Reference number(s)
4373-A

STANDARD MEDICARE PART B MANAGEMENT

EVOMELA (melphalan)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

As a high-dose conditioning treatment prior to hematopoietic progenitor (stem) cell transplantation in patients with multiple myeloma.

B. Compendial Uses

1. Primary therapy for symptomatic multiple myeloma
2. POEMS syndrome
3. Amyloidosis
4. Bone marrow transplant
5. Hodgkin's disease
6. Ovarian cancer
7. Melanoma
8. Gastrointestinal adenocarcinoma
9. Retinoblastoma

All other indications will be assessed on an individual basis. Submissions for indications other than those enumerated in this policy should be accompanied by supporting evidence from Medicare approved compendia.

II. CRITERIA FOR INITIAL APPROVAL

A. Multiple myeloma

Authorization of 12 months may be granted for treatment of multiple myeloma when used in one of the following settings:

1. High-dose conditioning treatment prior to stem cell transplant
2. Primary therapy for symptomatic members in combination with daratumumab, bortezomib, and prednisone for non-transplant candidates

B. POEMS

Authorization of 12 months may be granted for management of POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes) syndrome when both of the following criteria are met:

1. Therapy will be used in one of the following settings:
   i. As induction therapy for transplant eligible members

ii. For transplant ineligible members
2. Evomela will be used in combination with dexamethasone

C. Amyloidosis
Authorization of 12 months may be granted for the treatment of amyloidosis in combination with an autologous bone marrow transplant.

D. Bone marrow transplant
Authorization of 12 months may be granted for the bone marrow transplants when either of the following is met:
1. The requested drug will be used as part of a conditioning regimen prior to allogenic stem cell transplantation in one of the following regimens:
   i. In combination with busulfan
   ii. In combination with carmustine, etoposide, and cytarabine
2. The requested drug will be used as a conditioning regimen prior to autologous bone marrow transplantation in combination with busulfan.

E. Hodgkin's disease
Authorization of 12 months may be granted for the treatment of Hodgkin's disease in combination with carmustine, etoposide, cytarabine and hematopoietic stem cell transplant.

F. Ovarian cancer
Authorization of 12 months may be granted for the palliative treatment of non-resectable malignant epithelial ovarian cancer when administered intraperitoneally.

G. Melanoma
Authorization of 12 months may be granted for the treatment of melanoma if the disease is not metastatic.

H. Gastrointestinal adenocarcinoma
Authorization of 12 months may be granted for the treatment of gastrointestinal adenocarcinoma when administered intraperitoneally.

I. Retinoblastoma
Authorization of 12 months may be granted for the treatment of retinoblastoma when either of the following are met:
1. The requested drug will be administered as part of superselective ophthalmic artery chemotherapy in members undergoing primary or secondary treatment.
2. The requested drug will be administered as an intravitreal injection for the treatment of vitreous seeds.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

Authorization of 12 months may be granted when all of the following criteria are met:
A. The member is currently receiving therapy with Evomela
B. Evomela is being used to treat an indication enumerated in Section II
C. The member is receiving benefit from therapy. Benefit is defined as:
   1. No evidence of unacceptable toxicity while on the current regimen AND

2. No evidence of disease progression while on the current regimen

IV. SUMMARY OF EVIDENCE

The contents of this policy were created after examining the following resources:

1. The prescribing information for Evomela.
2. The available compendium
    a. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
    b. Micromedex DrugDex
    c. American Hospital Formulary Service- Drug Information (AHFS-DI)
    d. Lexi-Drugs
    e. Clinical Pharmacology
3. NCCN Guideline: Multiple myeloma

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Evomela are covered in addition to the following:

1. Primary therapy for symptomatic multiple myeloma
2. POEMS syndrome
3. Amyloidosis
4. Bone marrow transplant
5. Hodgkin's disease
6. Ovarian cancer
7. Melanoma
8. Gastrointestinal adenocarcinoma
9. Retinoblastoma

V. EXPLANATION OF RATIONALE

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for using Evomela as primary therapy for symptomatic multiple myeloma in combination with daratumumab, bortezomib, and prednisone for non-transplant candidates can be found in the NCCN Drugs and Biologics Compendium. Use of information in the NCCN Drugs and Biologics Compendium for off-label use of drugs and biologicals in an anti-cancer chemotherapeutic regimen is supported by the Medicare Benefit Policy Manual, Chapter 15, section 50.4.5 (Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen).

Support for using Evomela to treat Hodgkin's disease, ovarian cancer, melanoma, gastrointestinal adenocarcinoma and retinoblastoma can be found in the Micromedex DrugDex database. Use of information in the DrugDex database for off-label use of drugs and biologicals in an anti-cancer chemotherapeutic regimen is supported by the Medicare Benefit Policy Manual, Chapter 15, section 50.4.5 (Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen).

Support for using Evomela to treat POEMS syndrome can be found in the National Comprehensive Cancer Network's guideline for multiple myeloma. The NCCN Guideline for multiple myeloma supports the use of Evomela in combination with dexamethasone as either induction therapy for transplant eligible patients or for transplant ineligible patients.

Support for using Evomela to treat amyloidosis can be found in a study by Brown and Walls. Amyloidosis is often observed in patients with rheumatoid arthritis or multiple myeloma. Amyloidosis usually progresses slowly, with most patients surviving from 1 to 4 years (median, 14 months) following diagnosis. Melphalan (5 to 12 mg/day for 4 to 7 days repeated every 4 to 6 weeks) and prednisone therapy has been beneficial to patients with amyloidosis. Unfortunately, some patients treated with alkylating agents have developed acute leukemia.

Support for using Evomela to treat bone marrow transplant can be found in two studies. Van Besien et al published a paper on using melphalan as part of a conditioning regimen for allogenic transplant. High-dose melphalan-based chemotherapy allowed for durable engraftment of allogeneic bone marrow in 4 patients. Patients received conditioning regimens consisting of BEAM (carmustine, etoposide, cytarabine, melphalan) or busulfan plus melphalan. All 4 patients had prompt engraftment. Two patients had prolonged disease-free survival.
Attal et al published a study on using melphalan as part of a conditioning regimen for autologous stem cell transplant. High-dose chemotherapy and autologous bone marrow transplantation are more effective than conventional chemotherapy in patients with multiple myeloma. Two hundred patients with myeloma who were previously untreated were randomized to conventional chemotherapy with alternating cycles of VMCP (vincristine, melphalan, cyclophosphamide, and prednisone) and VBAP (vincristine, carmustine, doxorubicin, and prednisone) for a total of 18 cycles or to high-dose therapy after 4 to 6 cycles of the conventional regimen with melphalan (140 mg/m(2)) and total-body irradiation, followed by autologous bone marrow transplantation. The bone marrow was collected after the fourth chemotherapy cycle. Eighty-one percent of patients who received high-dose therapy responded; 57% of patients with the conventional regimen responded with a smaller proportion obtaining a complete response. The estimated five-year survival for patients treated with the high-dose regimen was 52% compared to only 12% of patients treated with conventional therapy.

VI. REFERENCES

1. Evomela [package insert]. East Windsor, NJ: Acrotech Biopharma LLC; April 2022.
2. The NCCN Drugs & Biologics Compendium® © 2021 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed October 17, 2022.
3. IBM Micromedex® DRUGDEX® (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com/ (cited: October 17, 2022).
4. Brown MP & Walls RS: Amyloidosis of immunoglobulin origin: useful treatment?. *Med J Aust* 1990; 152:95-97.
5. Van Besien K, Demuynck H, Lemaistre CF, et al: High-dose melphalan allows durable engraftment of allogeneic bone marrow. Bone Marrow Transplant 1995; 15:321-323.
6. Attal M, Harousseau JL, Stoppa AM, et al: A prospective, randomized trial of autologous bone marrow transplantation and chemotherapy in multiple myeloma. N Engl J Med 1996; 335:91-97.