

## Corporate Medical Policy

### Melphalan Hydrochloride (Evomela) for Intravenous Use

**File Name:** melphalan\_hydrochloride\_evomela\_for\_intravenous\_use  
**Origination:** 7/2016  
**Last CAP Review:** 3/2020  
**Next CAP Review:** n/a  
**Last Review:** 3/2020

#### Description of Procedure or Service

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Multiple myeloma is a systemic malignancy of plasma cells that accumulate in the bone marrow, usually associated with monoclonal antibody secretion, and results in bone marrow failure and bone destruction. It is the second most common hematologic disease with nearly 30,000 new cases projected in the U.S. in 2016 and over 11,000 deaths annually.

Melphalan hydrochloride (Evomela) is classified as an alkylating agent. Alkylating agents are a class of chemotherapy drugs that bind to DNA and prevent proper DNA replication. They have chemical components that can form permanent covalent bonds with nucleophilic substances in the DNA. Alkylating agents are used as part of chemotherapy in different types of cancers, including multiple myeloma.

According to the National Cancer Institute, melphalan (Evomela) is used for palliative treatment in multiple myeloma patients who cannot take melphalan (Evomela) by mouth and as a conditioning treatment to prepare multiple myeloma patients for a stem cell transplant.

Melphalan (Evomela) is also available in a tablet form. This policy only addresses intravenous use of Melphalan (Evomela).

**\*\*\*Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.**

#### Policy

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**BCBSNC will provide coverage for Melphalan Hydrochloride (Evomela) for intravenous use when it is determined to be medically necessary because the medical criteria and guidelines shown below are met.**

#### Benefits Application

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This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

#### When Evomela is covered

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Evomela may be considered medically necessary for the following clinical conditions:

1. For the diagnosis of multiple myeloma; **AND**

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2. As a high-dose conditioning treatment prior to hematopoietic progenitor (stem) cell transplantation; **OR**
3. For the palliative treatment of patients with an intolerance to oral melphalan.

## **When Evomela is not covered**

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Evomela is considered not medically necessary when the criteria under “When Melphalan (Evomela) is covered” are not met.

Evomela is considered investigational when used for indications outside of FDA labeling and nationally recognized compendia recommendations with the highest level of evidence (i.e. Level 1, 2A, 2B).

## **Policy Guidelines**

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The Food and Drug Administration has issued a black box warning for Evomela as follows:

### **WARNING: SEVERE BONE MARROW SUPPRESSION, HYPERSENSITIVITY, and LEUKEMOGENICITY:**

Severe bone marrow suppression with resulting infection or bleeding may occur. Controlled trials comparing intravenous (IV) melphalan to oral melphalan have shown more myelosuppression with the IV formulation. Monitor hematologic laboratory parameters.

Hypersensitivity reactions, including anaphylaxis, have occurred in approximately 2% of patients who received the IV formulation of melphalan. Discontinue treatment with Evomela for serious hypersensitivity reactions.

Melphalan produces chromosomal aberrations in vitro and in vivo. Evomela should be considered potentially leukemogenic in humans.

### **DOSAGE AND ADMINISTRATION:**

For Conditioning Treatment, the recommended dose of Evomela is 100 mg/m<sup>2</sup> /day administered over 30 minutes by intravenous infusion for 2 consecutive days (Day -3 and Day -2) prior to autologous stem cell transplantation (ASCT, Day 0).

For Palliative Treatment, the recommended dose of Evomela is 16 mg/m<sup>2</sup> administered as a single intravenous infusion over 15-20 minutes at 2-week intervals for 4 doses, then, after adequate recovery from toxicity, at 4-week intervals.

## **Billing/Coding/Physician Documentation Information**

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This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at [www.bcbsnc.com](http://www.bcbsnc.com). They are listed in the Category Search on the Medical Policy search page.

*Applicable service codes: J3490, J3590, J9999, C9399*

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

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## Scientific Background and Reference Sources

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American Cancer Society. Cancer Facts and Figures, 2016.

<http://www.cancer.org/research/cancerfactsstatistics/cancerfactsfigures2016/>

Food and Drug Administration (FDA) Prescribing Information.

[http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2016/207155s0001b1.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/207155s0001b1.pdf)

National Institutes of Health (NIH)/National Cancer Institute. Melphalan Hydrochloride.

<http://www.cancer.gov/about-cancer/treatment/drugs/melphalan-hydrochloride>

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Multiple Myeloma. Version 3.2016.

[https://www.nccn.org/professionals/physician\\_gls/pdf/myeloma.pdf](https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf)

Medical Director review 6/2016

Specialty Matched Consultant Advisory Panel 3/2017

Specialty Matched Consultant Advisory Panel 3/2018

Specialty Matched Consultant Advisory Panel 3/2019

Specialty Matched Consultant Advisory Panel 3/2020

Medical Director review 3/2020

## Policy Implementation/Update Information

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- 7/1/2016 New policy developed. Evomela may be considered medically necessary for the following clinical conditions: 1. For the diagnosis of multiple myeloma; 2. As a high-dose conditioning treatment prior to hematopoietic progenitor (stem) cell transplantation; 3. For the palliative treatment of patients with an intolerance to oral melphalan therapy. Medical Director review 6/2016. (mot)
- 4/28/17 Specialty Matched Consultant Advisory Panel review 3/29/2017. No change to policy statement. (lpr)
- 4/27/18 Specialty Matched Consultant Advisory Panel review 3/2018. No change to policy intent. (krc)
- 4/16/19 Specialty Matched Consultant Advisory Panel review 3/20/2019. No change to policy statement. (krc)
- 6/9/20 Specialty Matched Consultant Advisory Panel review 3/18/2020. (krc)
- 5/4/21 Policy archived. Medical Director review 3/2020. (krc)

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Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.

