Clinical Policy: Daratumumab (Darzalex)

Reference Number: PA.CP.PHAR.310
Effective Date: 01/18
Last Review Date: 07/17/19

Coding Implications
Revision Log

Description
The intent of the criteria is to ensure that patients follow selection elements established by Pennsylvania Health and Wellness ® clinical policy for daratumumab (Darzalex®).

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
It is the policy of Pennsylvania Health and Wellness ® that Darzalex is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Multiple Myeloma (must meet all):

1. Diagnosis of multiple myeloma;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. 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;
4. Request meets one of the following (a or b):
   a. Dose does not exceed the maximum indicated regimen in section IV;
   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: Refer to PA.CP.PMN.53.

II. Continued Approval

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

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met initial approval criteria, or the Continuity of Care policy applies (*see PA.LTSS.PHAR.01*);
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 IV;
   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 Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy, or the Continuity of Care policy applies (*see PA.LTSS.PHAR.01*); or
2. Refer to PA.CP.PMN.53

III. 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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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

IV. 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 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	See dosing regimen
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:	See dosing regimen

	16 mg/kg IV every 2 weeks Weeks 25 onwards until disease progression: 16 mg/kg IV every 4 weeks	
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

V. Product Availability

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

Background

Description/Mechanism of Action:

CD38 is a transmembrane glycoprotein (48 kDa) expressed on the surface of hematopoietic cells, including multiple myeloma and other cell types and tissues and has multiple functions, such as receptor mediated adhesion, signaling, and modulation of cyclase and hydrolase activity. Daratumumab is an IgG1κ human monoclonal antibody (mAb) that binds to CD38 and inhibits the growth of CD38 expressing tumor cells by inducing apoptosis directly through Fc mediated cross linking as well as by immune-mediated tumor cell lysis through complement dependent cytotoxicity (CDC), antibody dependent cell mediated cytotoxicity (ADCC) and antibody dependent cellular phagocytosis (ADCP). A subset of myeloid derived suppressor cells (CD38+MDSCs), regulatory T cells (CD38+T_{regs}) and B cells (CD38+B_{regs}) are decreased by daratumumab.

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	Approval Date
Criteria added for new FDA indication: combination use with bortezomib, mephalan, and prednisone for the treatment of newly	05.18	

Reviews, Revisions, and Approvals	Date	Approval Date
diagnosed MM patients ineligible for autologous stem cell transplant; prescriber requirement added; references reviewed and updated.		
3Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	07/17/19	

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.