

# Drug Policy:

## Darzalex™ and Darzalex Faspro™ (daratumumab IV/SC)

<b>POLICY NUMBER</b> UM ONC_1280	<b>SUBJECT</b> Darzalex™ and Darzalex Faspro™ (daratumumab IV/SC)		<b>DEPT/PROGRAM</b> UM Dept	<b>PAGE 1 OF 4</b>
<b>DATES COMMITTEE REVIEWED</b> 03/23/16, 01/05/17, 01/10/18, 01/09/19, 12/11/19, 01/08/20, 05/13/20, 06/10/20, 08/12/20, 09/09/20, 04/14/21, 09/08/21, 11/15/21, 12/08/21, 01/12/22, 04/13/22, 05/11/22, 07/13/22, 08/10/22, 11/09/22, 12/14/22, 03/08/23, 05/10/23, 08/09/23, 11/08/23, 12/13/2023, 09/18/24	<b>APPROVAL DATE</b> September 18, 2024	<b>EFFECTIVE DATE</b> September 27, 2024	<b>COMMITTEE APPROVAL DATES</b> 03/23/16, 01/05/17, 01/10/18, 01/09/19, 12/11/19, 01/08/20, 05/13/20, 06/10/20, 08/12/20, 09/09/20, 04/14/21, 09/08/21, 11/15/21, 12/08/21, 01/12/22, 04/13/22, 05/11/22, 07/13/22, 08/10/22, 11/09/22, 12/14/22, 03/08/23, 05/10/23, 08/09/23, 11/08/23, 12/13/2023, 09/18/24	
<b>PRIMARY BUSINESS OWNER:</b> UM		<b>COMMITTEE/BOARD APPROVAL</b> Utilization Management Committee		
<b>NCQA STANDARDS</b> UM 2		<b>ADDITIONAL AREAS OF IMPACT</b>		
<b>CMS REQUIREMENTS</b>	<b>STATE/FEDERAL REQUIREMENTS</b>		<b>APPLICABLE LINES OF BUSINESS</b> Commercial, Exchange, Medicaid	

### I. 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.

### II. INDICATIONS FOR USE/INCLUSION CRITERIA

#### A. Continuation requests for a not approvable medication shall be exempt from this Evolent policy provided:

1. The requested medication was used within the last year, **AND**
2. The member has not experienced disease progression and/or no intolerance to the requested medication, **AND**
3. Additional medication(s) are not being added to the continuation request.

## B. Multiple Myeloma (MM)

1. NOTE 1: Subcutaneous daratumumab, Darzalex Faspro, may be substituted for IV daratumumab for all the indications listed in this policy.
2. Newly Diagnosed Multiple Myeloma: For members with newly diagnosed multiple myeloma, the following regimens are supported by Evolent Policy for first line/initial therapy:
  - a. Daratumumab + lenalidomide + bortezomib +/- steroid (for transplant eligible members only)
  - b. Daratumumab + lenalidomide +/- steroid (for transplant ineligible members)
  - c. Daratumumab + bortezomib + thalidomide +/- steroid (transplant ineligible members)
  - d. 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:
    - i. Daratumumab + lenalidomide + bortezomib +/- steroid] for transplant eligible newly diagnosed MM patients, and
    - ii. Daratumumab + bortezomib + thalidomide + steroid for transplant in-eligible newly diagnosed MM patients, and
    - iii. 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 <http://pathways.newcenturyhealth.com>.
3. Relapsed/Refractory disease after 1-3 prior therapies: The following regimens are supported per Evolent Policy for daratumumab:
  - a. Daratumumab + carfilzomib +/- steroid
  - b. Daratumumab + pomalidomide +/- steroid (DPd)
  - c. Daratumumab + lenalidomide +/- steroid (DRd)
  - d. Daratumumab + bortezomib +/- cyclophosphamide +/- steroid
  - e. 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).
  - f. 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 <http://pathways.newcenturyhealth.com>.

## III. EXCLUSION CRITERIA

- A. 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.
- B. Dosing exceeds single dose limit of Darzalex IV 16 mg/kg or Darzalex Faspro SC 1,800 mg.
- C. 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:

1. Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
2. Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
3. 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.
4. 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).
5. 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.
6. That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
7. 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.

#### **IV. MEDICATION MANAGEMENT**

- A. Please refer to the FDA label/package insert for details regarding these topics.

#### **V. APPROVAL AUTHORITY**

- A. Review – Utilization Management Department
- B. Final Approval – Utilization Management Committee

#### **VI. ATTACHMENTS**

- A. None

#### **VII. REFERENCES**

- A. 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.
- B. 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.
- C. 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
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- F. Palumbo A, et al. CASTOR Investigators. Daratumumab, Bortezomib, and Dexamethasone for Multiple Myeloma. N Engl J Med. 2016 Aug 25;375(8):754-66.
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- I. Darzalex Faspro prescribing information. Janssen Biotech, Inc. Horsham, PA 2024.
- J. Clinical Pharmacology Elsevier Gold Standard 2024.
- K. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2024.
- L. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2024.
- M. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2024.
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- O. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: <https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf>.