Clinical Policy: Daratumumab (Darzalex)

Reference Number: CP.PHAR.310
Effective Date: 07.01.17
Last Review Date: 08.18
Line of Business: Medicaid, HIM-Medical Benefit

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Daratumumab (Darzalex®) is a CD38-directed cytolytic antibody.

FDA Approved Indication(s)

Darzalex is indicated:

- In combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone, for the treatment of patients with multiple myeloma (MM) who have received at least one prior therapy
- As monotherapy, for the treatment of patients with MM who have received at least three prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent or who are double-refractory to a PI and an immunomodulatory agent
- In combination with pomalidomide and dexamethasone for the treatment of patients with MM who have received at least two prior therapies including lenalidomide and a PI
- In combination with bortezomib, melphalan, and prednisone for the treatment of patients with newly diagnosed MM who are ineligible for autologous stem cell transplant

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Darzalex is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Multiple Myeloma (must meet all)**:**

1. Diagnosis of MM;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Darzalex is prescribed in one of the following ways (a, b, c, d, or e):
   a. In combination with either lenalidomide and dexamethasone or bortezomib and dexamethasone after at least one prior therapy;
   b. As monotherapy after three prior lines of therapy including at least one agent from both of the following categories of agents (i and ii):
      i. PI (e.g., ixazomib, bortezomib, carfilzomib);
      ii. Immunomodulatory agent (e.g., thalidomide, lenalidomide);
   c. As monotherapy in member who is double-refractory to a PI and an immunomodulatory agent;

d. In combination with pomalidomide and dexamethasone, after two prior therapies, including lenalidomine and a PI;
e. In combination with bortezomib, melphalan, and prednisone for newly diagnosed MM in member ineligible for autologous stem cell transplant;

5. Request meets one of the following (a or b):
   a. Dose does not exceed the maximum indicated regimen in section V;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): HIM.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Multiple Myeloma (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):
   a. New dose does not exceed the maximum indicated regimen in section V;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via health plan benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): HIM.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – HIM.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration

MM: multiple myeloma
NCCN: National Comprehensive Cancer Network
PI: proteasome inhibitor

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Ninlaro® (ixazomib)	4 mg PO on days 1, 8, and 15 of every 28-day treatment cycle	See dosing regimen
bortezomib (Velcade®)	1.3 mg/m^2 SC or IV; frequency of administration varies based on specific use	See dosing regimen
Kyprolis® (carfilzomib)	20 mg/m^2, 27 mg/m^2, and/or 56 mg/m^2 IV; frequency of administration varies based on specific use	See dosing regimen
Revlimid® (lenalidomide)	10 mg or 25 mg PO QD; dose and frequency of administration vary based on specific use	See dosing regimen
Thalomid® (thalidomide)	100 mg, 200 mg, or 400 mg PO QD; dose and frequency of administration vary based on specific use	See dosing regimen

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications
Not applicable

Appendix D: General Information
- Double-refractory: refractory, or did not respond, to both a PI and an immunomodulatory agent after being previously exposed to the agents

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
MM – monotherapy	Weeks 1 to 8: 16 mg/kg IV weekly Weeks 9 to 24: 16 mg/kg IV every 2 weeks Weeks 25 onwards until disease progression: 16 mg/kg IV every 4 weeks	See dosing regimen
MM – after at least one prior therapy	In combination with lenalidomide and low-dose dexamethasone: Weeks 1 to 8: 16 mg/kg IV weekly Weeks 9 to 24: 16 mg/kg IV every 2 weeks	See dosing regimen

Indication	Dosing Regimen	Maximum Dose
	Weeks 25 onwards until disease progression: 16 mg/kg IV every 4 weeks In combination with bortezomib and dexamethasone: Weeks 1 to 9: 16 mg/kg IV weekly Weeks 10 to 24: 16 mg/kg IV every 3 weeks Weeks 25 onwards until disease progression: 16 mg/kg IV every 4 weeks	
MM – after at least two prior therapies	In combination with pomalidomide and low-dose dexamethasone: Weeks 1 to 8: 16 mg/kg IV weekly Weeks 9 to 24: 16 mg/kg IV every 2 weeks Weeks 25 onwards until disease progression: 16 mg/kg IV every 4 weeks	See dosing regimen
MM – newly diagnosed	In combination with bortezomib, mephalan, and prednisone: Weeks 1 to 6: 16 mg/kg IV weekly Weeks 7 to 54: 16 mg/kg IV every 3 weeks Weeks 55 onwards until disease progression: 16 mg/kg IV every 4 weeks	See dosing regimen

VI. Product Availability

Single-dose vial: 100 mg/5 mL, 400 mg/20 mL

VII. References

1. Darzalex Prescribing Information. Horsham, PA: Janssen Biotech, Inc.; May 2018. Available at https://www.darzalex.com. Accessed May 16, 2018.
2. Daratumumab. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.NCCN.org. Accessed May 16, 2018.
3. Lee HC, Shah JJ, and Orlowski RZ. Novel approaches to treatment of double-refractory multiple myeloma. Am Soc Clin Oncol Educ Book. 2013: 302-306. Doi: 10.1200/EdBook_AM.2013.33.e302.
4. National Comprehensive Cancer Network. Multiple Myeloma Version 4.2018. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed May 16, 2018.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9145	Injection, daratumumab, 10 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy split from CP.PHAR.182 Excellus Oncology.	01.17	02.17
Policy converted to new template. -Re-organized appropriately prescribed regimen in initial criteria; defined double-refractory in footnote -Added new indication: In combination with pomalidomide and dexamethasone for the treatment of patients with MM who have received at least two prior therapies including lenalidomide and a PI.	07.17	11.17
Policy converted to new template. Annual review – no clinical changes.	08.17	11.17
Criteria added for new FDA indication: combination use with bortezomib, mephalan, and prednisone for the treatment of newly diagnosed MM patients ineligible for autologous stem cell transplant; HIM-Medical benefit added; prescriber requirement added; references reviewed and updated.	05.29.18	08.18

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of

insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

For Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the formulary exception policy.