Effective Date: 11/01/2018

Darzalex® (daratumumab)

FDA approval: November 16, 2015
HCPCS: J9415
Benefit: Medical

A. Policy Criteria:
   Note: must be supported by submission of chart notes and patient specific documentation.

   A. Coverage of the requested drug is provided when all the below criteria are met:
      a. Prescribed by or in consultation with an oncologist or hematologist
      b. Diagnosis of multiple myeloma
         i. As monotherapy for treatment failure with at least three prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent
            OR
            Tried and failed both PI and immunomodulatory agent
            OR
         ii. In combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone, for the treatment of patients who have received at least one prior therapy
         iii. In combination with pomalidomide and dexamethasone, for the treatment of patients who have received two prior therapies including lenalidomide and a PI
            OR
         iv. In combination with bortezomib, melphalan, and prednisone for newly diagnosed patients ineligible for autologous stem cell transplant
      c. Must not have received prior daratumumab or other anti-CD38 agent therapy

   B. Quantity Limitations, Authorization Period and Renewal Criteria
      a. Quantity Limit: based on FDA approved dosing
      b. Initial Authorization Period: 6 months
      c. Renewal Criteria:
         i. Treatment may be continued until treatment failure, disease progression or until unacceptable toxicity occurs
      d. Renewal Authorization Periods: 1 year

   C. Darzalex is considered investigational when used for all other conditions, including but not limited to:
      a. Newly diagnosed MM
      b. Leukemia
      c. Lymphoma

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Therapeutic considerations:

A. FDA approved indication
Darzalex is a human CD38-directed monoclonal antibody indicated for the treatment of patients with multiple myeloma (MM) who have received at least three prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory (IMiD) agent or who have tried and failed a PI and an immunomodulatory agent, OR 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, OR in combination with pomalidomide and dexamethasone for the treatment of patients who have received two prior therapies including lenalidomide and a PI, OR in combination with bortezomib, melphalan, and prednisone for newly diagnosed patient ineligible for autologous stem cell transplant.

*Please refer to most recent prescribing information. https://www.janssenmd.com/pdf/darzalex/DARZALEX_PI.pdf

B. Background Information
- MM is a form of blood cancer that occurs in infection-fighting plasma cells (a type of white blood cell) found in the bone marrow. These cancerous cells multiply, produce an abnormal protein and push out other healthy blood cells from the bone marrow. The disease may result in a weakened immune system and cause other bone or kidney problems.
- There are two main types of refractory multiple myeloma: primary refractory patients never achieve a response and progress while on initial therapy, and relapsed and refractory patients are nonresponsive while on salvage therapy.
- Darzalex 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). Myeloid derived suppressor cells (MDSCs) and a subset of regulatory T cells (CD38+Tregs) express CD38 and are susceptible to Darzalex mediated cell lysis.

C. Efficacy

*Please refer to most recent prescribing information.

D. Medication Safety Considerations
Black Box Warning: No

*Please refer to most recent prescribing information.

E. Dosing and administration
16 mg/kg injection according to the following schedule:

a. Monotherapy and in combination with lenalidomide or pomalidomide and low-dose dexamethasone:

<table>
<thead>
<tr>
<th>Schedule</th>
<th>Weeks</th>
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<tbody>
<tr>
<td>Weekly (total of 8 doses)</td>
<td>Weeks 1 to 8</td>
</tr>
<tr>
<td>Every two weeks (total of 8 doses)</td>
<td>Weeks 9 to 24</td>
</tr>
<tr>
<td>Every four weeks</td>
<td>Week 25 and onward until disease progression</td>
</tr>
</tbody>
</table>

b. In combination with bortezomib and dexamethasone:

<table>
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<th>Weeks</th>
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</thead>
<tbody>
<tr>
<td>Weekly (total of 9 doses)</td>
<td>Weeks 1 to 9</td>
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<tr>
<td>Every two weeks (total of 5 doses)</td>
<td>Weeks 10 to 24</td>
</tr>
<tr>
<td>Every four weeks</td>
<td>Week 25 and onward until disease progression</td>
</tr>
</tbody>
</table>

*Please refer to most recent prescribing information.

F. How supplied

Injection:
- 100 mg/5 mL solution in a single-dose vial
- 400 mg/20 mL solution in a single-dose vial

References:
3. Highmark Preliminary Medication Review: New Molecular Entity – Antineoplastics: elotuzumab (EmplicitiTm) [Bristol Myers Squibb] & daratumumab (DarzalexTM) [Janssen Biotech, Inc.]; Antineoplastics: Molecular Target Inhibitors – ixazomib (Ninlaro®) [Millennium Pharmaceuticals, Inc]; December 2015.
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Policy History

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* The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or [http://dailymed.nlm.nih.gov/dailymed/index.cfm](http://dailymed.nlm.nih.gov/dailymed/index.cfm)