VENTURA COUNTY HEALTH CARE PLAN

Utilization Review Policy

POLICY: Oncology – Darzalex™ (daratumumab injection for intravenous use – Janssen Biotech, Inc.)

DATE REVIEWED: 02/26/2020

OVERVIEW

Darzalex is a CD38-directed cytolytic antibody.[1] In multiple myeloma, Darzalex binds to CD38 and inhibits the growth of CD38-expressing tumor myeloma cells. It is approved in the following conditions:

1. in newly diagnosed patients, in combination with Revlimid (lenalidomide capsules) and dexamethasone, for the treatment of patients who are ineligible for autologous stem cell transplant and in relapsed/refractory disease, in combination with Revlimid and dexamethasone in patients who have received at least one prior therapy; AND
2. in newly diagnosed patients, in combination with Velcade (bortezumab injection), melphalan, and prednisone in those ineligible for autologous stem cell transplant; AND
3. in newly diagnosed patients, in combination with Velcade, Thalomid (thalidomide capsules), and dexamethasone, for treatment of patients who are eligible for autologous stem cell transplant; AND
4. in patients who have received at least one prior therapy, in combination with Velcade and dexamethasone; AND
5. in patients who have received at least two prior therapies (including Revlimid and a proteasome inhibitor), in combination with Pomalyst (pomalidomide capsules) and dexamethasone; AND
6. in patients who have received at least three prior lines of therapy (including a proteasome inhibitor and an immunomodulatory agent or who are double-refractory to a proteasome inhibitor and an immunomodulatory agent), as monotherapy.

Safety and efficacy is not established in patients < 18 years of age.

Guidelines

The NCCN Multiple Myeloma clinical practice guidelines (version 2.2020 – October 9, 2020) recommend Darzalex in treatment regimens for primary therapy.[2-3] Darzalex/Velcade/Thalomid/dexamethasone is recommended as primary therapy for transplant candidates. For patients who are non-transplant candidates, Darzalex/Revlimid/prednisone is a Preferred regimen, and Darxalex/Velcade/melphalan/prednisone is an Other regimen for primary treatment. For previously treated multiple myeloma, Darzalex/dexamethasone plus Velcade or Revlimid are among the Preferred regimens, whereas Darzalex monotherapy and Darzalex/dexamethasone are listed as other recommended regimens. The NCCN systemic light chain amyloidosis guidelines (version 1.2020 – December 6, 2019) list Darzalex as a therapy for previously treated disease.[4]

Dosing Information

Dosing varies depending on regimen prescribed. Refer to the prescribing information for more specific dosing for FDA-approved regimens. Dose reductions are not recommended. In cases of hematological toxicity, dose delay may be required to allow recovery of blood cell counts. When Darzalex was evaluated in systemic light chain amyloidosis, the dose used was similar to multiple myeloma.[4]

POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage of Darzalex. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication(s). Extended approvals are allowed if the patient continues to meet the criteria and dosing. Requests for doses outside of the established dosing

documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below.

Because of the of the specialized skills required for evaluation and diagnosis of patients treated with Darzalex, as well as the monitoring required for adverse events and long-term efficacy, approval requires Darzalex to be prescribed by or in consultation with a physician who specializes in the condition being treated.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Darzalex is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Multiple Myeloma**. Approve for 1 year if the patient meets BOTH of the following (A and B):
   - **A)** The patient meets ONE of the following (i or ii):
     - **i.** Darzalex is used in combination with at least one other agent.
       Note: Examples of agents that may be used in combination with Darzalex include Revlimid (lenalidomide capsules), Pomalyst (pomalidomide capsules), Thalomid (thalidomide capsules), melphalen, Velcade (bortezumab injection), or Kyprolis (carfilzomib injection); OR
     - **ii.** The patient has tried at least three different regimens for multiple myeloma.
       Note: Examples of agents used in other regimens include Velcade (bortezumab injection), Kyprolis (carfilzomib injection), Revlimid (lenalidomide capsules), cyclophosphamide, Ninlaro (ixazomib capsules); AND
   - **B)** Darzalex is prescribed by or in consultation with an oncologist or a hematologist.

   Dosing. Approve if the requested dosing meets the following:
   - **A)** The dose is 16 mg/kg intravenously (IV); AND
   - **B)** During Year 1, Darzalex is administered no more frequently than once weekly for up to nine infusions followed by infusions separated by 2 or more weeks; AND
   - **C)** After 1 year of therapy, doses are separated by at least 4 weeks.

Other Uses with Supportive Evidence

2. **Systemic Light Chain Amyloidosis.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   - **A)** The patient has received at least one other regimen for this condition.
     Note: Examples of agents used in other regimens include Velcade (bortezumab injection), Revlimid (lenalidomide capsules), cyclophosphamide, and melphalan; AND
   - **B)** The agent is prescribed by or in consultation with an oncologist or a hematologist.

   Dosing. Approve if the requested dosing meets the following (A, B, C):
   - **A)** The dose is 16 mg/kg intravenously (IV).
   - **B)** Darzalex is administered no more frequently than once weekly for up to eight infusions followed by infusions separated by 2 or more weeks; AND
   - **C)** After 6 months of therapy, doses are separated by at least 4 weeks.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Darzalex has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Darzalex [prescribing information]. Horsham, PA: Janssen Biotech, Inc.; September 2019.
2. The NCCN Drugs and Biologics Compendium. © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on February 17, 2020. Search term: daratumumab.
3. The NCCN Multiple Myeloma Clinical Practice Guidelines in Oncology (Version 2.2020 – October 9, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on February 18, 2020.
4. Kaufman GP, Schrier SL, Lafayette RA, et al. Daratumumab yields rapid and deep hematologic responses in patients with heavily pretreated AL amyloidosis. *Blood*. 2017;130(7):900-902.

HISTORY

Type of Revisio	Summary of Changes	Date Reviewed
New policy	--	11/14/2018
Early annual revision	**Multiple Myeloma:** Remove criterion that specifies that patients who have tried three previous regimens receive Darzalex as a single agent (not needed).	02/20/2019
Annual revision	**Multiple Myeloma:** Examples of agents for multiple myeloma were updated in the criteria. In the dosing section, treatment intervals were clarified to list the shortest interval between doses. **Systemic Light Chain Amyloidosis:** To align with NCCN guidelines, this was added an Other Use With Supportive Evidence. Criteria approve if the patient has tried at least one other regimen for this condition, and if prescribed by or in consultation with an oncologist or hematologist.	02/26/2020