Clinical Policy: Daunorubicin/Cytarabine (Vyxeos)

Reference Number: CP.PHAR.352
Effective Date: 12.01.17
Last Review Date: 11.26
Line of Business: Commercial, HIM/ICHRA, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Daunorubicin/cytarabine (Vyxeos®) is a liposomal combination of daunorubicin, an anthracycline topoisomerase inhibitor, and cytarabine, a nucleoside metabolic inhibitor.

FDA Approved Indication(s)

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.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Vyxeos is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Acute Myeloid Leukemia (must meet all)**:**

1. Diagnosis of one of the following (a, b, c, or d):
   a. t-AML;
   b. AML that is poor risk without *TP53* mutation or del(17p) abnormality;
   c. Cytogenetic changes consistent with myelodysplastic syndrome (MDS), which was formerly classified as AML-MRC;
   d. Antecedent MDS/chronic myelomonocytic leukemia (MDS/CMML);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 1 year;
4. Request meets one of the following (a, b, or c)*:
   a. Induction (up to 2 cycles): Dose does not exceed 44 mg/m^2 daunorubicin liposomal and 100 mg/m^2 cytarabine liposomal on days 1, 3, and 5 of cycle 1, and days 1 and 3 if a second cycle;
   b. Consolidation (up to 2 cycles): Dose does not exceed 29 mg/m^2 daunorubicin liposomal and 65 mg/m^2 cytarabine liposomal on days 1 and 3 of each cycle;
   c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Medicaid/HIM/ICHRA – 12 months

Commercial – 6 months or to the member's renewal date, whichever is longer

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Acute Myeloid Leukemia (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Vyxeos for AML and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. Member has not yet received ≥ 4 treatment cycles (up 2 to induction and 2 consolidation cycles);
4. If request is for a dose increase, request meets one of the following (a, b, or c)*:
   a. Induction (up to 2 cycles total): New dose does not exceed 44 mg/m^2 daunorubicin liposomal and 100 mg/m^2 cytarabine liposomal on days 1, 3, and 5 of cycle 1, and days 1 and 3 if a second cycle;
   b. Consolidation (up to 2 cycles total): New dose does not exceed 29 mg/m^2 daunorubicin liposomal and 65 mg/m^2 cytarabine liposomal on days 1 and 3 of each cycle;
   c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM/ICHRA – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – HIM.PA.154 for health insurance marketplace/ICHRA and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AML: acute myeloid leukemia
AML-MRC: acute myeloid leukemia with myelodysplasia-related changes
FDA: Food and Drug Administration
MDS-/CMML: myelodysplastic syndrome/ chronic myelomonocytic leukemia
NCCN: National Comprehensive Cancer Network
t-AML: therapy-related acute myeloid leukemia

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): hypersensitivity to daunorubicin, cytarabine, or any component of the formulation
- Boxed warning(s): do not interchange with other daunorubicin and/or cytarabine-containing products

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
t-AML, AML-MRC, and antecedent MDS/CMML	A full Vyxeos course consists of 1-2 cycles of induction and up to 2 cycles of consolidation. • *First Induction*: Daunorubicin 44 mg/m^2 and cytarabine 100 mg/m^2 liposome IV on days 1, 3 and 5 • *Second Induction* (Only for patients failing to achieve a response with the first induction cycle): Daunorubicin 44 mg/m^2 and cytarabine 100 mg/m^2 liposome IV on days 1 and 3. Administer second induction cycle 2 to 5 weeks after the first induction if there was no unacceptable toxicity to Vyxeos in patients who do not achieve remission with the first induction cycle. • *Consolidation:* Daunorubicin 29 mg/m^2 and cytarabine 65 mg/m^2 liposome IV on days 1 and 3. Administer the first consolidation cycle 5 to 8 weeks after the start of the last induction; administer the second consolidation cycle 5 to 8 weeks after the start of the first consolidation cycle in patients who do not show disease progression or unacceptable toxicity to Vyxeos.	See dosing regimens

VI. Product Availability

Single-dose vial: 44 mg daunorubicin and 100 mg cytarabine encapsulated in liposomes

VII. References

1. Vyxeos Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; January 2026. Available at: https://vyxeos.com. Accessed July 7, 2026.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed August 15, 2026.
3. National Comprehensive Cancer Network. Acute Myeloid Leukemia Version 5.2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf. Accessed August 15, 2026.
4. Lencet 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.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9153	Injection, liposomal, 1 mg daunorubicin and 2.27 mg cytarabine

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2022 annual review: no significant changes; references reviewed and updated. Template changes applied to other diagnoses/indications.	07.28.22	11.22
4Q 2023 annual review: no significant changes; references reviewed and updated.	08.07.23	11.23
4Q 2024 annual review: added Commercial line of business for use in medical coverage determinations; references reviewed and updated.	07.17.24	11.24
4Q 2025 annual review: added diagnosis option of AML that is poor risk without *TP53* mutation or del(17)p abnormality per NCCN; updated NCCN nomenclature for AML-MRC; revised Medicaid and HIM initial and continued approval durations to 12 months; references reviewed and updated.	07.11.25	11.25
4Q 2026 annual review: added ICHRA line of business; references reviewed and updated.	07.07.26	11.26

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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