POLICY NUMBER UM ONC_1326	SUBJECT Vyxeos™ (daunorubicin and cytarabine liposomal)		DEPT/PROGRAM UM Dept	PAGE 1 OF 3
DATES COMMITTEE REVIEWED 09/13/17, 09/21/18, 08/14/19, 12/11/19	APPROVAL DATE December 11, 2019	EFFECTIVE DATE December 11, 2019	COMMITTEE APPROVAL DATES (latest version listed last) 09/13/17, 09/21/18, 08/14/19, 12/11/19	
PRIMARY BUSINESS OWNER: UM APPROVED BY: Dr. Andrew Hertler		COMMITTEE/BOARD APPROVAL Utilization Management Committee		
URAC STANDARDS HUM 1		NCQA STANDARDS UM 2	ADDITIONAL AREAS OF IMPACT	
CMS REQUIREMENTS	STATE/FEDERAL REQUIREMENTS		APPLICABLE LINES OF BUSINESS All	

I. PURPOSE

To define and describe the accepted indications for Vyxeos (daunorubicin and cytarabine liposomal) usage in the treatment of cancer.

II. DEFINITIONS

Vyxeos (daunorubicin and cytarabine liposomal): is a liposomal combination of daunorubicin, an anthracycline topoisomerase inhibitor, and cytarabine, a nucleoside metabolic inhibitor. Daunorubicin binds with DNA and inhibits topoisomerase II and DNA polymerase activity resulting in altered regulation of gene expression and the formation of DNA-damaging free radicals. Cytarabine is a cell cycle phase-specific chemotherapy agent that affects cells in the S-phase of cell division; it inhibits DNA polymerase.

Vyxeos (daunorubicin and cytarabine liposomal) is FDA approved for the treatment of adults with newly-diagnosed therapy-related acute myeloid leukemia (t-AML) or AML with myelodysplasia-related changes (AML-MRC).

Vyxeos (daunorubicin and cytarabine liposomal) is available in 44 mg daunorubicin/100 mg cytarabine encapsulated in liposomes as lyophilized cake in a single-dose vial for reconstitution.

III. POLICY

New Century Health is responsible for processing all medication requests from network ordering providers. Medications not authorized by New Century Health may be deemed as not approvable and therefore not reimbursable. Treatment request outside the approved FDA manufacturer labeling or CMS approved compendia must follow CMS Medicare Benefit Policy Manual Chapter 15. If references are not produced, delays may occur to the processing of such request.

Inclusion Criteria: Vyxeos (daunorubicin and cytarabine liposomal) may be considered medically necessary when any of the following selection criteria is met:

1. **Acute Myeloid Leukemia (AML)**
    a. The member is being treated for AML related to therapy or with myelodysplasia-related changes **AND**
    b. The member is ≥ 60 years old and newly diagnosed **AND**
    c. The member has high risk AML with unfavorable cytogenetics features **AND**
    d. Vyxeos (daunorubicin and cytarabine liposomal) is being used as **ONE** of the following:

1. Induction therapy **OR**
2. Consolidation therapy

Exclusion Criteria: Vyxeos (daunorubicin and cytarabine liposomal) is not considered medically necessary when any of the following selection criteria is met:

1. The member was previously treated with prior cytotoxic therapy or radiotherapy for AML (except for hydroxyurea used for control of blood counts).
2. Concurrent use with hydroxyurea or any therapy for MDS.
3. The member has myocardial impairment or active/uncontrolled infection.
4. Dosing exceeds single dose limit of Vyxeos: 44 mg/m^2 daunorubicin liposomal and 100 mg/m^2 cytarabine liposomal.
5. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature may be deemed as not approvable and therefore not reimbursable.

IV. PROCEDURE

Requests for Vyxeos (daunorubicin and cytarabine liposomal) shall be reviewed for appropriateness per FDA approved product labeling, the National Comprehensive Cancer Network (NCCN) and American Society of Clinical Oncology (ASCO) clinical guidelines, or CMS approved compendia.

1. **Dosage and Administration: Calculate dose based on Daunorubicin and patient's body surface area (BSA).**
    a. First induction: 44 mg/m2 daunorubicin liposomal and 100 mg/m2 cytarabine liposomal IV over 90 minutes on days 1, 3, and 5; patients who do not achieve a response may receive a second induction.
    b. Second induction (given 2 to 5 weeks after the first induction cycle): 44 mg/m2 daunorubicin liposomal and 100 mg/m2 cytarabine liposomal IV on days 1 and 3.
    c. Consolidation therapy (given 5 to 8 weeks after the start of the last induction): 29 mg/m2 daunorubicin liposomal and 65 mg/m2 cytarabine liposomal IV on days 1 and 3. Patients without disease progression or unacceptable toxicity should receive a second cycle of consolidation therapy given 5 to 8 weeks after the start of the previous consolidation.
2. **Dosage Adjustments: Dosage adjustments are not required for renal or hepatic impairment.**
3. **Monitoring**
    a. Assess blood counts prior to each consolidation cycle.
    b. Obtain liver function studies prior to initiating induction and before each consolidation cycle. Assess more frequently when co-administered with another hepatotoxic agent.
    c. Obtain renal function studies prior to initiating induction and before each consolidation cycle.
    d. Pregnancy testing should be done prior to initiating treatment. Male and female patients should use effective contraception during treatment and for 6 months following the last dose.

V. APPROVAL AUTHORITY

1. Review – UM Department
2. Final Approval – UM Committee

VI. ATTACHMENTS

None

VII. REFERENCES

1. Vyxeos prescribing information. Jazz Pharmaceuticals, Inc. Palo Alto, CA 2010.
2. Clinical Pharmacology Elsevier Gold Standard. 2010.
3. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, Co. 2010.
4. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium. 2010.
5. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD. 2010.