Clinical Policy: Daunorubicin/Cytarabine (Vyxeos)

Reference Number: CP.PHAR.352
Effective Date: 12.01.17
Last Review Date: 11.17
Line of Business: 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 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 (which may include office chart notes and lab results) 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. One of the following diagnoses (a or b):
   a. t-AML;
   b. AML-MRC;
2. Age ≥ 18 years;
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

1. Refer to CP.PHAR.57 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 Centene benefit or member has previously met initial approval criteria;

2. Member is responding positively to therapy (e.g., no disease progression or unacceptable toxicity);
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: 44 mg/m^2 daunorubicin liposomal and 100 mg/m^2 cytarabine liposomal;
   b. Consolidation: 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 Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to CP.PHAR.57 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 – CP.PHAR.57 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: 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

<table>
<tr><th>Indication</th><th>Dosing Regimen</th><th>Maximum Dose</th></tr>
<tr><td>t-AML or AML-MRC</td><td>A full Vyxeos course consists of 1-2 cycles of induction and up to 2 cycles of consolidation.
<table>
<tr><th>Cycle</th><th>Vyxeos Dose and Schedule</th></tr>
<tr><td>First Induction</td><td>Daunorubicin 44 mg/m^2 and cytarabine 100 mg/m^2 liposome IV over 90 minutes on days 1, 3 and 5</td></tr>
<tr><td>Second Induction*</td><td>Daunorubicin 44 mg/m^2 and cytarabine 100 mg/m^2 liposome IV over 90 minutes on days 1 and 3</td></tr>
<tr><td>Consolidation**</td><td>Daunorubicin 29 mg/m^2 and cytarabine 65 mg/m^2 liposome IV over 90 minutes on days 1 and 3</td></tr>
</table>
*Only for patients failing to achieve a response with the first induction cycle; administered 2 to 5 weeks after the first
**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.</td><td>44 mg/m^2 daunorubicin liposomal and 100 mg/m^2 cytarabine liposomal</td></tr>
</table>

VI. Product Availability

Liposome for injection (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://www.accessdata.fda.gov/drugsatfda_docs/label/2017/209401s000lbl.pdf. Accessed September 6, 2017.
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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	09.06.17	11.17

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.