



Medical Policy Manual **Approved Revision: Do Not Implement Until 4/2/21**

Daratumumab

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 in a mammalian cell line 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 by immune-mediated tumor cell lysis through complement dependent cytotoxicity, antibody dependent cell mediated cytotoxicity and antibody dependent cellular phagocytosis. Myeloid derived suppressor cells and a subset of regulatory T cells express CD38 and are susceptible to daratumumab mediated cell lysis.

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

- Daratumumab is considered **medically appropriate** for **ALL** of the following:
 - Individual is 18 years of age or older
 - **Therapy** will not be used in combination with other anti-CD38 therapies (i.e., daratumumab, isatuximab, etc.)
 - Diagnosis of **ANY ONE** of the following:
 - Multiple Myeloma and **ANY ONE** of the following:
 - Used in the treatment of newly diagnosed disease in individuals who are ineligible for autologous stem cell transplant (ASCT) in combination with **ANY ONE** of the following regimens:
 - Lenalidomide and dexamethasone
 - Bortezomib, melphalan and prednisone
 - **Cyclophosphamide, bortezomib, and dexamethasone**
 - Used in the treatment of newly diagnosed disease in individuals who are eligible for autologous stem cell transplant (ASCT) in combination with **ANY ONE** of the following regimens:
 - **Bortezomib, lenalidomide, and dexamethasone**
 - Bortezomib, thalidomide, and dexamethasone (VTd)
 - **Cyclophosphamide, bortezomib, and dexamethasone**
 - Used for disease relapse after 6 months following primary induction therapy with the same regimen in combination with **ANY ONE** of the following regimens:
 - Lenalidomide and dexamethasone for non-transplant candidates
 - **Cyclophosphamide, bortezomib, and dexamethasone**
 - Used as subsequent therapy in combination with dexamethasone and **ANY ONE** of the following:
 - Lenalidomide
 - Bortezomib



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- Carfilzomib
- Cyclophosphamide **and bortezomib**
- 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 (e.g. bortezomib, carfilzomib, etc.)
- Treatment as a single agent if **ANY ONE** of the following:
 - Individual has 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.)
 - Individual is double-refractory to a proteasome inhibitor and an immunomodulatory agent
- Systemic Light Chain Amyloidosis and **ALL** of the following:
 - Used as single agent therapy
 - Used for the treatment of relapsed/refractory disease

RENEWAL CRITERIA

- Daratumumab is considered **medically appropriate** for renewal if **ALL** of the following criteria are met:
 - Individual continues to meet initial approval criteria (not including prerequisite therapy)
 - Disease response with treatment as defined by stabilization of disease and decrease in size of tumor or tumor spread.
 - Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: severe infusion reactions, including anaphylactic reactions, neutropenia, thrombocytopenia, etc.
 - **Additional requirements for uses below:**
 - 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).**

INDICATION(S)	DOSAGE & ADMINISTRATION
Multiple Myeloma	<p><u>Newly diagnosed disease in patients ineligible for ASCT in combination with: bortezomib, melphalan and prednisone</u></p> <ul style="list-style-type: none"> • 16 mg/kg body weight given as an intravenous infusion in a six week cycle: <ul style="list-style-type: none"> -Weekly Weeks 1 to 6 (six doses; cycle 1) -Every three weeks Weeks 7 to 54 (sixteen doses; cycles 2 thru 9) -Every four weeks Week 55 onwards (cycle 10 and beyond) <p style="text-align: center;"><i>Treat until disease progression or unacceptable toxicity</i></p>
	<p><u>Newly diagnosed disease in patients eligible for ASCT in combination with bortezomib, thalidomide and dexamethasone</u></p> <ul style="list-style-type: none"> • 16 mg/kg body weight given as an intravenous infusion in a 4 week cycle • Induction: <ul style="list-style-type: none"> -Weekly..... Weeks 1 to 8 (eight doses; cycles 1 and 2) -Every two weeksWeeks 9 to 16 (four doses; cycles 3 and 4)) <p style="text-align: center;"><i>Stop for high dose chemotherapy and ASCT</i></p> • Consolidation: <ul style="list-style-type: none"> -Every two weeks..... Weeks 1 to 8 (four doses; cycles 5 and 6)
	<p><u>Newly diagnosed disease in patients eligible for ASCT in combination with bortezomib, lenalidomide and dexamethasone</u></p>



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	<ul style="list-style-type: none"> 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 to 102 for a maximum of 2 years of maintenance treatment <p><u>Newly diagnosed OR relapsed disease in combination with cyclophosphamide, bortezomib and dexamethasone</u> Induction</p> <ul style="list-style-type: none"> 8 mg/kg body weight given as an intravenous infusion on days 1 and 2 (Week 1; total 2 doses) <u>Followed by 16 mg/kg body weight given as an intravenous infusion in a 4 week cycle:</u> -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) <p>Maintenance (after ASCT)</p> <ul style="list-style-type: none"> 16 mg/kg body weight given as an intravenous infusion every 4 weeks for up to 12 cycles (48 weeks) <p><u>Treatment as one of the following:</u></p> <ul style="list-style-type: none"> 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, and low-dose dexamethasone in patients with relapsed/refractory disease 16 mg/kg body weight given as an intravenous (IV) 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) <i>Treat until disease progression or unacceptable toxicity</i> <p><u>Combination therapy with carfilzomib and dexamethasone for relapsed/refractory disease</u></p> <ul style="list-style-type: none"> 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) <i>Treat until disease progression or unacceptable toxicity</i> <p><u>Combination therapy with bortezomib and dexamethasone for relapsed /refractory disease:</u></p> <ul style="list-style-type: none"> 16 mg/kg body weight given as an intravenous (IV) 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) <i>Treat until disease progression or unacceptable toxicity</i>
Systemic Light Chain Amyloidosis	<ul style="list-style-type: none"> 16 mg/kg body weight given as an intravenous (IV) 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



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**To facilitate administration, the first prescribed 16 mg/kg dose at Week 1 may be split over two consecutive days i.e. 8 mg/kg on Day 1 and Day 2 respectively.*

Note: Initiate antiviral prophylaxis to prevent herpes zoster reactivation within 1 week after starting Darzalex and continue for 3 months following treatment.

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).

Refer to **DOSAGE LIMITS** below

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

Lexi-comp Online. (2020, March). AHFS DI. Daratumumab. Retrieved December 3, 2020 from Lexi-comp Online with AHFS.



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National Comprehensive Cancer Network. (2020). NCCN Drugs & Biologics Compendium®. Daratumumab. Retrieved December 3, 2020 from the National Comprehensive Cancer Network.

U. S. Food and Drug Administration. (2020, August). Center for Drug Evaluation and Research. Darzalex™ (daratumumab) injections, for intravenous use. Retrieved December 3, 2020 from https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761036s005lbl.pdf.

EFFECTIVE DATE 4/2/21

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