Clinical Policy: Daunorubicin/Cytarabine (Vyxeos)

Reference Number: ERX.SPA.270
Effective Date: 12.01.18
Last Review Date: 11.20
Line of Business: Commercial, Medicaid

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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 AML;
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: 6 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Vyxeos for a covered indication 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. New 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: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 – ERX.PA.01 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
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
AML	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 over 90 minutes on days 1, 3 and 5 • *Second Induction* (Only for patients failing to achieve a response with the first induction cycle; administered 2 to 5 weeks after the first): Daunorubicin 44 mg/m^2 and cytarabine 100 mg/m^2 liposome IV over 90 minutes on days 1 and 3 • *Consolidation:* Daunorubicin 29 mg/m^2 and cytarabine 65 mg/m^2 liposome IV over 90 minutes 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	See dosing regimens

Indication	Dosing Regimen	Maximum Dose
	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.	

VI. Product Availability

Single-dose vial: 44 mg daunorubicin and 100 mg cytarabine

VII. References

1. Vyxeos Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; March 2021. Available at: https://vyxeos.com/. Accessed April 15, 2021.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed April 15, 2021.
3. National Comprehensive Cancer Network. Acute Myeloid Leukemia Version 3.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf. Accessed August 11, 2020.
4. Godley LA, Larson RA. Therapy-related Myeloid Leukemia. Seminars in oncology. 2008;35(4):418-429. doi:10.1053/j.seminoncol.2008.04.012.
5. Vardiman J, Reichard K. Acute myeloid leukemia with myelodysplasia-related changes. Am J Clin Pathol. 2015 Jul;144(1):29-43.
6. 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. Available at https://www.ncbi.nlm.nih.gov/pubmed/30024784.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	08.07.18	11.18
4Q 2019 annual review: antecedent MDS/CMML added per NCCN; cycle details added per PI; FDA/NCCN dosing limitation added; references reviewed and updated.	08.27.19	11.19
4Q 2020 annual review: AML criteria collapsed in recognition of the interrelated transformative nature of the three disease states and to encompass new subtypes and treatment algorithms; references reviewed and updated.	08.18.20	11.20
RT4: updated AML criteria from adults only to pediatric extension of 1 year old and older.	04.19.21	

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

be bound by the foregoing terms and conditions, in addition to the Site Use Agreement for Health Plans associated with Envolve Pharmacy Solutions.