Clinical Policy: Daunorubicin/Cytarabine (Vyxeos)

Reference Number: PA.CP.PHAR.352
Effective Date: 10/2018
Last Review Date: 10/2023

Coding Implications
Revision Log

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 PA Health & Wellness® 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 t-AML, AML-MRC, antecedent myelodysplastic syndrome/chronic myelomonocytic leukemia (MDS/CMML) or poor-risk AML with and without TP53-mutation or del17p abnormality;
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*).

Approval duration: 6 months

B. Other diagnoses/indications (must meet all)

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53
2. The requested dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use.

II. Continued Therapy

A. Acute Myeloid Leukemia (must meet all)**:**
1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies;
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*).

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53
   a. The requested dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use.

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 – PA.CP.PMN.53 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-CMLL: 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 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. 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 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 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.; September 2022. Available at: https://vyxeos.com/. Accessed August 7, 2023.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed August 7, 2023.
3. National Comprehensive Cancer Network. Acute Myeloid Leukemia Version 4.2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf. Accessed August 7, 2023.
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. Accessed August 7, 2023.

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
Policy created	10/2018	
4Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	10/2019	
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; cycle details added per PI; FDA/NCCN dosing limitation added; references reviewed and updated.	08/2020	
4Q 2021 annual review: updated diagnosis of coverage for t-AML, AML-MRC and antecedent MDS/CMML as per PI and NCCN Compendium; updated appendices; updated section V Dosage and Administration; removed temporary HCPCS code C9024 and added J9153; references reviewed and updated.	10/2021	
4Q 2022 annual review: no significant changes; references reviewed and updated.	10/2022	
4Q 2023 annual review: no significant changes; references reviewed and updated.	10/2023	