Vyxeos® (daunorubicin and cytarabine – liposome)
(Intravenous)

-E-

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I. Length of Authorization

Coverage will be provided for a maximum of 2 cycles of induction (6 doses total) and 2 cycles of consolidation (4 doses total) within 6 months. Coverage may not be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Vyxeos single-dose vial: 23 vials total

B. Max Units (per dose and over time) [HCPCS Unit]:

- 1012 billable units per 155 days

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient is at least 1 year of age (unless otherwise specified); **AND**
- Baseline left ventricular ejection fraction (LVEF) is within normal limits and will be reassessed prior to consolidation and as clinically required; **AND**
- Cumulative lifetime anthracycline (e.g., daunorubicin, etc.) dose does not exceed 550 mg/m^2 (or 400 mg/m^2 in patients who received radiation to the mediastinum); **AND**
- Will not be used in combination with other chemotherapy; **AND**

Acute Myeloid Leukemia (AML) † ‡ Φ [1-3]

- Patient has therapy-related acute myeloid leukemia (t-AML) OR AML with myelodysplasia-related changes (AML-MRC) †; **AND**
  - Used as induction therapy for newly diagnosed disease; **OR**
  - Used as re-induction therapy if previously given as first induction therapy; **OR**
  - Used as consolidation therapy if previously given as induction therapy; **OR**

- Patient has antecedent myelodysplastic syndrome/chronic myelomonocytic leukemia (antecedent MDS/CMML) ‡; **AND**
    - Patient is at least 18 years of age; **AND**
        - Used as induction therapy for patients who are candidates for intensive induction therapy; **OR**
        - Used as re-induction therapy if previously given as first induction therapy; **AND**
            - Patient has residual disease; **OR**
        - Used as consolidation if previously given as induction therapy

Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1,3]

Authorizations may not be renewed.

V. Dosage/Administration [1,3]

Indication	Dose

t-AML, antecedent MDS/CMML, & AML-MRC	<u>First Induction</u>
	• daunorubicin 44 mg/m^2 and cytarabine 100 mg/m^2 liposome intravenously days 1, 3 and 5 for 1 cycle
	• ***<u>NOTE:</u>*** *Only applies to t-AML, antecedent MDS/CMML, AML-MRC*
	<u>Re-Induction (Second Induction)</u>
	• daunorubicin 44 mg/m^2 and cytarabine 100 mg/m^2 liposome intravenously days 1 and 3 for 1 cycle
	  ○ Only for patients who fail to respond to the first induction cycle
	  ○ May be administered 2 to 5 weeks after the first induction cycle if there was no unacceptable toxicity
	• ***<u>NOTE:</u>*** *Only applies to t-AML, antecedent MDS/CMML, AML-MRC*
	<u>Consolidation</u>
	• daunorubicin 29 mg/m^2 and cytarabine 65 mg/m^2 liposome intravenously days 1 and 3 for 1 to 2 cycles
	  ○ Administer the first consolidation cycle 5 to 8 weeks after the start of the last induction cycle

	○ Administer the second consolidation cycle 5 to 8 weeks after the start of the first consolidation cycle if there was no unacceptable toxicity or disease progression

VI. Billing Code/Availability Information

HCPCS Code:

- J9153 – Injection, liposomal, 1 mg daunorubicin and 2.27 mg cytarabine; 1 billable unit = 1 1 mg daunorubicin and 2.27 mg cytarabine

NDC:

- Vyxeos (44 mg daunorubicin and 100 mg cytarabine) liposome, single-dose vial: 68727−0745−xx

VII. References (STANDARD)

1. Vyxeos [package insert]. Palo Alto, CA; Jazz Pharmaceuticals, Inc., September 2022. Accessed July 2024.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for cytarabine/daunorubicin liposome. National Comprehensive Cancer Network, 2024. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed July 2024.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Acute Myeloid Leukemia. Version 3.2024. National Comprehensive Cancer Network, 2024. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed July 2024.
4. Lin TL, Ryan RJ, Fadert S, et al. Outcomes in older patients with high-risk/secondary AML who achieved remission with CPX-351 versus 7+3 but did not undergo transplant: Phase 3 exploratory analysis. J Clin Onco; DOI: 10.1200/JCO.2020.38.15_suppl.7537 Journal of Clinical Oncology38, no. 15_suppl(May 20, 2020)7537-7537.

VIII. References (ENHANCED)

1e. Lancet JE, Uy, GL, Cortes JE, et al. Final results of a phase III randomized trial of CPX-351 versus 7+3 in older patients with newly diagnosed high risk (secondary) AML. Journal of Clinical Oncology 2016 34:15_suppl, 7000-7000.

2e. Welch JS, Petti AA, Miller CA, et al. TP53 and Decitabine in Acute Myeloid Leukemia and Myelodysplastic Syndromes. N Engl J Med 2016; 375:2023-2036.

3e. Löwenberg B, Ossenkoppele GJ, van Putten W, et al. High-Dose Daunorubicin in Older Patients with Acute Myeloid Leukemia. N Engl J Med 2009; 361:1235-1248.

4e. Stone RM, Mandrekar S, Sanford BL, et al. The Multi-Kinase Inhibitor Midostaurin (M) Prolongs Survival Compared with Placebo (P) in Combination with Daunorubicin (D)/Cytarabine (C) Induction (ind), High-Dose C Consolidation (consol), and As Maintenance (maint) Therapy in Newly Diagnosed Acute Myeloid Leukemia (AML) Patients (pts) Age 18-60 with FLT3 Mutations (muts): An International Prospective Randomized (rand) P-Controlled Double-Blind Trial (CALGB 10603/RATIFY [Alliance]). Blood 2015; 126:6.

5e. Mayer RJ, Davis RB, Schiffer CA, et al. Intensive Postremission Chemotherapy in Adults with Acute Myeloid Leukemia. N Engl J Med 1994; 331:896-903.

6e. Cooper TM, Absalon MJ, Alonzo TA, et al. Phase I/II Study of CPX-351 Followed by Fludarabine, Cytarabine, and Granulocyte-Colony Stimulating Factor for Children With Relapsed Acute Myeloid Leukemia: A Report From the Children's Oncology Group. J Clin Oncol. 2020 Jul 1;38(19):2170-2177. doi: 10.1200/JCO.19.03306.

7e. Prime Therapeutics Management. Vyxeos Clinical Literature Review Analysis. Last updated July 2024. Accessed July 2024.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C92.00	Acute myeloblastic leukemia not having achieved remission
C92.01	Acute myeloblastic leukemia in remission
C92.50	Acute myelomonocytic leukemia not having achieved remission
C92.51	Acute myelomonocytic leukemia in remission
C92.60	Acute myeloid leukemia with 11q23-abnormality not having achieved remission
C92.61	Acute myeloid leukemia with 11q23-abnormality in remission
C92.A0	Acute myeloid leukemia with multilineage dysplasia not having achieved remission
C92.A1	Acute myeloid leukemia with multilineage dysplasia in remission
C93.00	Acute monoblastic/monocytic leukemia not having achieved remission
C93.01	Acute monoblastic/monocytic leukemia in remission

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdictio	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC