Vyxeos (daunorubicin and cytarabine)

Background
Vyxeos is a cancer agent that is a liposomal combination of daunorubicin, an anthracycline topoisomerase inhibitor, and cytarabine, a nucleoside metabolic inhibitor. Vyxeos is indicated for the treatment of newly-diagnosed therapy-related acute myeloid leukemia (t-AML) or AML with myelodysplasia-related changes (AML-MRC) which is a rapidly progressing cancer that forms in the bone marrow and results in an increased number of abnormal white blood cells in the bloodstream and bone marrow. Therapy-related acute myeloid leukemia (t-AML) occurs as a complication of chemotherapy or radiation AML-MRC is characterized by a history of certain blood disorders and other significant mutations within cancer cells (1).

Regulatory Status
FDA-approved indication: Vyxeos is a liposomal combination of daunorubicin, an anthracycline topoisomerase inhibitor, and cytarabine, a nucleoside metabolic inhibitor that 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) (1).

Vyxeos has a boxed warning for not interchanging with other daunorubicin and/or cytarabine containing products (1).

Vyxeos contains the anthracycline daunorubicin, which has a known risk of cardiotoxicity. Prior therapy with anthracyclines, pre-existing cardiac disease, previous radiotherapy to the mediastinum, or concomitant use of cardiotoxic drugs may increase the risk of
daunorubicin induced cardiac toxicity. Prior to administering Vyxeos, obtain an electrocardiogram (ECG) and assess cardiac function by multi-gated radionuclide angiography (MUGA) scan or echocardiography (ECHO) (1).

Reconstituted Vyxeos contains 5 mg/mL copper gluconate, of which 14% is elemental copper. The maximum theoretical total exposure of copper under the recommended Vyxeos dosing regimen is 106 mg/m². Monitor total serum copper, serum nonceruloplasmin bound copper, 24-hour urine copper levels and serial neuropsychological examinations (1).

Safety and efficacy in pediatric patients below the age of 18 have not been established (1).

Related policies
Idhifa, Rydapt

Policy
This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Vyxeos may be considered medically necessary in patients 18 years or older with therapy-related acute myeloid leukemia (t-AML) or AML with myelodysplasia-related changes (AML-MRC) and if the conditions indicated below are met.

Vyxeos is considered investigational in patients below 18 years of age and for all other indications.

Prior-Approval Requirements

Age
18 years of age and older

Diagnoses

The patient must have ONE of the following:

1. Therapy-related acute myeloid leukemia (t-AML)
2. Acute myeloid leukemia with Myelodysplasia-related changes (AML-MRC)

AND ALL of the following:
a. Inadequate response, intolerance (high risk for relapse) or contraindication to the use of daunorubicin and cytarabine separately
b. Prescriber agrees NOT to interchange with other daunorubicin and/or cytarabine containing products
c. Prescriber agrees to do an electrocardiogram (ECG) and assess cardiac function by multi-gated radionuclide angiography (MUGA) scan or echocardiography (ECHO) prior to administering Vyxeos
d. Prescriber agrees to monitor complete blood counts and urine copper levels on a regular basis

Prior – Approval Renewal Requirements

Age
18 years of age and older

Diagnoses

The patient must have ONE of the following:

1. Therapy-related acute myeloid leukemia (t-AML)
2. Acute myeloid leukemia with Myelodysplasia-related changes (AML-MRC)

AND ALL of the following:

a. NO disease progression or unacceptable toxicity
b. Prescriber agrees NOT to interchange with other daunorubicin and/or cytarabine containing products
c. Prescriber agrees to monitor complete blood counts and urine copper levels on a regular basis

Policy Guidelines

Pre - PA Allowance
None

Prior - Approval Limits
Duration 12 months

Prior – Approval Renewal Limits
Duration 12 months
Rationale

Summary
Vyxeos is indicated for the treatment of newly-diagnosed therapy-related acute myeloid leukemia (t-AML) or AML with myelodysplasia-related changes (AML-MRC) which is a rapidly progressing cancer that forms in the bone marrow and results in an increased number of abnormal white blood cells in the bloodstream and bone marrow. Safety and efficacy in pediatric patients below the age of 18 have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate and cost effective use of Vyxeos while maintaining optimal therapeutic outcomes.

References

Policy History

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>August 2017</td>
<td>Addition to PA</td>
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<tr>
<td>September 2017</td>
<td>Annual review</td>
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<tr>
<td>December 2017</td>
<td>Annual editorial review</td>
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<td></td>
<td>Addition of prescriber agreeing to monitor complete blood counts and</td>
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<td>urine copper levels on a regular basis per SME</td>
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<td>March 2018</td>
<td>Annual editorial review</td>
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<td>Clarification to add intolerance (high risk for relapse) or contraindication to the use of daunorubicin and cytarabine separately</td>
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Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 20, 2019 and is effective on July 1, 2019.