Evolent Clinical Guideline 3239 for Vyxeos™ (daunorubicin and cytarabine liposomal)

Guideline Number:	Applicable Codes	
Evolent_CG_3239		
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Original Date:	**Last Revised Date:**	**Implementation Date:**
September 2017	December 2025	December 2025

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STATEMENT

Purpose

To define and describe the accepted indications for Vyxeos (daunorubicin and cytarabine liposomal) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

INDICATIONS

Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided

- The member has not experienced disease progression on the requested medication AND
- The requested medication was used within the last year without a lapse of more than 30 days of having an active authorization AND
- Additional medication(s) are not being added to the continuation request.

Acute Myeloid Leukemia (AML)

- Vyxeos (daunorubicin and cytarabine liposomal) may be used for induction and consolidation therapy for adult members aged 60 years or older, with one of the following 5 subtypes of newly diagnosed AML:
  - Therapy related AML
  - AML with a history of MDS – No prior HMA (Hypomethylating Agent Therapy, e.g., azacitidine)
  - AML with a history of MDS - Treated with prior HMA (Hypomethylating Agent Therapy received, e.g., azacitidine)
  - AML with a history of CMML (Chronic Myelo-Monocytic Leukemia)
  - De-Novo AML with MDS - related cytogenetic abnormalities
- NOTE: Vyxeos (daunorubicin and cytarabine liposomal) is not supported by Evolent Vyxeos Policy as induction treatment in adult members less than 60 years of age with newly diagnosed AML. This policy position is based on the lack of Level 1 evidence (randomized phase III trials and/or meta-analyses) to show superior outcomes with Vyxeos compared to regimens containing conventional formulations of daunorubicin and cytarabine. Other Evolent recommended agents/regimens, in members younger than 60 years of age (including but not limited to regimens) are available at **Evolent Pathways**.

- Vyxeos (daunorubicin and cytarabine liposomal) may be used for induction and consolidation therapy for pediatric members 1-17 years of age, who have therapy-related AML or AML with MDS-associated cytogenetic abnormalities.

CONTRAINDICATIONS/WARNINGS

- Contraindications
  - Serious hypersensitivity to daunorubicin, cytarabine, or any component of the formulation
- US Boxed Warning
  - Daunorubicin and cytarabine (liposomal) 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.

EXCLUSION CRITERIA

- Members without one of the 5 types of AML described in the indication section above.
- Members with Acute Promyelocytic Leukemia.
- Members with t(8;21) positive or inversion 16 positive (Core Binding Factor positive) AML.
- CNS Leukemia.
- Dosing exceeds single dose limit of Vyxeos: 44 mg/m^2 daunorubicin liposomal and 100 mg/m^2 cytarabine liposomal (for induction) or 29 mg/m^2 daunorubicin liposomal and 65 mg/m^2 cytarabine liposomal (for consolidation).
- Investigational use of Vyxeos (daunorubicin and cytarabine liposomal) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:
  - Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
  - Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
  - Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definitions of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
  - Whether the experimental design, considering the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use

randomization, double blind trials, placebos, or crossover).

- That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
- That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
- That abstracts (including meeting abstracts) without the full article from the approved peer- reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

CODING AND STANDARDS

Codes

- J9153 - Injection, liposomal, 1 mg daunorubicin and 2.27 mg cytarabine

Applicable Lines of Business

☐	CHIP (Children's Health Insurance Program)
☒	Commercial
☒	Exchange/Marketplace
☒	Medicaid
☐	Medicare Advantage

POLICY HISTORY

Date	Summary
December 2025	• Converted to new Evolent guideline template • This guideline replaces UM ONC_1326 Vyxeos (daunorubicin and cytarabine liposomal) • Updated exclusion criteria • Updated references
December 2024	• Added Evolent disclaimer language • Added Coding Information section with HCPCS code • Updated NCH verbiage to Evolent

LEGAL AND COMPLIANCE

Guideline Approval

Committee

Reviewed / Approved by Evolent Specialty Services Clinical Guideline Review Committee

Disclaimer

Evolent Clinical Guidelines do not constitute medical advice. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Evolent uses Clinical Guidelines in accordance with its contractual obligations to provide utilization management. Coverage for services varies for individual members according to the terms of their health care coverage or government program. Individual members' health care coverage may not utilize some Evolent Clinical Guidelines. Evolent clinical guidelines contain guidance that requires prior authorization and service limitations. A list of procedure codes, services or drugs may not be all inclusive and does not imply that a service or drug is a covered or non-covered service or drug. Evolent reserves the right to review and update this Clinical Guideline in its sole discretion. Notice of any changes shall be provided as required by applicable provider agreements and laws or regulations. Members should contact their Plan customer service representative for specific coverage information.

REFERENCES

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