Evomela® (melphalan)
(Intravenous)

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I. Length of Authorization

Conditioning Treatment: Coverage is provided for six months and may NOT be renewed.

All Other Indications: Coverage is provided for six months and may be renewed.

II. Dosing Limits

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

- Evomela 50 mg single-dose vial for reconstitution: 10 vials

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

- Conditioning Treatment: 250 billable units for 2 doses only prior to ASCT
- All Other Indications: 40 billable units every 14 days for 4 doses only, then 40 billable units every month thereafter

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

Universal Criteria [1]

- Patient does not have a history of serious allergic reactions to melphalan; **AND**
- Patient must have had an intolerance to melphalan or Alkeran® IV prior to consideration of Evomela®; **AND**

Multiple Myeloma (MM) † [1,2]

- Used as high-dose myeloablative conditioning treatment **Φ**; **AND**
  - Patient will receive an autologous stem cell transplant (ASCT); **OR**
- Used as primary therapy for symptomatic disease in non-transplant candidates **‡**; **AND**
  - Used in combination with daratumumab, bortezomib, and prednisone; **AND**
  - Patient is unable to tolerate oral melphalan therapy; **OR**
- Used for the management of POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes) syndrome **‡**; **AND**

- Used in combination with dexamethasone; **AND**
- Patient is unable to tolerate oral melphalan therapy; **AND**
- Patient is transplant ineligible OR used as induction therapy if transplant eligible

† FDA indication(s); ‡ Compendia recommended indication(s); Φ Orphan Drug

IV. Renewal Criteria [1]

Coverage can be renewed based upon the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe gastrointestinal toxicity (e.g., nausea, vomiting, diarrhea, mucositis), severe hepatotoxicity, severe bone marrow suppression, hypersensitivity reactions, secondary malignancies (e.g., myeloproliferative syndrome, acute leukemia), etc.; **AND**

Conditioning Treatment

- Coverage cannot be renewed.

All Other Indications

- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread

V. Dosage/Administration [1]

Indication	Dose
MM – Conditioning Treatment	The recommended dose of Evomela is 100 mg/m²/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). *Note: For patients who weigh more than 130% of their ideal body weight, body surface area should be calculated based on adjusted ideal body weight.*
All Other Indications	The recommended dose of Evomela is 16 mg/m² 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. • Reduce dose up to 50% in patients with renal impairment (BUN ≥30 mg/dL)

VI. Billing Code/Availability Information

HCPCS Code:

- J9246 - Injection, melphalan (evomela), 1 mg: 1 billable unit = 1 mg

NDC:

- Evomela 50 mg lyophilized powder in single-dose vial for reconstitution: 72893-0001-xx

VII. References

1. Evomela [package insert]. East Windsor, NJ; Acrotech Biopharma, LLC.; April 2022. Accessed June 2022.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for melphalan. National Comprehensive Cancer Network, 2022. 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 June 2022.
3. Aljitawi OS, Ganguly S, Abhyankar SH, et al. Phase IIa cross-over study of propylene glycol-free melphalan (LGD-353) and Alkeran in multiple myeloma autologous transplantation. Bone Marrow Transplant. 2014;49(8):1042-1045
4. Hari P, Aljitawi OS, Arce-Lara C, et al. A phase IIb, multicenter, open-label, safety, and efficacy study of high-dose, propylene glycol-free melphalan hydrochloride for injection (EVOMELA) for myeloablative conditioning in multiple myeloma patients undergoing autologous transplantation. Biol Blood Marrow Transplant. 2015;21(12):2100-2105.
5. Mai EK, Benner A, Bertsch U, et al. Single Versus Tandem High-Dose Melphalan Followed by Autologous Blood Stem Cell Transplantation in Multiple Myeloma: Long-Term Results From the Phase III GMMG-HD2 Trial. Br J Haematol. 2016 Jun;173(5):731-41. doi: 10.1111/bjh.13994.
6. Moreau P, Facon T, Attal M, et al. Comparison of 200 mg/m(2) Melphalan and 8 Gy Total Body Irradiation Plus 140 mg/m(2) Melphalan as Conditioning Regimens for Peripheral Blood Stem Cell Transplantation in Patients With Newly Diagnosed Multiple Myeloma: Final Analysis of the Intergroupe Francophone Du Myélome 9502 Randomized Trial. Blood. 2002 Feb 1;99(3):731-5. doi: 10.1182/blood.v99.3.731.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C90.00	Multiple myeloma not having achieved remission
C90.02	Multiple myeloma in relapse
C90.10	Plasma cell leukemia not having achieved remission
C90.12	Plasma cell leukemia in relapse
C90.20	Extramedullary plasmacytoma not having achieved remission
C90.22	Extramedullary plasmacytoma in relapse
C90.30	Solitary plasmacytoma not having achieved remission

C90.32	Solitary plasmacytoma in relapse
D47.9	Neoplasm of uncertain behavior of lymphoid, hematopoietic and related tissue, unspecified
E31.9	Polyglandular dysfunction, unspecified
G62.9	Polyneuropathy, unspecified
G90.9	Disorder of the autonomic nervous system, unspecified
L98.9	Disorder of the skin and subcutaneous tissue, unspecified
Z85.79	Personal history of other malignant neoplasms of lymphoid, hematopoietic and related tissues

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

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 Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered 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		
Jurisdiction	**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, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
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