Proudly Canadian

Pr Vyxeos®

daunorubicin and cytarabine liposome for injection

DISCOVERING VYXEOS®

The Canadian story of the first dual-drug liposomal formulation

Scan to see more of our story: Watch the Made in Canada *video*

Jazz Pharmaceuticals

Clinical use:
Pediatrics (<18 years): The safety and effectiveness of VYXEOS in the treatment of newly diagnosed t-AML and AML-MRC has not been established in children and adolescent patients under 18 years of age.
Geriatrics (≥65 years of age): No significant differences in safety were observed in patients aged 65 or older.

Serious warnings and precautions:
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.

Relevant warnings and precautions:
- VYXEOS must not be substituted or interchanged with other daunorubicin and/or cytarabine-containing products
- Tissue necrosis
- Cardiotoxicity is a known risk of anthracycline treatment
- Driving and operating machinery
- VYXEOS should be used in patients with a history of Wilson's disease or other copper-related disorder only if the benefits outweigh the risks. Discontinue VYXEOS in patients with signs or symptoms of acute copper toxicity
- Gastrointestinal mucositis and diarrhea
- Hematologic: Severe myelosuppression resulting in fatal infections and haemorrhage has been reported in patients after administration with VYXEOS. Patients should be carefully monitored during VYXEOS treatment for possible clinical complications due to myelosuppression. Patient blood counts should be regularly monitored during VYXEOS treatment and appropriate supportive measures should be used for clinical complications due to myelosuppression
- Hepatic impairment may increase the risk of toxicity associated with daunorubicin and cytarabine. Evaluation of hepatic function using conventional clinical laboratory tests is recommended prior to administration of VYXEOS and periodically during treatment. VYXEOS should only be used in patients with severe hepatic impairment if the benefits outweigh the risks
- Serious hypersensitivity reactions, including anaphylactic reactions, have been reported with daunorubicin and cytarabine
- Increased susceptibility to infections
- Renal impairment may increase the risk of toxicity associated with daunorubicin and cytarabine. Evaluation of renal function using conventional clinical laboratory tests is recommended prior to administration of VYXEOS and periodically during treatment. VYXEOS should only be used in patients with end-stage renal disease if the benefits outweigh the risks
- Cardiac function and blood uric acid levels should be closely monitored. Appropriate therapy should be initiated if hyperuricemia develops
- Pregnancy: There are no data on the use of VYXEOS in pregnant women. Patients should be advised to avoid becoming pregnant during VYXEOS treatment. Male patients and women of childbearing potential must use effective methods of contraception during treatment and for 6 months following last dose of VYXEOS
- Male fertility may be compromised by treatment with VYXEOS according to animal studies
- Nursing women should be advised not to breastfeed during treatment with VYXEOS

For more information:
Consult the VYXEOS Product Monograph at: www.jazzpharma.com for important information relating to adverse reactions, drug interactions, and dosing information, which has not been discussed in this piece.
The Product Monograph is also available by calling our medical department at: 1-800-520-5568.

REFERENCES: 1. Tardi P, Johnstone S, Harasym N, *et al.* In vivo maintenance of synergistic cytarabine:daunorubicin ratios greatly enhances therapeutic efficacy. *Leuk Res* 2009;33:129–139. **2.** Tolcher AW, Mayer LD. Improving combination cancer therapy: the CombiPlex® development platform. *Future Oncol* 2018;14:1317–1332. **3.** Lancet JE, Uy GL, Cortes JE, *et al.* CPX-351 (cytarabine and daunorubicin) liposome for injection versus conventional cytarabine plus daunorubicin in older patients with newly diagnosed secondary acute myeloid leukemia. *J Clin Oncol* 2018;36:2684–2692. **4.** Current VYXEOS® Product Monograph, Jazz Pharmaceuticals Canada, Inc. **5.** Lancet JE, Cortes JE, Hogge DE, *et al.* Phase 2 trial of CPX-351, a fixed 5:1 molar ratio of cytarabine/daunorubicin, vs cytarabine/daunorubicin in older adults with untreated AML. *Blood* 2014;123(21):3239–3246. **6.** Granfeldt Østgård LS, Medeiros BC, Sengeløv H, *et al.* Epidemiology and clinical significance of secondary and therapy-related acute myeloid leukemia: A national population-based cohort study. *J Clin Oncol* 2015;33:3641–3649. **7.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Acute Myeloid Leukemia V.2.2021. © National Comprehensive Cancer Network, Inc. 2021. All rights reserved. Accessed February, 2021. To view the most recent and complete version of the guideline, go online to NCCN.org. **8.** Talati C, Lancet JE. CPX-351: changing the landscape of treatment for patients with secondary acute myeloid leukemia. *Future Oncol* 2018;14:1147–1154.

BC: British Columbia
MDS: Myelodysplastic syndromes
MPN: Myeloproliferative neoplasm
CMMoL AML: Chronic myelomonocytic leukemia AML
*Conventional chemotherapy includes the 7+3/5+2 regimen for induction and consolidation, using cytarabine and daunorubicin.[3]

†sAML defined as AML occurring after therapy and/or an antecedent myeloid disease, e.g., MDS or MPN, excluding chronic myeloid leukemia, regardless of prior cytotoxic therapy for these disorders. This includes the sub-types t-AML, AML-MRC and CMMoL AML.[6,7]
‡High-risk AML defined as t-AML or AML-MRC.

CA-VYX-2300015

Jazz Pharmaceuticals

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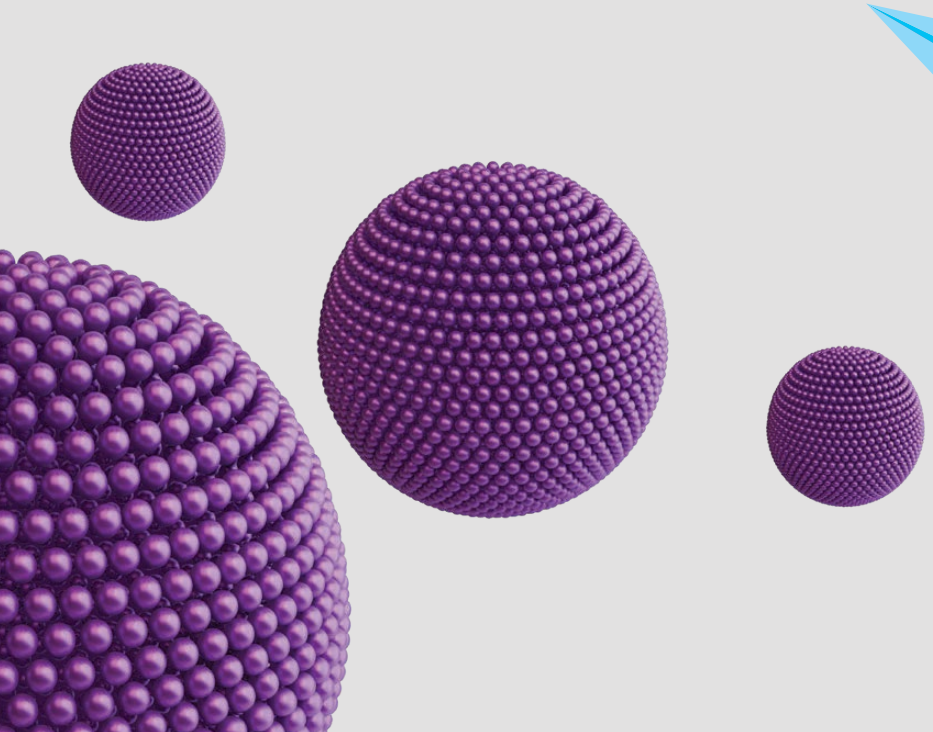
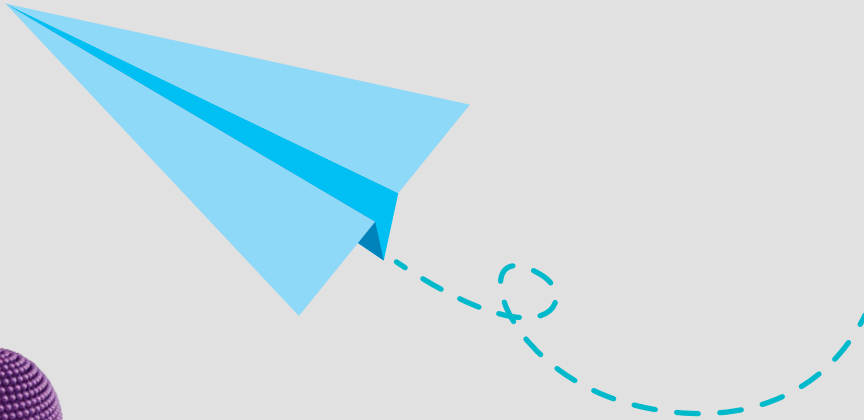
Pr Vyxeos®

Laying the foundations in a new era of AML treatment[8]

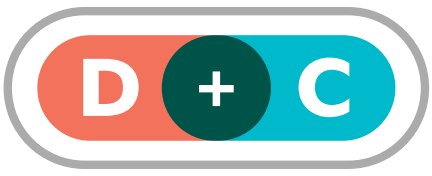




Further information for healthcare professionals can be found at www.vyxeos.ca

FOR THE PAST FEW DECADES

Daunorubicin (D) and cytarabine (C) were administered individually for the treatment of acute myeloid leukemia (AML)[1]



D and C were later combined in conventional chemotherapy* – resulting in increased response rates with little increase in toxicity[1-3]

IN THE EARLY 2000s

A team of Canadian researchers from Celator Pharmaceuticals in Vancouver, BC, discovered an opportunity to optimize combination therapy with an innovative delivery system

The CombiPlex® Platform: A technology-based approach brought to life

The dual-drug screening phase was used to identify the optimal ratio for synergistic activity

Optimized anti-leukemia activity (as shown *in vitro*) with daunorubicin and cytarabine in a synergistic ratio[2,4]

Delivered in an advanced liposome to maintain the fixed molar ratio for a prolonged period of time[4]

SYNERGY GREATER THAN D C

Evaluated in high-risk patients with secondary AML (sAML)†‡ in:

2008–2009

Phase II trial[5]
A multicentre, randomized, open-label, parallel-arm study

126 PATIENTS were enrolled across **18 sites** in Canada and the US, including: British Columbia Cancer Research Centre, McGill University, Dalhousie University

2012–2014

Phase III trial[3,4]
A multicentre, randomized, open-label, parallel-arm, superiority study

309 PATIENTS were enrolled across **39 sites** in Canada and the US, including: University of Alberta, British Columbia Cancer Research Centre, Princess Margaret Cancer Centre, University of Montreal

TODAY

Proudly Canadian

PrVyxeos®

The first dual-drug advanced liposomal formulation after 20 years of development[2]

PrVYXEOS® (daunorubicin and cytarabine liposome for injection) is indicated for the treatment of adults with newly diagnosed therapy-related acute myeloid leukemia (t-AML) or AML with myelodysplasia-related changes (AML-MRC)[4]

Formulated to optimize the synergistic activity of daunorubicin and cytarabine[3]

Designed using the CombiPlex® Platform by Celator Pharmaceuticals (now a subsidiary of Jazz Pharmaceuticals) in Vancouver, BC

Tested in pre-clinical and clinical trials across multiple Canadian sites