Daratumumab (Darzalex®)

NDC CODE(S) 57894-0502-XX DARZALEX 100MG/5ML Solution (JANSSEN BIOTECH)
57894-0502-XX DARZALEX 400MG/20ML Solution (JANSSEN BIOTECH)

DESCRIPTION

Daratumumab is an immunoglobulin G1 kappa human monoclonal antibody against CD38 antigen produced using recombinant DNA technology. Daratumumab binds to CD38 and inhibits the growth of CD38 expressing tumor cells by inducing apoptosis directly through Fc mediated cross linking as well as through immune-mediated tumor cell lysis, complement dependent cytotoxicity, antibody dependent cell mediated cytotoxicity and antibody dependent cellular phagocytosis.

POLICY

- Daratumumab for the treatment of the following is considered ***medically necessary*** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**
  - Multiple Myeloma
  - Systemic Light Chain Amyloidosis
- Daratumumab for the treatment of other conditions/diseases is considered ***investigational.***

MEDICAL APPROPRIATENESS

INITIAL APPROVAL CRITERIA

- Patient is at least 18 years of age; **AND**

Universal Criteria

- Therapy will not be used in combination with other anti-CD38 therapies (i.e., daratumumab, isatuximab, etc.); **AND**

Multiple Myeloma

- Used in the treatment of newly diagnosed disease in patients who are ineligible for autologous stem cell transplant (ASCT) in combination with ONE of the following regimens:
  - Lenalidomide and dexamethasone; **OR**
  - Bortezomib, melphalan, and prednisone; **OR**
  - Cyclophosphamide, bortezomib, and dexamethasone; **OR**
- Used in the treatment of newly diagnosed disease in patients who are eligible for autologous stem cell transplant (ASCT) in combination with ONE of the following regimens:
  - Bortezomib, lenalidomide, and dexamethasone; **OR**
  - Bortezomib, thalidomide, and dexamethasone (VTd); **OR**
  - Cyclophosphamide, bortezomib, and dexamethasone; **OR**
- Used for disease relapse after 6 months following primary induction therapy with the same regimen in combination with ONE of the following regimens:
  - Lenalidomide and dexamethasone for non-transplant candidates; **OR**
  - Cyclophosphamide, bortezomib, and dexamethasone; **OR**
- Used as subsequent therapy for relapsed or progressive disease in combination with dexamethasone and ONE of the following:

- Lenalidomide; **OR**
- Bortezomib; **OR**
- Carfilzomib; **OR**
- Cyclophosphamide and bortezomib; **OR**
- Selinexor; **OR**

- Used in combination with pomalidomide and dexamethasone after at least two prior therapies including an immunomodulatory agent (e.g., lenalidomide, pomalidomide, etc.) and a proteasome inhibitor (bortezomib, carfilzomib, etc.); **OR**
- Used as single agent therapy; **AND**
  - Patient received at least three prior lines of therapy including a proteasome inhibitor (e.g., bortezomib, carfilzomib, etc.) and an immunomodulatory agent (e.g., lenalidomide, pomalidomide, etc.); **OR**
  - Patient is double-refractory to a proteasome inhibitor and an immunomodulatory agent

Systemic Light Chain Amyloidosis

- Used as single agent therapy; **AND**
- Used for the treatment of relapsed/refractory disease

RENEWAL CRITERIA

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in the Initial Approval Criteria; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe infusion reactions including anaphylactic reactions, neutropenia, thrombocytopenia, etc.; **AND**
  - Use for newly diagnosed disease in combination with bortezomib, thalidomide, and dexamethasone after 24 weeks of induction/consolidation therapy may not be renewed.
  - Use for newly diagnosed disease in combination with bortezomib, lenalidomide and dexamethasone may be renewed for up to a maximum of 2 years of maintenance therapy.
  - Use for newly diagnosed or relapsed disease in combination with cyclophosphamide, bortezomib and dexamethasone may be renewed for up to a maximum of 80 weeks *(32 weeks of induction therapy and 48 weeks of maintenance therapy).*

DOSAGE/ADMINISTRATION

INDICATION	DOSE
Multiple Myeloma	<u>Newly diagnosed disease in patients ineligible for ASCT in combination with bortezomib, melphalan and prednisone</u> ▪ 16 mg/kg body weight given as an intravenous infusion in a 6 week cycle: ▫ Weekly — Weeks 1 to 6 (six doses; cycle 1) ▫ Every three weeks — Weeks 7 to 54 (16 doses; cycles 2 to 9) ▫ Every four weeks — Week 55 onwards (cycle 10 and beyond) *Treat until disease progression or unacceptable toxicity*
	<u>Newly diagnosed disease in patients eligible for ASCT in combination with bortezomib, thalidomide and dexamethasone</u>

	▪ 16 mg/kg body weight given as an intravenous infusion in a 4 week cycle: ▪ Induction – ▫ Weekly Weeks 1 to 8 (eight doses; cycles 1 and 2) ▫ Every two weeks Weeks 9 to 16 (four doses; cycles 3 and 4) *Stop for high dose chemotherapy and ASCT* ▪ Consolidation – ▫ Every two weeks Weeks 1 to 8 (four doses; cycles 5 and 6)
	<u>Newly diagnosed disease in patients eligible for ASCT in combination with bortezomib, lenalidomide and dexamethasone</u> ▪ 16 mg/kg body weight given as an intravenous infusion as follows: ▪ Induction – **3 week cycle** ▫ Weekly Weeks 1 to 12 (twelve doses; cycles 1 to 4) ▪ Consolidation – (*after ASCT*) – **3 week cycle** ▫ Weekly Weeks 13 to 18 (six doses; cycles 5 and 6) ▪ Maintenance – **4 week cycle** ▫ Every 4 or 8 weeks Weeks 1 to102 -maximum of 2 years of maintenance treatment
	<u>Newly diagnosed OR relapsed disease in combination with cyclophosphamide, bortezomib and dexamethasone</u> Induction ▪ 8 mg/kg body weight given as an intravenous infusion on days 1 and 2 (Week 1; total 2 doses) ▪ Followed by 16 mg/kg body weight given as an intravenous infusion in a 4 week cycle: ▫ Weekly Weeks 2 to 8 (seven doses; cycles 1 and 2) ▫ Every two weeks Weeks 9 to 24 (eight doses; cycles 3 to 6) ▫ Every four weeks Week 25 to 32 (two doses; cycles 7 and 8) Maintenance (*after ASCT*) ▪ 16 mg/kg body weight given as an intravenous infusion every 4 weeks for up to 12 cycles (48 weeks)
	<u>Treatment as one of the following:</u> • Monotherapy for patients with relapsed/refractory multiple myeloma • Combination therapy with lenalidomide and low-dose dexamethasone for newly diagnosed patients ineligible for ASCT • Combination therapy with lenalidomide, ~~or~~ pomalidomide, or selinexor and low-dose dexamethasone in patients with relapsed/refractory disease ▪ 16 mg/kg body weight given as an intravenous infusion in a 4 week cycle: ▫ Weekly Weeks 1 to 8 (eight doses; cycles 1 and 2) ▫ Every two weeks 9 to 24 (eight doses; cycles 3 to 6) ▫ Every four weeks Week 25 onwards (cycle 7 and beyond) *Treat until disease progression or unacceptable toxicity*
	<u>Combination therapy with carfilzomib and dexamethasone for relapsed/refractory disease</u> ▪ 8 mg/kg body weight given as an intravenous infusion on days 1 and 2 (Week 1; total 2

	▪ doses) ▪ Followed by 16 mg/kg body weight given as an intravenous infusion in a 4 week cycle: ▫ Weekly Weeks 2 to 8 (seven doses; cycles 1 and 2) ▫ Every two weeks Weeks 9 to 24 (eight doses; cycles 3 to 6) ▫ Every four weeks Week 25 onwards (cycle 7 and beyond) *Treat until disease progression or unacceptable toxicity*
	<u>Combination therapy with bortezomib and dexamethasone for relapsed/refractory disease</u> ▪ 16 mg/kg body weight given as an intravenous infusion in a 3 week cycle: ▫ Weekly Weeks 1 to 9 (nine doses; cycles 1 to 3) ▫ Every three weeks Weeks 10 to 24 (five doses; cycles 4 to 8) ▫ Every four weeks Week 25 onwards (cycle 9 and beyond) *Treat until disease progression or unacceptable toxicity*
Systemic Light Chain Amyloidosis	▪ 16 mg/kg body weight given as an intravenous infusion: ▫ Weekly Weeks 1 to 8 (eight doses) ▫ Every two weeks Weeks 9 to 24 (eight doses) ▫ Every four weeks Week 25 onwards until disease progression or unacceptable toxicity

LENGTH OF AUTHORIZATION

Coverage will be provided for six months and may be renewed (unless otherwise specified).

- Use for newly diagnosed multiple myeloma in combination with bortezomib, thalidomide, and dexamethasone may not be renewed.
- Use for newly diagnosed disease in combination with bortezomib, lenalidomide and dexamethasone may be renewed for up to a maximum of 2 years of maintenance therapy.
- Use for newly diagnosed or relapsed disease in combination with cyclophosphamide, bortezomib and dexamethasone may be renewed for up to a maximum of 80 weeks *(32 weeks of induction therapy and 48 weeks of maintenance therapy)*.

DOSING LIMITS

Max Units (per dose and over time) [HCPCS Unit]:

- Up to 180 billable units per dose
  - Weekly Week 1 to 8, then every two weeks, Week 9-24, then every four weeks Week 25 onwards

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification,

explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

SOURCES

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2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for daratumumab. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed April 2021.
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14. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Multiple Myeloma Version 4.2021. National Comprehensive Cancer Network, 2021. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed April 2021.
15. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Systemic Light Chain Amyloidosis 1.2021. National Comprehensive Cancer Network, 2021. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed April 2021.
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EFFECTIVE DATE 9/30/2021

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