Regimen Monograph

A - Regimen Name

LIPOCYTADAUN(CONS) Regimen

Liposomal DAUNOrubicin / liposomal cytarabine

Disease Site

Hematologic
Leukemia - Acute Myeloid (AML)

Intent

Curative
Palliative

Regimen Category

Evidence-Informed :

Regimen is considered appropriate as part of the standard care of patients; meaningfully improves outcomes (survival, quality of life), tolerability or costs compared to alternatives (recommended by the Disease Site Team and national consensus body e.g. pan-Canadian Oncology Drug Review, pCODR). Recommendation is based on an appropriately conducted phase III clinical trial relevant to the Canadian context OR (where phase III trials are not feasible) an appropriately sized phase II trial. Regimens where one or more drugs are not approved by Health Canada for any indication will be identified under Rationale and Use.

Rationale and Uses

For consolidation treatment (after 1-2 cycles of induction) in patients with newly diagnosed therapy-related acute myeloid leukemia (t-AML) or AML with myelodysplasia-related changes (AML-MRC) who are fit for intensive chemotherapy*

*Patients must achieve complete remission (CR) or CR with incomplete neutrophil or platelet recovery (CRi) during induction.

Supplementary Public Funding

liposomal DAUNOrubicin / liposomal cytarabine
New Drug Funding Program (Liposomal Daunorubicin and Liposomal Cytarabine (Outpatient) - Previously Untreated Acute Myeloid Leukemia) (NDFP Website)

Additional Information	**The information provided in this document is intended for use only in the management of adults with leukemia, and for cancer centres with expertise in treating acute leukemia.**

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B - Drug Regimen

Liposomal daunorubicin / liposomal cytarabine (Vyxeos®) is **not interchangeable** with other daunorubicin- and/or cytarabine-containing products.

Consolidation* (after 1 or 2 Cycles of Induction)**:**

liposomal DAUNOrubicin / liposomal cytarabine	29** mg /m²	IV	Days 1 and 3

*Administered 5 to 8 weeks after start of the last induction or 1st consolidation, according to the product monograph. Do not start consolidation until ANC > 0.5 x 10^9/L and platelets > 50 x 10^9/L.

**Determine the dose based on the liposomal daunorubicin component. Each 29 mg/m^2 daunorubicin component delivers cytarabine 65 mg/m^2.

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C - Cycle Frequency

For up to 2 cycles unless disease progression or unacceptable toxicity occurs

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D - Premedication and Supportive Measures

Antiemetic Regimen: Moderate

- Also refer to CCO Antiemetic Recommendations.

Screen for hepatitis B virus in all cancer patients starting systemic treatment. Refer to the hepatitis B virus screening and management guideline.

Other Supportive Care:

- Consider prophylactic anti-infectives (e.g., anti-bacterials, anti-virals, anti-fungals) for febrile neutropenia prophylaxis.
- Consider prophylaxis for tumour lysis in patients at risk.

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E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated.

Assess cardiac function (e.g., ECG, and MUGA / Echo) prior to starting treatment and monitor routinely.

Calculate total cumulative anthracycline doses (daunorubicin or equivalent) prior to each cycle. Total cumulative daunorubicin doses should not exceed:

- 550mg/m^2
- 400mg/m^2 in patients with previous thoracic radiation

In the pivotal trial, patients were required to have at baseline, a prior lifetime cumulative anthracycline exposure of < 368 mg/m^2 daunorubicin (or equivalent).

Dosage with toxicity

Toxicity	Action
Cardiotoxicity (i.e., cardiomyopathy, impaired cardiac function)	Discontinue.
Acute copper toxicity	Discontinue.

Management of Infusion-related reactions:

Also refer to the CCO guideline for detailed description of Management of Cancer Medication-Related Infusion Reaction.

Severity	Management	Re-challenge
Mild	• Stop the infusion. • Manage the symptoms. **Restart:** • Once symptoms resolve, restart the infusion at 50% of the prior rate +/- pre-medications (antihistamines and/or corticosteroids).	• Re-challenge with pre-medications.
Moderate	• Stop the infusion. • Manage the symptoms. • Do not restart.	• Pre-medicate with antihistamines and/or corticosteroids. • Re-challenge at the same rate.
Severe	• Stop treatment. • Aggressively manage symptoms.	• Discontinue permanently (do not re-challenge).

Hepatic Impairment

Liposomal daunorubicin / liposomal cytarabine should only be used in severe hepatic impairment if benefits outweigh risks.

Bilirubin (µmol/L)	Liposomal Daunorubicin / Liposomal Cytarabine Dosage
≤ 50	No dose adjustment required
> 50	No data

Renal Impairment

Creatinine Clearance (mL/min)	Liposomal Daunorubicin / Liposomal Cytarabine Dosage
≥ 15	No dose adjustment required
< 15	No data. Use only if benefits outweigh risks.

Dosage in the Elderly

No dose adjustment required in patients ≥ 65 years old. Although there were no overall differences in safety between older and younger patients, bleeding events occurred more frequently in patients ≥ 65 years old.

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F - Adverse Effects

Refer to liposomal DAUNOrubicin / liposomal cytarabine drug monograph(s) for additional details of adverse effects.

Very common (≥ 50%)	Common (25-49%)	Less common (10-24%)	Uncommon (< 10%), but may be severe or life-threatening
• Myelosuppression ± infection, bleeding (may be severe) • Rash, pruritus	• Edema • Nausea, vomiting • Diarrhea • Mucositis • Constipation • Musculoskeletal pain • Abdominal pain • Cough, dyspnea • Headache • Fatigue • Arrhythmia • Anorexia, weight loss • Sleep disorder	• Cardiotoxicity • Changes in blood pressure • Dizziness • Delusions, hallucinations • Injection site reaction • Pleural effusion • Anxiety • Eye disorders • Nephrotoxicity	• Anaphylaxis • Tumour lysis syndrome • Pneumonitis • Extravasation • Hypothyroidism

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G - Interactions

Refer to liposomal DAUNOrubicin / liposomal cytarabine drug monograph(s) for additional details.

- Do not administer with other cardiotoxic agents unless cardiac function is closely monitored; avoid anthracycline-based therapy for up to 28 weeks after stopping trastuzumab.
- Monitor liver function more frequently when liposomal daunorubicin / liposomal cytarabine is given with hepatotoxic agents.

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H - Drug Administration and Special Precautions

Refer to liposomal DAUNOrubicin / liposomal cytarabine drug monograph(s) for additional details.

Administration:

Liposomal daunorubicin / liposomal cytarabine (Vyxeos®) is **not interchangeable** with other daunorubicin- and/or cytarabine-containing products.

- Dose should be determined based on the liposomal daunorubicin component and the individual's BSA.
- Calculate drug volume based on the concentration of the liposomal daunorubicin component (2.2 mg/mL).
- Reconstitute each vial with SWFI; mix by careful swirling and gentle inversion. Refer to the product monograph for details.
- Dilute in 500mL NS or D5W; mix by gentle inversion.
- Administer as IV infusion over 90 minutes using an infusion pump through a CVC or PICC line. An in-line membrane filter (minimum pore diameter ≥ 15 µm) may be used.
- Daunorubicin is a vesicant. Exercise care to ensure that there is no extravasation when liposomal daunorubicin / liposomal cytarabine is administered.
- Do NOT administer by intramuscular, intrathecal or subcutaneous route.
- Flush line with NS after administration.
- Do not mix with or administer as an infusion with other medications.
- Store unopened vials in the original carton at 2-8°C. Protect from light. Keep in an upright position.

Contraindications:

- Patients who are hypersensitive to this drug or any of its components

Other Warnings/Precautions:

- Liposomal daunorubicin / liposomal cytarabine is not recommended in patients with reduced LVEF.
- Avoid use of live vaccines in patients receiving liposomal daunorubicin / liposomal cytarabine. Inactivated vaccines may be administered; however, response may be diminished.
- Patients should exercise caution when driving or operating heavy machinery as fatigue and dizziness have been reported with liposomal daunorubicin / liposomal cytarabine.
- Caution in patients with Wilson's disease; the formulation contains copper. A hepatologist and nephrologist should be consulted before starting treatment. Perform serum/urine copper levels and serial neuropsychological assessments at baseline and as clinically indicated.

Pregnancy/Lactation:

- This regimen is not recommended for use in pregnancy. Adequate contraception should be used by patients and their partners while on treatment and after the last treatment dose. Recommended methods and duration of contraception may differ depending on the treatment. Refer to the drug monograph(s) for more information.
- Breastfeeding is not recommended during this treatment and after the last treatment dose. Refer to the drug monograph(s) for recommendations after the last treatment dose (if available).
- Fertility effects: Probable

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I - Recommended Clinical Monitoring

Treating physicians may decide to monitor more or less frequently for individual patients but should always consider recommendations from the product monograph.

Refer to the hepatitis B virus screening and management guideline for monitoring during and after treatment.

Recommended Clinical Monitoring

- Cardiac function tests (e.g., ECG, and MUGA / Echo); Baseline, prior to consolidation, and as clinically indicated
- CBC; Baseline, before each cycle, and as clinically indicated
- Liver function tests; Baseline, before each cycle, and as clinically indicated
- Renal function tests; Baseline, before each cycle, and as clinically indicated
- Clinical toxicity assessment for infusion-related or injection site reactions, tumour lysis syndrome, infections, bleeding, skin, respiratory and GI effects; At each visit
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

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J - Administrative Information

Approximate Patient Visit	2 hours

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K - References

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.

Liposomal DAUNOrubicin / liposomal cytarabine drug monograph. Ontario Health (Cancer Care Ontario).

December 2023 Modified Dosage in hepatic impairment, Dosage in renal impairment, and Pregnancy/lactation sections

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M - Disclaimer

Regimen Abstracts

A Regimen Abstract is an abbreviated version of a Regimen Monograph and contains only top level information on usage, dosing, schedule, cycle length and special notes (if available). It is intended for healthcare providers and is to be used for informational purposes only. It is not intended to constitute or be a substitute for medical advice, and all uses of the Regimen Abstract are subject to clinical judgment. Such information is provided on an "as-is" basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information's quality, accuracy, currency, completeness, or reliability, and Cancer Care Ontario disclaims all liability for the use of this information, and for any claims, actions, demands or suits that arise from such use.

Information in regimen abstracts is accurate to the extent of the ST-QBP regimen master listings, and has not undergone the full review process of a regimen monograph. Full regimen monographs will be published for each ST-QBP regimen as they are developed.

Regimen Monographs

Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.

The information set out in the drug monographs, regimen monographs, appendices and symptom management information (for health professionals) contained in the Drug Formulary (the "Formulary") is intended for healthcare

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The format and content of the drug monographs, regimen monographs, appendices and symptom management information contained in the Formulary will change as they are reviewed and revised on a periodic basis. The date of last revision will be visible on each page of the monograph and regimen. Since standards of usage are constantly evolving, it is advised that the Formulary not be used as the sole source of information. It is strongly recommended that original references or product monograph be consulted prior to using a chemotherapy regimen for the first time.

Some Formulary documents, such as the medication information sheets, regimen information sheets and symptom management information (for patients), are intended for patients. Patients should always consult with their healthcare provider if they have questions regarding any information set out in the Formulary documents.

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