Clinical Policy: Daunorubicin/Cytarabine (Vyxeos)

Reference Number: PA.CP.PHAR.352
Effective Date: 10.17.18
Last Review Date: 10/30/2019

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 adults with newly-diagnosed therapy-related acute myeloid leukemia (t-AML) or AML with myelodysplasia-related changes (AML-MRC).

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 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 or AML-MRC;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Dose does not exceed:
   a. Induction (up to 2 cycles): 44 mg/m^2 daunorubicin liposomal and 100 mg/m^2 cytarabine liposomal;
   b. Consolidation (up to 2 cycles): 29 mg/m^2 daunorubicin liposomal and 65 mg/m^2 cytarabine liposomal.

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 Pennsylvania Health and 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, new dose does not exceed:

a. Induction (up to 2 cycles total): 44 mg/m^2 daunorubicin liposomal and 100 mg/m^2 cytarabine liposomal;
b. Consolidation (up to 2 cycles total): 29 mg/m^2 daunorubicin liposomal and 65 mg/m^2 cytarabine liposomal.

Approval duration: 6 months

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

1. Currently receiving medication via Pennsylvania Health and 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: myelodysplastic syndrome
MDS/MPN: myelodysplastic/ myeloproliferative neoplasm
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

Appendix D: General Information

- t-AML is a clinical syndrome occurring as a late complication following cytotoxic therapy and/ or ionizing radiotherapy for an unrelated disease.
- AML-MRC includes those forms of AML occurring in patients with a history of a myelodysplastic syndrome (MDS) or a myelodysplastic/myeloproliferative neoplasm (MDS/MPN); it also includes those forms of AML with morphologic features or cytogenetic abnormalities characteristic of an MDS.

- The World Health Organization, as discussed in Vardiman et al, defines AML-MRC as cases with 20% or more blasts in the peripheral blood or bone marrow and one or more of the following: (1) history of MDS or MDS/MPN, (2) multilineage dysplasia (dysplasia in ≥ 50% of the cells in at least two lineages), or (3) specific myelodysplasia-related cytogenetic abnormalities - e.g. –7/del(7q), –5/del(5q), i(17q)/t(17p), –13/del(13q), del(13q), del(12p)/t(12p), del(9q), idic(X)(q13), t(11;16)(q23;p13.3), t(3;21)(q26.2;q22.1), t(1;3)(p36.3;q21.1), t(2;11)(p21;q23), t(5;12)(q33;p12), t(5;7)(q33;q11.2), t(5;17)(q33;p13), t(5;10)(q33;q21), t(3;5)(q25;q34).

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
t-AML or AML-MRC	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 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 regimen

VI. Product Availability

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

VII. References

1. Vyxeos Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; August 2017. Available at: https://vyxeos.com/. Accessed July 23, 2018.
2. Godley LA, Larson RA. Therapy-related Myeloid Leukemia. Seminars in oncology. 2008;35(4):418-429. doi:10.1053/j.seminoncol.2008.04.012.
3. Vardiman J, Reichard K. Acute myeloid leukemia with myelodysplasia-related changes. Am J Clin Pathol. 2015 Jul;144(1):29-43.
4. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed July 23, 2018.

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
C9024	Injection, liposomal, 1 mg daunorubicin and 2.27 mg cytarabine

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	10/18	
4Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	10/30/19	