Clinical Policy: Daratumumab (Darzalex)

Reference Number: CP.PHAR.310
Effective Date: 02/17
Last Review Date: 02/17

Coding Implications
Revision Log

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

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

Policy/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 multiple myeloma;
2. Darzalex is prescribed in one of the following ways (a or b):
   a. After one prior therapy, either of the following (i or ii):
      i. Lenalidomide and dexamethasone;
      ii. Bortezomib and dexamethasone;
   b. As monotherapy, and (i or ii):
      i. History of at least one prior therapy from each of the following drug classes:
         a) Proteasome inhibitor (PI) (e.g., ixazomib, bortezomib, carfilzomib);
         b) Immunomodulatory agent (e.g., thalidomide, lenalidomide);
      ii. Member is double-refractory to a PI and an immunomodulatory agent.

Approval duration: 3 months

B. Other diagnoses/indications: Refer to CP.PHAR.57 - Global Biopharm Policy.

II. Continued Approval

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

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member has none of the following reasons to discontinue:
   a. Disease progression or unacceptable toxicity;
   b. Life-threatening infusion reaction;
   c. Third occurrence of any Grade 3* or greater adverse reaction (severe/hospitalization indicated);
   d. First occurrence of any Grade 4* (life-threatening) adverse reaction.

**National Cancer Institute Common Toxicity Criteria for Adverse Events, version 4.0.*

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
2. Refer to CP.PHAR.57 - Global Biopharm Policy**.**

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.

Formulations:
Darzalex is a preservative-free solution for intravenous infusion supplied as:
- 100 mg/5 mL single-dose vial
- 400 mg/20 mL single-dose vial

FDA Approved Indications:
Darzalex is a CD38-directed cytolytic antibody/intravenous formulation indicated
- In combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone, for the treatment of patients with multiple myeloma who have received at least one prior therapy.
- As monotherapy, for the treatment of patients with multiple myeloma 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.

Appendices
Appendix A: Abbreviation Key
CDC: Complement dependent cytotoxicity
ADCC: Antibody dependent cell mediated cytotoxicity
ADCP: Antibody dependent cellular phagocytosis
PI: Proteasome inhibitor

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
Policy split from CP.PHAR.182 Excellus Oncology.	01/17	02/17

References

1. Darzalex prescribing information. Horsham, PA: Janssen Biotech, Inc.; November 2016. Available at https://www.darzalexhcp.com/shared/product/darzalex/darzalex-prescribing-information.pdf. Accessed January 9, 2017.
2. Multiple myeloma (Version 3.2017). In: National Comprehensive Cancer Network Guidelines. Available at NCCN.org. Accessed January 10, 2017.

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.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.