Evolent Clinical Guideline 3160 for Darzalex™ and Darzalex Faspro™ (daratumumab IV/SC)

Guideline Number:	Applicable Codes	
Evolent_CG_3160		
"Evolent" refers to Evolent Health LLC and Evolent Specialty Services, Inc. *© 2016 - 2025 Evolent. All rights Reserved.*		
Original Date:	**Last Revised Date:**	**Implementation Date:**
March 2016	December 2025	December 2025

TABLE OF CONTENTS

STATEMENT

Purpose

To define and describe the accepted indications for Darzalex and Darzalex Faspro (daratumumab IV/SC) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

INDICATIONS

Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided

- The member has not experienced disease progression on the requested medication AND
- The requested medication was used within the last year without a lapse of more than 30 days of having an active authorization AND
- Additional medication(s) are not being added to the continuation request.

Multiple Myeloma (MM)

- NOTE 1: Subcutaneous daratumumab, Darzalex Faspro, may be substituted for IV daratumumab for all the indications listed in this policy.
- Newly Diagnosed Multiple Myeloma: For members with newly diagnosed multiple myeloma, the following regimens are supported by Evolent Policy for first line/initial therapy:
    - Daratumumab + lenalidomide + bortezomib +/- steroid (for transplant eligible members only)
    - Daratumumab + bortezomib + thalidomide +/- steroid (for transplant eligible members only)
    - Daratumumab + lenalidomide +/- steroid (for transplant ineligible members only)
    - Daratumumab + bortezomib + cyclophosphamide +/- steroid
    - NOTE 2: Daratumumab + carfilzomib + lenalidomide +/- steroid is not supported by Evolent Policy for daratumumab for the treatment of newly diagnosed MM (transplant eligible or transplant ineligible). This policy position is based on the lack of Level 1 Evidence(randomized clinical trials and/or meta-analyses) to show superior outcomes with the above regimen in comparison to:
        - Daratumumab + lenalidomide + bortezomib +/- steroid for transplant eligible

newly diagnosed MM patients, and

- Daratumumab + bortezomib + thalidomide +/- steroid for transplant eligible newly diagnosed MM patients, and
- An exception may be made if the member is intolerant to/has a contraindication to bortezomib. Please refer to alternative agents/regimens recommended by Evolent including but not limited to regimens available at **Evolent Pathways**.

- Relapsed/Refractory disease after 1-3 prior therapies: The following regimens are supported per Evolent Policy for daratumumab:
  - Daratumumab + carfilzomib +/- steroid
  - Daratumumab + pomalidomide +/- steroid (DPd)
  - Daratumumab + lenalidomide +/- steroid (DRd)
  - Daratumumab + bortezomib +/- cyclophosphamide +/- steroid
  - Daratumumab monotherapy in members who failed 3 prior lines of therapy or double refractory on a proteasome inhibitor (e.g., bortezomib, carfilzomib, ixazomib) & an immunomodulatory agent (e.g., lenalidomide, pomalidomide, thalidomide).
  - NOTE 3: [Daratumumab + selinexor +/- steroid] is not supported by Evolent Policy for daratumumab for the treatment of relapsed/refractory MM. This policy position is based on the lack of Level 1 Evidence (randomized clinical trials and/or meta-analyses) demonstrating superiority of the above regimen compared to Evolent recommended alternatives agents/regimens, including but not limited to regimens at **Evolent Pathways**.

Smoldering Multiple Myeloma (SMM)

- Subcutaneous daratumumab, Darzalex Faspro, may be used as monotherapy in adult members for the treatment of high-risk smoldering multiple myeloma.

CONTRAINDICATIONS/WARNINGS

- Contraindications
  - History of severe hypersensitivity to daratumumab or any component of the formulation.
  - History of severe hypersensitivity to daratumumab, hyaluronidase, or any component of the formulation.

EXCLUSION CRITERIA

- Disease progression while on a Darzalex and Darzalex Faspro (daratumumab IV/SC) containing regimen, or disease progression on Sarclisa (isatuximab) or Sarclisa (isatuximab) containing regimen.
- Dosing exceeds single dose limit of Darzalex IV 16 mg/kg or Darzalex Faspro SC 1,800 mg.

- Investigational use of Darzalex and Darzalex Faspro (daratumumab IV/SC) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:
    - Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
    - Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
    - Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definitions of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
    - Whether the experimental design, considering the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
    - That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
    - That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
    - That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

CODING AND STANDARDS

Codes

- J9144 - Injection, daratumumab, 10 mg and hyaluronidase-fihj
- J9145 - Injection, daratumumab, 10 mg

Applicable Lines of Business

☐	CHIP (Children's Health Insurance Program)
☒	Commercial
☒	Exchange/Marketplace
☒	Medicaid
☐	Medicare Advantage

POLICY HISTORY

Date	Summary
December 2025	• Added new indication • Updated references
August 2025	• Converted to new Evolent guideline template • This guideline replaces UM ONC_1280 Darzalex and Darzalex Faspro (daratumumab IV/SC) • Updated indication section • Updated references
September 2024	• Updated references • Updated NCH verbiage to Evolent

LEGAL AND COMPLIANCE

Guideline Approval

Committee

Reviewed / Approved by Evolent Specialty Services Clinical Guideline Review Committee

Disclaimer

Evolent Clinical Guidelines do not constitute medical advice. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Evolent uses Clinical Guidelines in accordance with its contractual obligations to provide utilization management. Coverage for services varies for individual members according to the terms of their health care coverage or government program. Individual members' health care coverage may not utilize some Evolent Clinical Guidelines. Evolent clinical guidelines contain guidance that requires prior authorization and service limitations. A list of procedure codes, services or drugs may not be all inclusive and does not imply that a service or drug is a covered or non-covered service or drug. Evolent reserves the right to review and update this Clinical Guideline in its sole discretion. Notice of any changes shall be provided as required by applicable provider agreements and laws or regulations. Members should contact their Plan customer service representative for specific coverage information.

REFERENCES

1. Dimopoulos MA, et al; AQUILA Investigators. Daratumumab or Active Monitoring for High-Risk Smoldering Multiple Myeloma. *N Engl J Med*. 2025 May 8;392(18):1777-1788. doi: 10.1056/NEJMoa2409029.

2. Voorhees PM, et al. Daratumumab plus RVd for newly diagnosed multiple myeloma: final analysis of the safety run-in cohort of GRIFFIN. *Blood Adv*. 2021 Feb 23;5(4):1092-1096. doi: 10.1182/bloodadvances.2020003642.
3. Costa LJ, et al. Daratumumab, Carfilzomib, Lenalidomide, and Dexamethasone With Minimal Residual Disease Response-Adapted Therapy in Newly Diagnosed Multiple Myeloma. *J Clin Oncol*. 2022 Sep 1;40(25):2901-2912. doi: 10.1200/JCO.21.01935.
4. Sonneveld P, et al; PERSEUS Trial Investigators. Daratumumab, Bortezomib, Lenalidomide, and Dexamethasone for Multiple Myeloma. *N Engl J Med*. 2024 Jan 25;390(4):301-313. doi: 10.1056/NEJMoa2312054.
5. Voorhees PM, et al. Daratumumab, lenalidomide, bortezomib, and dexamethasone for transplant-eligible newly diagnosed multiple myeloma: the GRIFFIN trial. *Blood*. 2020 Aug 20;136(8):936-945.doi: 10.1182/blood.2020005288.
6. Dimopoulos MA, et al; POLLUX Investigators. Daratumumab, Lenalidomide, and Dexamethasone for Multiple Myeloma. *N Engl J Med*. 2016 Oct 6;375(14):1319-1331. doi: 10.1056/NEJMoa1607751.
7. Palumbo A, et al; CASTOR Investigators. Daratumumab, Bortezomib, and Dexamethasone for Multiple Myeloma. *N Engl J Med*. 2016 Aug 25;375(8):754-66. doi: 10.1056/NEJMoa1606038.
8. Joseph NS, et al. Long-Term Follow-Up Results of Lenalidomide, Bortezomib, and Dexamethasone Induction Therapy and Risk-Adapted Maintenance Approach in Newly Diagnosed Multiple Myeloma. *J Clin Oncol*. 2020 Jun 10;38(17):1928-1937. doi: 10.1200/JCO.19.02515.
9. Darzalex Faspro prescribing information. Janssen Biotech, Inc. Horsham, PA 2025.
10. Darzalex prescribing information. Janssen Biotech, Inc. Horsham, PA 2025.
11. Clinical Pharmacology Elsevier Gold Standard 2025.
12. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2025.
13. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2025.
14. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2025.
15. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. *J Clin Oncol*. 2014 Apr 20;32(12):1277-80.
16. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: **https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf**.
17. Current and Resolved Drug Shortages and Discontinuations Reported to the FDA: **http://www.accessdata.fda.gov/scripts/drugshortages/default.cfm**.