BlueCross BlueShield of North Carolina

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Corporate Medical Policy

Daratumumab (Darzalex®)

File Name:	daratumumab_darzalex
Origination:	2/2016
Last CAP Review:	4/2020
Next CAP Review:	4/2021
Last Review:	6/2020

Description of Procedure or Service

Daratumumab (Darzalex) is an immunoglobulin G1 kappa (IgG1k) human monoclonal antibody against CD38 antigen, produced in a mammalian cell line using recombinant DNA technology.

CD38 is a transmembrane glycoprotein (48 kDa) expressed on the surface of hematopoietic cells, including multiple myeloma and other cell types and tissues and has multiple functions, such as receptor mediated adhesion, signaling, and modulation of cyclase and hydrolase activity.

Daratumumab (Darzalex) is the first monoclonal antibody approved for treating multiple myeloma. Multiple myeloma is a form of blood cancer that occurs in infection-fighting plasma cells (a type of white blood cell) found in the bone marrow. These cancerous cells multiply, produce an abnormal protein and push out other healthy blood cells from the bone marrow. The disease may result in a weakened immune system and cause other bone or kidney problems.

Daratumumab and hyaluronidase-fihj (Darzalex Faspro™) is a subcutaneous combination drug that contains daratumumab and hyaluronidase. Hyaluronidase has been shown to increase the absorption rate of daratumumab into systemic circulation. In May 2020, Darzalex Faspro was approved by the FDA for the same labeled indications as daratumumab for the treatment of multiple myeloma.

******Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

Policy

BCBSNC will provide coverage for daratumumab (Darzalex) and daratumumab and hyaluronidase-fihj (Darzalex Faspro) when it is determined to be medically necessary because the medical criteria and guidelines noted below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Daratumumab (Darzalex) is covered

Daratumumab (Darzalex) and daratumumab and hyaluronidase-fihj (Darzalex Faspro) are considered medically necessary for the treatment of multiple myeloma:

- As monotherapy in patients who have received at least three prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent **OR** who are double-refractory or have relapsed twice on a PI and an immunomodulatory agent*; **OR**
- In combination with dexamethasone and either lenalidomide or bortezomib, in patients who have received at least one prior therapy; **OR**
- In combination with pomalidomide and dexamethasone, in patients who have received at least two prior therapies including lenalidomide and a proteasome inhibitor and have demonstrated disease progression on or within 60 days of completion of the last therapy; **OR**
- In combination with bortezomib, melphalan and prednisone in patients with newly diagnosed disease who are ineligible for autologous stem cell transplantation; **OR**
- In combination with lenalidomide and dexamethasone in patients with newly diagnosed disease who are ineligible for autologous stem cell transplantation; **OR**
- In combination with bortezomib, thalidomide, and dexamethasone in patients with newly diagnosed disease who are eligible for autologous stem cell transplantation.

*PI inhibitors: [e.g., bortezomib (Velcade), carfilzomib (Kyprolis), ixazomib (Ninlaro)];
Immunomodulatory agents: (e.g., thalidomide, lenalidomide, pomalidomide);
Refractory=resistant to treatment

Use of daratumumab (Darzalex) and daratumumab and hyaluronidase-fihj (Darzalex Faspro) may be considered medically necessary for clinical indications not listed above when the drug is prescribed for the treatment of cancer either:

- In accordance with FDA label (when clinical benefit has been established, see Policy Guidelines); **OR**

- In accordance with specific strong endorsement or support by nationally recognized compendia, when such recommendation is based on strong/high levels of evidence, and/or uniform consensus of clinical appropriateness has been reached.

When Daratumumab (Darzalex) is not covered

Daratumumab (Darzalex) and daratumumab and hyaluronidase-fihj (Darzalex Faspro) are considered not medically necessary and therefore not covered when above criteria are not met.

Daratumumab (Darzalex) and daratumumab and hyaluronidase-fihj (Darzalex Faspro) are considered investigational when used for:

1. Non-cancer indications; **OR**

2. When criteria are not met regarding FDA labeling **OR** strong endorsement/support by nationally recognized compendia, as stated under "When Daratumumab (Darzalex) is covered."

Policy Guidelines

The recommended dose for Darzalex is 16mg/kg body weight administered as an intravenous infusion.

The recommended dose for Darzalex Faspro is 1,800 mg/30,000 units (1,800 mg daratumumab and 30,000 units hyaluronidase) administered subcutaneously over approximately 3-5 minutes.

Monotherapy and in combination with lenalidomide or pomalidomide and low-dose dexamethasone:
Dosing schedule should be weekly for weeks 1-8; every two weeks for weeks 9-24; every four weeks from week 25 onward until disease progression.

In combination with bortezomib and dexamethasone:
Dosing schedule should be weekly for weeks 1-9; every three weeks for weeks 10-24; every four weeks from week 25 onward until disease progression.

In combination with bortezomib, melphalan and prednisone:
Dosing schedule should be weekly for weeks 1-6; every three weeks for weeks 7-54; every four weeks from week 55 onward until disease progression.

In combination with bortezomib, thalidomide and dexamethasone:
Dosing schedule for induction should be weekly for weeks 1-8, every two weeks for weeks 9-16, and should be stopped for high dose chemotherapy and autologous stem cell transplantation (ASCT); for consolidation upon re-initiation of treatment after ASCT, the dosing should be every two weeks for weeks 1-8.

Drugs prescribed for treatment of cancer in accordance with FDA label may be considered medically necessary when clinical benefit has been established, and should not be determined to be investigational as defined in Corporate Medical Policy (CMP), "Investigational (Experimental) Services."

Please refer to CMP "Investigational (Experimental) Services" for a summary of evidence standards from nationally recognized compendia.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable service codes: C9399, J3490, J3590, J9144, J9145, J9999, S0353, S0354

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

US Food and Drug Administration (FDA). Center for Biologics Evaluation and Research. Available at:
http://www.fda.gov/newsevents/newsroom/pressannouncements/ucm472875.htm.
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US Food and Drug Administration (FDA). Prescribing Information. Available at:
http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/761036Orig1s000lbledt.pdf
Accessed February 3, 2016.

Senior Medical Director review 2/2016.

Specialty Matched Consultant Advisory Panel review- 4/2016

Medical Director review 8/2016

Medical Director review 3/2017

Specialty Matched Consultant Advisory Panel review- 4/2017

Darzalex (daratumumab) [prescribing information]. Horsham, PA: Janssen Biotech, Inc; June 2017. Available at: http://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/DARZALEX-pi.pdf. Accessed 3/2018.

Chari A, Suvannasankha A, Fay JW, et al. Daratumumab plus pomalidomide and dexamethasone in relapsed and/or refractory multiple myeloma [published online ahead of print July 21, 2017]. Blood. 2017 Aug 24;130(8):974-981. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5570682/?report=printable. Accessed March 28, 2018.

Dimopoulos MA, Oriol A, Nahi H, et al. Daratumumab, lenalidomide, and dexamethasone for multiple myeloma. N Engl J Med. 2016;375(14):1319-1331. Available at: http://www.nejm.org/doi/pdf/10.1056/NEJMoa1607751. Accessed March 28, 2018.

Palumbo A, Chanan-Khan A, Weisel K, et al. Daratumumab, bortezomib, and dexamethasone for multiple myeloma. N Engl J Med. 2016;375(8):754-766. Available at: http://www.nejm.org/doi/pdf/10.1056/NEJMoa1606038. Accessed March 28, 2018.

National Comprehensive Cancer Network (NCCN) Guidelines Version 4.2018 Multiple Myeloma. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed May 2018.

Specialty Matched Consultant Advisory Panel review- 4/2018

Medical Director review 6/2018

Janssen Biotech, Inc. Darzalex (daratumumab) injection for intravenous use. Highlights of prescribing information. February 2019. Available at: http://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/DARZALEX-pi.pdf. Accessed April 2019

Specialty Matched Consultant Advisory Panel review- 4/2019

Janssen Biotech, Inc. Darzalex (daratumumab) injection for intravenous use. Highlights of prescribing information. September 2019. Available at: http://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/DARZALEX-pi.pdf. Last accessed November 2019.

Medical Director review 12/2019

Specialty Matched Consultant Advisory Panel review- 4/2020

Janssen Biotech, Inc. Darzalex Faspro (daratumumab and hyaluronidase-fihj) injection, for subcutaneous use. Highlights of prescribing information. May 2020. Available at: http://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/DARZALEX+Faspro-pi.pdf. Last accessed June 2020.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Multiple Myeloma, version 4.2020. Revised May 8, 2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Last accessed June 2020.

Medical Director review 6/2020

Policy Implementation/Update Information

2/29/16 New policy issued. Daratumumab (Darzalex) is considered medically necessary for the treatment of multiple myeloma in patients: who have received 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. Senior medical director review 2/2016. References added. Notification given 2/29/2016 for effective date 4/29/2016. (lpr)

7/1/16 Specialty Matched Consultant Review panel meeting 4/27/16. No change to policy statement. Added HCPCS code C9476 to "Billing/Coding" section for effective date 7/1/16. (lpr)

12/30/16 Medical Director review 8/2016. No change to policy statement. Deleted the following HCPCS codes C9476, C9399, J3490, J3590, J9999 and added HCPCS codes J9145, S0353, S0354 to Billing/Coding section. Notification given 12/30/16 for effective date 4/1/17. (lpr)

5/26/17 Added the following statement to "When Covered" section: "Use of Daratumumab (Darzalex) may be considered medically necessary for clinical indications not listed above when the drug is prescribed for the treatment of cancer either: In accordance with FDA label (when clinical benefit has been established, see Policy Guidelines); OR In accordance with specific strong endorsement or support by nationally recognized compendia, when such recommendation is based on strong/high levels of evidence, and/or uniform consensus of clinical appropriateness has been reached". Under "When Not Covered" section, added the statement "Daratumumab (Darzalex) is considered investigational when used for: 1)Non-cancer indications; **OR** 2) When criteria are not met regarding FDA labeling **OR** strong endorsement/ support by nationally recognized compendia, as stated under "When Daratumumab (Darzalex) is covered." Added the following statements under "Policy Guidelines" section: 1)Drugs prescribed for treatment of cancer in accordance with FDA label may be considered medically necessary when clinical benefit has been established, and should not be determined to be investigational as defined in Corporate Medical Policy, Investigational (Experimental) Services." 2) Please refer to CMP "Investigational (Experimental) Services" for a summary of evidence standards from nationally recognized compendia. Medical director review 3/2017. Specialty Matched Consultant Advisory Panel review 4/26/2017. No change to policy statement. (lpr)

6/29/18 Added the following statements to "When Covered" section: "In combination with dexamethasone and either lenalidomide or bortezomib, in patients who have received at least one prior therapy; **OR** In combination with pomalidomide and dexamethasone, in patients who have received at least two prior therapies including lenalidomide and a proteasome inhibitor and have demonstrated disease progression on or within 60 days of completion of the last therapy." Added the following statement under "Policy Guidelines" section: "In combination with bortezomib and dexamethasone: Dosing schedule should be weekly for weeks 1-9; every three weeks for weeks 10-24; every four weeks from week 25 onward until disease progression." and clarified existing dosing scheduled as "Monotherapy and in combination with lenalidomide or pomalidomide and low-dose dexamethasone." References added. Specialty Matched Consultant Advisory Panel review 4/25/2018. Medical Director review 6/2018. (krc)

4/30/19 Added the following statement to "When Covered" section: "In combination with bortezomib, melphalan and prednisone in patients with newly diagnosed disease who are ineligible for autologous stem cell transplantation," and updated Policy Guidelines with the associated dosing regimen for this indication. References added. Specialty Matched Consultant Advisory Panel review 4/17/2019. (krc)

12/10/19 Added the following statements to "When Covered" section: "In combination with lenalidomide and dexamethasone in patients with newly diagnosed disease who are ineligible for autologous stem cell transplantation," and "in combination with bortezomib, thalidomide, and dexamethasone in patients with newly diagnosed disease who are eligible for autologous stem cell transplantation," and updated Policy Guidelines with the associated dosing regimen for these indications. Reference added. Medical Director review 12/2019. (krc)

6/9/20 Specialty Matched Consultant Advisory Panel review 4/15/2020. No change to policy statements. (krc)

6/30/20 Under "When Covered," added Darzalex Faspro (daratumumab and hyaluronidase-fihj) for the treatment of multiple myeloma with same policy statements as Darzalex. Updated Description and Policy Guidelines sections to reflect addition of Darzalex Faspro to policy. Added HCPCS codes C9399, J3490, J3590, J9999 to Billing/Coding section. References added. Medical Director review 6/2020. (krc)

10/1/20 Added HCPCS code C9062 to Billing/Coding section effective 10/1/2020. (krc)

12/31/20 Added HCPCS code J9144 to Billing/Coding section effective 1/1/2021 and deleted code C9062 termed 12/31/2020. (krc)