Daratumumab (Darzalex®) and Daratumumab and hyaluronidase-fihj (Darzalex Faspro®)

Prior Authorization Drug Coverage Policy

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Lines of Business: Commercial
Policy type: Prior Authorization

This Drug Coverage Policy provides parameters for the coverage of daratumumab (Darzalex®) and daratumumab and hyaluronidase-fihj (Darzalex Faspro®). Consideration of medically necessary indications are based upon U.S. Food and Drug Administration (FDA) indications, recommended uses within the Centers of Medicare & Medicaid Services (CMS) five recognized compendia, including the National Comprehensive Cancer Network (NCCN) Drugs & Biologics Compendium (Category 1 or 2A recommendations), and peer-reviewed scientific literature eligible for coverage according to the CMS, Medicare Benefit Policy Manual, Chapter 15, section 50.4.5 titled, "Off-Label Use of Anti-Cancer Drugs and Biologics." This policy evaluates whether the drug therapy is proven to be effective based on published evidence-based medicine.

Drug Description[1,2]

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.

Hyaluronidase (recombinant human) is an endoglycosidase used to increase the dispersion and absorption of co-administered drugs when administered subcutaneously. Hyaluronan is a polysaccharide found in the extracellular matrix of the subcutaneous tissue. It is depolymerized by the naturally occurring enzyme hyaluronidase. Hyaluronidase increases permeability of the subcutaneous tissue by depolymerizing Hyaluronan.

FDA Indications[1,2]

Daratumumab (Darzalex®) is FDA indicated for treatment of multiple myeloma:

- In combination with lenalidomide and dexamethasone in newly diagnosed patients who are ineligible for autologous stem cell transplant and in patients with relapsed or refractory multiple myeloma who have received at least one prior therapy
- In combination with bortezomib, melphalan and prednisone in newly diagnosed patients who are ineligible for autologous stem cell transplant
- In combination with bortezomib, thalidomide, and dexamethasone in newly diagnosed patients who are eligible for autologous stem cell transplant
- In combination with bortezomib and dexamethasone in patients who have received at least one prior therapy
- In combination with carfilzomib and dexamethasone in patients with relapsed or refractory multiple myeloma who have received one to three prior lines of therapy
- in combination with pomalidomide and dexamethasone in patients who have received at least two prior therapies including lenalidomide and a proteasome inhibitor
- As monotherapy, 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

Daratumumab and hyaluronidase-fihj (Darzalex Faspro®) is FDA indicated for treatment of multiple myeloma and light chain amyloidosis.

- In combination with bortezomib, melphalan and prednisone in newly diagnosed patients who are ineligible for autologous stem cell transplant
- In combination with lenalidomide and dexamethasone in newly diagnosed patients who are ineligible for autologous stem cell transplant and in patients with relapsed or refractory multiple myeloma who have received at least one prior therapy
- In combination with bortezomib, thalidomide, and dexamethasone in newly diagnosed patients who are eligible for autologous stem cell transplant
- In combination with bortezomib and dexamethasone in patients who have received at least one prior therapy
- In combination with pomalidomide and dexamethasone in patients who have received at least one prior line of therapy including lenalidomide and a proteasome inhibitor
- As monotherapy, 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
- In combination with bortezomib, cyclophosphamide and dexamethasone is indicated for the treatment of adult patients with newly diagnosed light chain (AL) amyloidosis.

NCCN Compendium Supported Indications[3,4]

- Multiple Myeloma
- Systemic Light Chain Amyloidosis

Coverage Determinations[1,2]

Daratumumab and daratumumab and hyaluronidase-fihj will require prior authorization. This agent is considered medically necessary for the following oncology indications if all criteria below are met:

Multiple Myeloma (MM)

- The member has a diagnosis of multiple myeloma **AND**
- The member will be treated with daratumumab/daratumumab and hyaluronidase-fihj based on one of the following:
    - In combination with bortezomib, melphalan and prednisone in patients who are:
        - Newly diagnosed **AND**
        - Ineligible for autologous stem cell transplant **OR**
    - In combination with bortezomib, thalidomide, and dexamethasone in patients who are:
        - Newly diagnosed **AND**
        - Eligible for autologous stem cell transplant **OR**
    - In combination with bortezomib and dexamethasone in patients with relapsed or relapsed and refractory disease who had:
        - Received at least one prior line of therapy **AND**
        - At least a partial response to one or more prior therapies **AND**
        - Documented disease progression **OR**
    - Daratumumab (Darzalex®) only:
        - In combination with carfilzomib and dexamethasone in patients with relapsed or refractory multiple myeloma who have received one to three prior lines of therapy
    - Daratumumab (Darzalex®) only:
        - In combination with pomalidomide and dexamethasone in patients with relapsed and/or refractory disease who had:
            - Received at least two prior lines of therapies including lenalidomide and a proteasome inhibitor for at least two consecutive cycles **AND**
            - Documented disease progression **OR**
    - Daratumumab and hyaluronidase-fihj (Darzalex Faspro®) only:
        - In combination with pomalidomide and dexamethasone in patients with relapsed and/or refractory disease who had:
            - Received at least one prior line of therapies including lenalidomide and a proteasome inhibitor **AND**
            - Documented disease progression **OR**
    - In combination with lenalidomide and dexamethasone in patients who are:
        - Newly diagnosed **AND**
        - Ineligible for autologous stem cell transplant **OR**
    - In combination with lenalidomide and dexamethasone in patients with relapsed or refractory disease who had:

        - Received one or more prior lines of therapy **AND**
        - A response to one or more prior lines of therapy **AND**
        - Documented disease progression **OR**
    - As monotherapy in relapsed or refractory patients who had:
        - Documented disease progression on or within 60 days of the last dose of the most recent prior therapy **AND**
        - A response to at least one prior therapy **AND**
        - Received an alkylating agent alone or in combination with other multiple myeloma therapies **AND**
        - Received at least three prior lines of therapy that included a proteasome inhibitor and an immunomodulatory agent **OR**
        - Disease double refractory to the most recent proteasome inhibitor and immunomodulatory agent

Recommended dosage (Daratumumab):

- In combination with lenalidomide or pomalidomide and low-dose dexamethasone, and for monotherapy: 16 mg/kg IV weekly for cycles 1-2 (total of 8 doses), every 2 weeks for cycles 3-6 (total of 8 doses), then every 4 weeks for cycles 7+, 28 days per cycle
- In combination with bortezomib, melphalan, and prednisone: 16 mg/kg IV weekly for cycle 1 (total of 6 doses), every 3 weeks for cycles 2-9 (total of 16 doses), then every 4 weeks for cycles 10+, 42 days per cycle
- In combination with bortezomib, thalidomide, and dexamethasone:
    - Induction: 16 mg/kg IV weekly for cycles 1-2 (total of 8 doses), then every 2 weeks for cycles 3-4 (total of 4 doses), 28 days per cycle
    - Consolidation: 16 mg/kg IV every 2 weeks for cycles 1-2 (total of 4 doses), 28 days per cycle
- In combination with bortezomib and dexamethasone: 16 mg/kg IV weekly for cycle 1-3 (total of 9 doses), every 3 weeks for cycles 4-8 (total of 5 doses), then every 4 weeks for cycles 9+, 21 days per cycle
- Note: to facilitate administration, the first prescribed 16mg/kg dose at Week 1 may be split over two consecutive days. For example, 8mg/kg on day 1 and day 2 respectively.

Recommended dosage (Daratumumab and hyaluronidase-fihj):

- In combination with lenalidomide or pomalidomide and low-dose dexamethasone, and for monotherapy: 1,800 mg daratumumab and 30,000 units hyaluronidase subcutaneously weekly on weeks 1 to 8 (8 doses), 1,800 mg daratumumab and 30,000 units hyaluronidase every other week on weeks 9 to 24 (8 doses), and then 1,800 mg daratumumab and 30,000 units hyaluronidase every 4 weeks starting on week 25 until disease progression
- In combination with bortezomib, melphalan, and prednisone: 1,800 mg daratumumab and 30,000 units hyaluronidase subcutaneously weekly on weeks 1 to 6 (6 doses), 1,800 mg daratumumab and 30,000 units hyaluronidase every 3 weeks on weeks 7 to 54 (16

doses), and then 1,800 mg daratumumab and 30,000 units hyaluronidase every 4 weeks starting on week 55 until disease progression

- In combination with bortezomib, thalidomide, and dexamethasone:
  - Induction: 1,800 mg daratumumab and 30,000 units hyaluronidase subcutaneously weekly on weeks 1 to 8 (8 doses), and then 1,800 mg daratumumab and 30,000 units hyaluronidase subcutaneously every 2 weeks on weeks 9 to 16 (4 doses), followed by high-dose chemotherapy and an ASCT
  - Consolidation: 1,800 mg daratumumab and 30,000 units hyaluronidase subcutaneously every 2 weeks on weeks 1 to 8 (4 doses)
- In combination with bortezomib and dexamethasone: 1,800 mg daratumumab and 30,000 units hyaluronidase subcutaneously weekly on weeks 1 to 9 (9 doses), 1,800 mg daratumumab and 30,000 units hyaluronidase every 3 weeks on weeks 10 to 24 (5 doses), and then 1,800 mg daratumumab and 30,000 units hyaluronidase every 4 weeks starting on week 25 until disease progression

Systemic Light Chain Amyloidosis

- The member has a diagnosis of systemic light chain amyloidosis **AND**
- The member has relapsed or refractory disease **AND**
- The member will be treated with daratumumab as monotherapy

Recommended dosage (Daratumumab): 16 mg/kg IV weekly for cycles 1-2 (total of 8 doses), then every 2 weeks for cycles 3-6 (total of 8 doses), 28 days per cycle

Recommended dosage (Daratumumab and hyaluronidase-fihj): 1,800 mg daratumumab and 30,000 units hyaluronidase subcutaneously weekly on weeks 1 to 8 (8 doses), 1,800 mg daratumumab and 30,000 units hyaluronidase every 2 weeks on weeks 9 to 24 (8 doses), and then 1,800 mg daratumumab and 30,000 units hyaluronidase every 4 weeks starting on week 25 until disease progression or for a maximum of 2 years.

All indications:

- Daratumumab will be approved through clinical review for up to a 6-month duration

Coverage Limitations

Treatment with daratumumab/daratumumab and hyaluronidase-fihj is not considered medically necessary for members with the following concomitant conditions:

- The member has experienced disease progression on daratumumab/daratumumab and hyaluronidase-fihj.
- The member has smoldering multiple myeloma.
- Indications not supported by NCCN category 2A or higher recommendations may not be considered medically necessary

Contraindications/Warnings/Precautions[1,2]

- Patients with a history of severe hypersensitivity to daratumumab/daratumumab and hyaluronidase-fihj or any of the components of the formulation.
- Daratumumab and hyaluronidase-fihj (Darzalex Faspro®) is not indicated and is not recommended for the treatment of patients with light chain (AL) amyloidosis who have NYHA Class IIIB or Class IV cardiac disease or Mayo Stage IIIB outside of controlled clinical trials
- Warnings/Precautions:
    - Infusion Reactions
    - Interference with cross-matching and red blood cell antibody screening. Type and screen patients prior to starting treatment. Inform blood banks that patient has received daratumumab
    - Neutropenia
    - Thrombocytopenia

For specific recommendations on contraindications, warnings and precautions, patient monitoring, and on dose adjustments and discontinuation, please refer to the current prescribing information.

Billing

- Description: inj., daratumumab, 10 mg
    - HCPCS: J9145
- Description: inj., daratumumab, 10 mg and hyaluronidase-fihj
    - HCPCS: J9144

Disclaimer

Drug Coverage Policies are developed as needed, regularly reviewed, updated at least annually, and are subject to change. Other policies and coverage determination guidelines may apply. Federal and state regulatory requirements and member specific benefit plan documents, if applicable, must be reviewed prior to this Drug Coverage Policy. This Drug Coverage Policy is for informational purposes only and does not constitute medical advice or dictate how providers should practice medicine. This policy should not be reproduced, stored in a retrieval system, or altered from its original form without written permission from Oncology Analytics, Inc.

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