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5.21.070

Section:	Prescription Drugs	**Effective Date:**	July 1, 2024
Subsection:	Antineoplastic Agents	**Original Policy Date:**	December 11, 2015
Subject:	Darzalex	**Page:**	1 of 6

Last Review Date: June 13, 2024

Darzalex

Description

Darzalex (daratumumab)

Background
Darzalex (daratumumab) is a CD38 monoclonal antibody indicated for the treatment of multiple myeloma (MM) as monotherapy in patients who have received at least three prior lines of therapy. Additionally, Darzalex can be used in combination with various other oncology medications for the treatment of multiple myeloma in newly diagnosed patients, as well as in patients that have failed prior lines of therapy. Multiple myeloma is a cancer that forms in a type of white blood cell called plasma cells. CD38 is a transmembrane protein found on the surface of hematopoietic cells (cells that give rise to all other blood cells), including multiple myeloma and other cell types. Darzalex binds to the CD38 receptors and inhibits the growth of tumor cells by inducing cell death (1-2).

Regulatory Status
FDA-approved indications: Darzalex is a human CD38-directed monoclonal antibody indicated for the treatment of adult patients with multiple myeloma: (1)

1. In combination with lenalidomide and dexamethasone in newly diagnosed patients with multiple myeloma 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
2. In combination with bortezomib, melphalan, and prednisone for the treatment of patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant
3. In combination with bortezomib, thalidomide, and dexamethasone in newly diagnosed patients who are eligible for autologous stem cell transplant

4. In combination with bortezomib and dexamethasone for the treatment of patients with multiple myeloma who have received at least one prior therapy
5. In combination with carfilzomib and dexamethasone in patients with relapsed or refractory multiple myeloma who have received one to three prior lines of therapy
6. In combination with pomalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor
7. 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

Safety and effectiveness of Darzalex have not been established in pediatric patients (1).

Related Policies
Darzalex Faspro, Sarclisa

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Darzalex may be considered **medically necessary** if the conditions indicated below are met.

Darzalex may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

Multiple myeloma (MM)

AND ONE of the following:

1. Newly diagnosed multiple myeloma (MM) **AND ONE** of the following:
    a. Patient is ineligible for autologous stem cell transplant

i. Used in combination with **ONE** of the following:
1. Bortezomib, melphalan, and prednisone
2. Lenalidomide and dexamethasone

b. Patient is eligible for autologous stem cell transplant
i. Used in combination with bortezomib, thalidomide, and dexamethasone

2. Used in combination with carfilzomib and dexamethasone
a. Patient has relapsed or refractory multiple myeloma **AND** patient has received one to three prior lines of therapy

3. Used in combination with lenalidomide and dexamethasone
a. Patient has relapsed or refractory multiple myeloma **AND** patient has received at least one prior therapy

4. Used in combination with bortezomib and dexamethasone
a. Patient has received at least one prior therapy

5. Used in combination with pomalidomide and dexamethasone
a. Patient has received at least two prior therapies that include a proteasome inhibitor (PI) and lenalidomide

6. Used as monotherapy **AND ONE** of the following:
a. Patient has received at least three prior lines of therapy including a proteasome inhibitor (PI) and immunomodulatory agent
b. Patient has had a double-refractory failure to a proteasome inhibitor (PI) and an immunomodulatory agent

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

Multiple myeloma (MM)

AND the following:

1. **NO** disease progression or unacceptable toxicity

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Darzalex (daratumumab) is a monoclonal antibody indicated for the treatment of patients with multiple myeloma as monotherapy, who have received at least three prior lines of therapy. Additionally, this can be used in combination with various other oncology medications for the treatment of multiple myeloma in newly diagnosed patients, as well as in patients that have failed prior lines of therapy. Safety and effectiveness of Darzalex have not been established in pediatric patients (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Darzalex while maintaining optimal therapeutic outcomes.

References

1. Darzalex [package insert]. Horsham, PA: Janssen Biotech, Inc.; January 2023.
2. NCCN Drugs & Biologics Compendium® Daratumumab 2024. National Comprehensive Cancer Network, Inc. Accessed on April 23, 2024.

Policy History

Date	Action
December 2015	New policy
March 2016	Annual review Policy number changed from 5.04.70 to 5.21.70

June 2016	Annual editorial review and reference update
September 2016	Annual review
December 2016	Addition of the option of 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
March 2017	Annual review
July 2017	Addition of patient will use in combination with Pomalyst (pomalidomide) and dexamethasone and has received at least two prior therapies that include the following: a Proteasome inhibitor (PI) and Revlimid (lenalidomide)
September 2017	Annual review
June 2018	Annual editorial review and reference update Addition of the use of this medication for the treatment of multiple myeloma for newly diagnosed patients when used in combination with bortezomib (Velcade), melphalan, and prednisone in patients who are ineligible for autologous stem cell transplantation Increase in length of approval for initiation from 6 months to 12 months
June 2019	Annual review and reference update
July 2019	Addition of indication: newly diagnosed multiple myeloma in combination with lenalidomide and dexamethasone in patients who are ineligible for autologous stem cell transplant
September 2019	Annual review and reference update
October 2019	Addition of indication: newly diagnosed multiple myeloma in combination with bortezomib, thalidomide, and dexamethasone in patients who are eligible for autologous stem cell transplant
December 2019	Annual review
June 2020	Annual review and reference update
September 2020	Annual review and reference update. Addition of indication: relapsed or refractory multiple myeloma in combination with carfilzomib and dexamethasone in patients who have received one to three prior lines of therapy
March 2021	Annual editorial review and reference update Changed monotherapy requirement (6a) from “patient has received at least 3 prior lines of therapy TWO of which must include a PI and IMiD” to “patient has received at least 3 prior lines of therapy including a PI and an IMiD” to align with the package insert
March 2022	Annual review and reference update

June 2022	Annual review and reference update
March 2023	Annual review and reference update. Changed policy number to 5.21.070
December 2023	Annual review and reference update
March 2024	Annual review and reference update
June 2024	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 13, 2024 and is effective on July 1, 2024.