiority in overall survival compared with the 7+3 control

- For more clinical trial data, see full labeling

New Product Monograph

- For more information view the product monograph available at:

  http://www.empr.com/vyxeos/drug/34723/