Clinical Policy: Daratumumab (Darzalex)
Reference Number: CP.PHAR.310
Effective Date: 07.01.17
Last Review Date: 08.19
Line of Business: Medicaid, HIM-Medical Benefit

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

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 lenalidomide* and a PI;
e. In combination with bortezomib*, melphalan, and prednisone for newly diagnosed MM and member is ineligible for autologous stem cell transplant; *Prior authorization is required.

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): CP.PMN.53 for Medicaid and HIM-Medical Benefit.

II. Continued Therapy
   A. Multiple Myeloma (must meet all):
      1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Darzalex for a covered indication and has received this medication for at least 30 days;
      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): CP.PMN.53 for Medicaid and HIM-Medical Benefit.

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 – CP.PMN.53 for Medicaid and HIM-Medical Benefit or evidence of coverage documents.

IV. Appendices/General Information
   Appendix A: Abbreviation/Acronym Key
   FDA: Food and Drug Administration MM: multiple myeloma
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.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ninlaro® (ixazomib)</td>
<td>4 mg PO on days 1, 8, and 15 of every 28-day treatment cycle</td>
<td>See dosing regimen</td>
</tr>
<tr>
<td>bortezomib (Velcade®)</td>
<td>1.3 mg/m² SC or IV; frequency of administration varies based on specific use</td>
<td>See dosing regimen</td>
</tr>
<tr>
<td>Kyprolis® (carfilzomib)</td>
<td>20 mg/m², 27 mg/m², and/or 56 mg/m² IV; frequency of administration varies based on specific use</td>
<td>See dosing regimen</td>
</tr>
<tr>
<td>Revlimid® (lenalidomide)</td>
<td>10 mg or 25 mg PO QD; dose and frequency of administration vary based on specific use</td>
<td>See dosing regimen</td>
</tr>
<tr>
<td>Thalomid® (thalidomide)</td>
<td>100 mg, 200 mg, or 400 mg PO QD; dose and frequency of administration vary based on specific use</td>
<td>See dosing regimen</td>
</tr>
</tbody>
</table>

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/Box Warnings

None reported

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>MM – monotherapy</td>
<td>Weeks 1 to 8: 16 mg/kg IV weekly 16 mg/kg IV every 2 weeks 16 mg/kg IV every 4 weeks</td>
<td>See dosing regimen</td>
</tr>
<tr>
<td>MM – after at least one prior therapy</td>
<td>In combination with lenalidomide and low-dose dexamethasone: Weeks 1 to 8: 16 mg/kg IV weekly 16 mg/kg IV every 2 weeks 16 mg/kg IV every 4 weeks In combination with bortezomib and dexamethasone: Weeks 1 to 9:</td>
<td>See dosing regimen</td>
</tr>
</tbody>
</table>
### Indication | Dosing Regimen | Maximum Dose
--- | --- | ---
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 | | 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 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

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**VI. Product Availability**
Single-dose vial: 100 mg/5 mL, 400 mg/20 mL

**VII. References**

**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.

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>J9145</td>
<td>Injection, daratumumab, 10 mg</td>
</tr>
</tbody>
</table>
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.

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**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.

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