

Corporate Medical Policy

Polatuzumab vedotin-piiq (Polivy™)

File Name:	polatuzumab_vedotin_polivy
Origination:	7/2019
Last CAP Review:	4/2020
Next CAP Review:	4/2021
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Description of Procedure or Service

Polatuzumab vedotin-piiq (Polivy™) is a CD79b-directed antibody-drug conjugate that is indicated in combination with bendamustine and a rituximab product for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, after at least two prior systemic chemotherapies.

DLBCL is the most common subtype of non-Hodgkin lymphoma (NHL), representing approximately one-third of NHL patients. It is an aggressive and quickly progressing NHL in which survival without treatment is measured in months. While there have been many advancements in the treatment of DLBCL, a cure is not achieved in most patients using conventional therapy, and roughly 30 to 40% of patients suffer relapse. For patients who are refractory to initial treatment and for patients who relapse after an initial response, only a small percentage will experience prolonged disease-free survival with salvage chemoimmunotherapy treatment alone. The preferred treatment for a first relapse of DLBCL or primary refractory DLBCL is salvage chemoimmunotherapy followed by autologous hematopoietic stem cell transplantation (HSCT). However, the outcome for relapsed/refractory DLBCL patients who are ineligible for transplant remains poor.

Polatuzumab vedotin-piiq (Polivy) is a CD79b-directed antibody-drug conjugate with activity against dividing B-cells, which was approved by the U.S. Food and Drug Administration (FDA) in June 2019 for the treatment of relapsed or refractory DLBCL. The monoclonal antibody is linked to a small molecule anti-mitotic agent monomethyl auristatin E (MMAE), and works by binding to CD79b (a B-cell specific surface protein) of the B-cell receptor. Upon binding, polatuzumab vedotin is internalized and the linker is cleaved by lysosomal proteases enabling intracellular delivery of MMAE. MMAE binds to microtubules, inhibits cell division, and induces apoptosis, thus killing dividing cells,

Related Policies:

CAR-T Therapy

Monoclonal Antibodies for Non-Hodgkin Lymphoma and Acute Myeloid Leukemia in the Non-Hematopoietic Stem Cell Transplant Setting

Hematopoietic Stem-Cell Transplant for Non-Hodgkin Lymphomas

*****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

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BCBSNC will provide coverage for polatuzumab vedotin-piiq (Polivy™) 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 Polatuzumab vedotin-piiq (Polivy) is covered

Polatuzumab vedotin-piiq (Polivy) is considered medically necessary for the treatment of adult patients with diffuse large B-cell lymphoma (DLBCL) when the following criteria are met:

- The patient has relapsed or refractory disease; **and**
- Polatuzumab vedotin is administered in combination with bendamustine and a rituximab product; **and**
- The patient has received at least two prior systemic chemotherapies; **and**
- The patient is not a candidate for autologous hematopoietic stem cell transplantation (HSCT); **and**
- The patient has not previously undergone allogeneic HSCT; **and**
- The patient does not have active central nervous system lymphoma or histologically transformed lymphoma.

Authorization: 12 months

Use of polatuzumab vedotin-piiq (Polivy) 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 Polatuzumab vedotin-piiq (Polivy) is not covered

Polatuzumab vedotin-piiq (Polivy) is considered **investigational** and therefore not covered when the above criteria are not met.

Polatuzumab vedotin-piiq (Polivy) 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 Polatuzumab vedotin-piiq (Polivy) is covered.”

Policy Guidelines

The recommended dose of Polivy is 1.8 mg/kg given as an intravenous infusion over 90 minutes every 21 days for 6 cycles, in combination with bendamustine and a rituximab product. Patients

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may receive subsequent infusions administered over 30 minutes if the previous infusion is well tolerated. Patients should be premedicated with an antihistamine and antipyretic at least 30 minutes prior to receiving Polivy.

According to the manufacturer's safety information for Polivy, the most common adverse reactions ($\geq 20\%$ incidence) include neutropenia, thrombocytopenia, anemia, peripheral neuropathy, fatigue, diarrhea, fever, decreased appetite, and pneumonia.

Evidence Summary

The efficacy of polatuzumab vedotin-piiq (Polivy) was evaluated in an open-label, multicenter clinical trial (NCT02257567) that included a cohort of 80 patients with relapsed or refractory DLBCL after at least one prior regimen. Patients included in the trial were at least 18 years of age with histologically confirmed relapsed/refractory DLBCL, and were eligible if not a candidate for autologous HSCT at study entry. Patients were excluded from the study who had Grade 2 or higher peripheral neuropathy, prior allogeneic HSCT, active central nervous system lymphoma, or transformed lymphoma. Patients were randomized 1:1 to receive either polatuzumab vedotin in combination with bendamustine and a rituximab product (BR) or BR alone for six 21-day cycles. Polatuzumab was administered intravenously at 1.8 mg/kg on Day 2 of Cycle 1 and on Day 1 of Cycles 2-6. Bendamustine was administered intravenously at 90 mg/m² daily on Days 2 and 3 of Cycle 1 and on Days 1 and 2 of Cycles 2-6. A rituximab product was administered intravenously at a dose of 375 mg/m² on Day 1 of Cycles 1-6. Of the 80 patients included in the DLBCL cohort of the trial, the median number of prior therapies was 2 (range: 1-7), with 29% receiving one prior therapy, 25% receiving two prior therapies, and 46% receiving three or more prior therapies. Eighty percent of patients had refractory disease to last therapy. The primary efficacy endpoints were based on complete response (CR) rate at the end of treatment and duration of response (DOR), as determined by an independent review committee (IRC). Other efficacy measures included IRC-assessed based overall response. Complete response was observed in 16 of 40 patients (40%) in the polatuzumab vedotin plus BR arm, and in 7 of 40 patients (18%) in the BR arm. Of the 25 patients who achieved a partial or complete response in the polatuzumab vedotin plus BR arm, 16 (64%) had a DOR of at least 6 months, and 12 (48%) had a DOR of at least 12 months. Of the 10 patients achieving a partial or complete response in the BR arm, 3 (30%) had a DOR lasting at least 6 months, and 2 (20%) had a DOR lasting at least 12 months. The results indicate that the addition of polatuzumab vedotin-piiq to bendamustine and a rituximab product resulted in a greater CR rate and DOR in a cohort study of patients with relapsed or refractory DLBCL after at least one prior regimen.

The following information is derived from FDA prescribing information, as peer reviewed published trial results have not been identified.

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.bcbssc.com. They are listed in the Category Search on the Medical Policy search page.

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Applicable codes: J9309, 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

Genentech, Inc. Polivy (polatuzumab vedotin-piiq) for injection, for intravenous use. Highlights of prescribing information. June 2019. Available at: https://www.gene.com/download/pdf/polivy_prescribing.pdf. Last accessed July 2019.

U.S. Food and Drug Administration. FDA approves first chemoimmunotherapy regimen for patients with relapsed or refractory diffuse large B-cell lymphoma. Available at: <https://www.fda.gov/news-events/press-announcements/fda-approves-first-chemoimmunotherapy-regimen-patients-relapsed-or-refractory-diffuse-large-b-cell>. Accessed July 2019.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. B-Cell Lymphomas, version 4.2019. Revised June 18, 2019. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed July 2019.

Sehn LH, Herrera AF, Matasar MJ, et al. Polatuzumab vedotin (Pola) plus bendamustine (B) with rituximab (R) or obinutuzumab (G) in relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL): Updated results of a phase (Ph) Ib/II study. *Blood* 2018;132(Suppl 1):1683. Available at: http://www.bloodjournal.org/content/132/Suppl_1/1683. Accessed July 2019.

Medical Director review 7/2019

Specialty Matched Consultant Advisory Panel review 4/2020

Policy Implementation/Update Information

- 7/30/19 New policy developed. Polivy is considered medically necessary for diffuse large B-cell lymphoma (DLBCL). Added HCPCS codes C9399, J3490, J3590, J9999, S0353, and S0354 to Billing/Coding section. References added. Medical Director review 7/2019. (krc)
- 12/31/19 Added HCPCS code J9309 to Billing/Coding section and deleted codes C9399, J3490, J3590, and J9999 effective 1/1/2020. (krc)
- 6/9/20 Specialty Matched Consultant Advisory Panel review 4/15/2020. No change to policy statements. (krc)

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.