Medical Policy

Utilization Management and Clinical Medical Policy

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Polatuzumab vedotin-piiq (Polivy)	**MP-RX-FP-73-23**	☒ **MMM MA** ☒ **MMM MultiHealth**	**11/30/2023**	**5/6/2026**
			Last Review Date: **5/6/2026**	**Frequently Revision:** **Annual**

Service Category:

- ☐ Anesthesia
- ☐ Surgery
- ☐ Radiology Procedures
- ☐ Pathology and Laboratory Procedures
- ☐ Medicine Services and Procedures
- ☐ Evaluation and Management Services
- ☐ DME/Prosthetics or Supplies
- ☒ Other: Part B Drugs

Service Description:

This document addresses the use of polatuzumab vedotin-piiq (Polivy®), a CD79b-directed antibody and microtubule inhibitor conjugate approved by the Food and Drug Administration (FDA) for the treatment of certain patients with diffuse large B-cell lymphoma (DLBCL), not otherwise specified (NOS) or high-grade B-cell lymphoma (HGBL), and patients with relapsed or refractory DLBCL, NOS, after at least two prior therapies.

Background Information:

Polivy is a monoclonal antibody-drug conjugate (ADC) that consists of a humanized igG1 antibody specific for CD79b and a small molecule, monomethyl auristatin E (MMAE), a microtubule- disrupting agent. The anticancer activity is due to the binding of the ADC to CD79b-expressing cells, cleavage of MMAE component, and killing dividing cells by inhibiting cell division and inducing apoptosis. The target CD79b is a surface protein found exclusively on B- cells and Polivy is indicated to treat diffuse large B-cell lymphoma (DLBCL).

The FDA approved indications for Polivy include in combination with bendamustine and a rituximab product for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma, not otherwise specified, after at least two prior therapies. Accelerated approval was based on positive results from a phase 2 trial comparing Polivy plus bendamustine and rituximab (BR) to BR alone.

Patients included in this study were not eligible for autologous hematopoietic stem cell transplantation (HSCT). Polivy is also FDA approved for previously untreated diffuse large B-cell lymphoma, not otherwise specified or high-grade B-cell lymphoma in combination with a rituximab product, cyclophosphamide, doxorubicin, and prednisone (R-CHP) for individuals who have an International Prognostic Index score of 2 or greater. NCCN provides additional recommendations with category 1 or 2A levels of evidence for the use of Polivy. These include its use as first-line treatment for previously untreated DLBCL and high-grade B-cell lymphomas in combination with R-CHP (category 1); treatment of histologic transformation to DLBCL; and use in post-transplant lymphoproliferative disorders (PTLD). NCCN also recommends Polivy for second-line or subsequent therapy in relapsed or refractory DLBCL, high-grade B-cell lymphomas, HIV-related lymphomas, and PTLD (category 2A), including use as a single agent; in combination with bendamustine and/or rituximab; in combination with gemcitabine and oxaliplatin (GemOx) with rituximab; in combination with mosunetuzumab-axgb; and as preapheresis holding or postpheresis bridging therapy for patients eligible for CAR T-cell therapy.

Definitions and Measures

Policy Name: Polatuzumab vedotin-piiq (Polivy)	Policy Number: MP-RX-FP-73-23	Scope: ☒ MMM MA ☒ MMM MultiHealth	Origination Date: 11/30/2023	Effective Date: 5/6/2026
			Last Review Date: 5/6/2026	Frequently Revision: Annual

- DLBCL: Diffuse large B-cell lymphoma
- Hematopoietic stem cells: Primitive cells capable of replication and formation into mature blood cells in order to repopulate the bone marrow.
- HGBL: High-grade B-cell lymphoma
- Line of Therapy:
  - First-line therapy: The first or primary treatment for the diagnosis, which may include surgery, chemotherapy, radiation therapy or a combination of these therapies.
  - Second-line therapy: Treatment given when initial treatment (first-line therapy) is not effective or there is disease progression.
  - Third-line therapy: Treatment given when both initial (first-line therapy) and subsequent treatment (second-line therapy) are not effective or there is disease progression.
- Monoclonal antibody: A protein developed in the laboratory that can locate and bind to specific substances in the body and on the surface of cancer cells.
- Non-Hodgkin Lymphoma (NHL): A group of malignant solid tumors or lymphoid tissues. Refractory Disease: Illness or disease that does not respond to treatment,
- NOS: Not otherwise specified
- Relapse or recurrence: After a period of improvement, during which time a disease (for example, cancer) could not be detected, the return of signs and symptoms of illness or disease. For cancer, it may come back to the same place as the original (primary) tumor or to another place in the body.

Approved Indications

Polatuzumab vedotin-piiq (Polivy®) is indicated by the FDA for the treatment of:

A. Adult patients who have previously untreated diffuse large B-cell lymphoma (DLBCL), not otherwise specified (NOS) or high-grade B-cell lymphoma (HGBL) and who have an International Prognostic Index score of 2 or greater: in combination with a rituximab product, cyclophosphamide, doxorubicin, and prednisone (R-CHP).
B. Adult patients with relapsed or refractory DLBCL, NOS, after at least two prior therapies: in combination with bendamustine and a rituximab product.

Other Uses

NCCN also recommends polatuzumab vedotin-piiq (Polivy®) in additional B-cell lymphoma settings beyond DLBCL, including HIV-related B-cell lymphomas and post-transplant lymphoproliferative disorders (PTLD). NCCN recommendations include use as a single agent and in combination with bendamustine and/or rituximab, as well as in other combination regimens (e.g., with gemcitabine/oxaliplatin [GemOx] plus rituximab or with mosunetuzumab-axgb) and, when clinically appropriate, as bridging therapy related to cellular therapy pathways. Polivy was studied as monotherapy early in its development (NCT01290549), and ongoing clinical trials continue to evaluate Polivy in various combination regimens. Further studies in larger populations are needed to define the optimal combination regimen and place in therapy in lymphoma subtypes beyond DLBCL.

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
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			Last Review Date: 5/6/2026	Frequently Revision: Annual

Medical Necessity Guidelines:

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Polivy® (Polatuzumab vedotin-piiq)

A. Criteria For Initial Approval (*Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met **all** approval criteria.)*

i. Individual has a diagnosis of relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified (including high-grade B-cell lymphomas), including histologic transformation of an indolent lymphoma to DLBCL/high-grade B-cell lymphoma, HIV-related B-cell lymphoma; or monomorphic post-transplant lymphoproliferative disorder (B-cell type) (Label, NCCN 2A); **AND**
   - A. Individual has received at least one prior lines of therapy (NCCN 2A); **AND**
   - B. Individual is using as a single agent or in combination with bendamustine and/or a rituximab (including rituximab biosimilars); **OR**
   - C. Individual is using in combination with gemcitabine and oxaliplatin (GemOx) with rituximab (NCCN 2A); **OR**
   - D. Individual is using in combination with mosunetuzumab-axgb (NCCN 2A).

OR

ii. Individual has a diagnosis of relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified (including high-grade B-cell lymphomas, including histologic transformation of an indolent lymphoma to DLBCL/high-grade B-cell lymphoma), HIV-related B-cell lymphoma; or monomorphic post-transplant lymphoproliferative disorder (B-cell type); **AND**
   - A. Individual is a candidate for CAR T-cell therapy; **AND**
   - B. Polatuzumab vedotin-piiq is being used as ONE of the following:
     1. In combination with rituximab as a preapheresis holding therapy option prior to leukapheresis (preapheresis refers to therapy administered before collection of T-cells for CAR T-cell manufacturing) (NCCN 2A); **OR**
     2. As a single agent or in combination with bendamustine and/or a rituximab product (including rituximab biosimilars) as a postapheresis bridging option until CAR T-cell product is available (NCCN 2A). When bendamustine is used, administration should be delayed until after leukapheresis when clinically appropriate.

OR

Policy Name: Polatuzumab vedotin-piiq (Polivy)	Policy Number: MP-RX-FP-73-23	Scope: ☒ MMM MA ☒ MMM MultiHealth	Origination Date: 11/30/2023	Effective Date: 5/6/2026
			Last Review Date: 5/6/2026	Frequently Revision: Annual

iii. Individual has a diagnosis of diffuse large B-cell lymphoma (DLBCL), not otherwise specified (including high-grade B-cell lymphomas) or monomorphic or systemic polymorphic post-transplant lymphoproliferative disorder (B-cell type); **AND**

A. Individual is using in combination with rituximab (or a rituximab biosimilar), cyclophosphamide, doxorubicin, and prednisone (Pola-R-CHP) (NCCN 1); **AND**

B. Individual has International Prognostic Index (IPI) ≥2; **OR**

C. Individual has stage I–II disease (excluding stage II with extensive mesenteric disease) with stage-modified International Prognostic Index (smIPI) >1.

OR

iv. Individual has a diagnosis of diffuse large B-cell lymphoma (DLBCL), not otherwise specified (including high-grade B-cell lymphomas); **AND**

A. Individual is Non-Candidate for CAR T-Cell Therapy; **AND**

B. Individual is using as a single agent or in combination with bendamustine and/or a rituximab (including rituximab biosimilars); **OR**

C. Individual is using in combination with gemcitabine and oxaliplatin (GemOx) with rituximab (NCCN 2A); **OR**

D. Individual is using in combination with mosunetuzumab-axgb (NCCN 2A).

OR

v. Individual has a diagnosis of Mantle Cell Lymphoma; **AND**

A. Individual has relapsed, refractory, or progressive disease (relapse #2 or greater); **AND**

B. Individual has received prior second-line therapy including one of the following (NCCN 2A):

1. A non-covalent Bruton tyrosine kinase inhibitor (ncBTKi); **OR**
2. CAR T-cell therapy; **OR**
3. Other continuous or fixed-duration treatment regimens;

AND

C. Individual meets one of the following clinical scenarios (NCCN 2A):

1. No response or progressive disease following second-line therapy; **OR**
2. Partial response, no response, or progressive disease following CAR T-cell therapy or fixed-duration regimens;

AND

D. Polatuzumab vedotin-piiq is being used in combination with mosunetuzumab-axgb (NCCN 2A).

B. Criteria For Continuation of Therapy

i. MMM considers continuation of Polatuzumab vedotin-piiq (Polivy®) therapy medically necessary in members requesting reauthorization for an indication listed in Section A above (Criteria for Initial Approval) when there is no evidence of an unacceptable toxicity or disease progression while on the current regimen, and the recommended duration of therapy has not been exceeded. The following information should be submitted for reauthorization:

A. A current oncology note documenting the patient's response to treatment showing no progression of disease

Policy Name: Polatuzumab vedotin-piiq (Polivy)	Policy Number: MP-RX-FP-73-23	Scope: ☒ MMM MA ☒ MMM MultiHealth	Origination Date: 11/30/2023	Effective Date: 5/6/2026
			Last Review Date: 5/6/2026	Frequently Revision: Annual

B. Current imaging studies and other objective measures showing no progression of disease when compared with previous results

ii. Consistent with the product FDA approved information, MMM considers continuation of Polatuzumab vedotin-piiq (Polivy) therapy medically necessary for up to 6 months (6 cycles total).

C. Authorization Duration

i. Initial Approval Duration: 6 Cycles (every 21 days; approximately 5 months)

D. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

i. Requests for Polatuzumab vedotin-piiq (Polivy) may not be approved when the above criteria (Section A: Criteria for Initial Approval) are not met and for all other indications.

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Polatuzumab vedotin-piiq (Polivy)	MP-RX-FP-73-23	☒ MMM MA ☒ MMM MultiHealth	11/30/2023	5/6/2026
			Last Review Date: 5/6/2026	Frequently Revision: Annual

Limits or Restrictions:

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

i. N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Drug	Co-administered Medications	Recommended Dosing Schedule	Recommended Treatment Duration
Patients with Previously Untreated DLBCL, NOS or HGBL	A rituximab product, cyclophosphamide, doxorubicin, and prednisone	1.8 mg/kg as an intravenous infusion every 21 days	6 Cycles
Patients with Relapsed or Refractory DLBCL, NOS	bendamustine and a rituximab product	1.8 mg/kg as an intravenous infusion every 21 days	6 Cycles
Exceptions			
None			

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
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			Last Review Date: 5/6/2026	Frequently Revision: Annual

Codes Information:

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

ICD-10 Diagnostic Codes:

Codes	Description
C82.00-C82.99	Follicular Lymphoma
C83.10–C83.19	Mantle Cell Lymphoma
C83.30-C83.39	Diffuse large B-cell lymphoma
C83.80–C83.89, C85.80–C85.89	Other specified types of non-Hodgkin lymphoma
C85.10-C85.29	Unspecified B-cell lymphoma/ Mediastinal (thymic) large B-cell lymphoma
B20	Human Immunodeficiency Virus (HIV) disease (when specified as HIV-related B-cell lymphoma)
D47.Z1	Post-transplant lymphoproliferative disorder (PTLD)

HCPCS Codes:

Codes	Description
J9309	Injection, polatuzumab vedotin-piiq, 1 mg [Polivy]

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Reference Information:

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4. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2024; Updated periodically.
5. Morschhauser F, Flinn IW, Advani R, et al. Polatuzumab vedotin or pinatuzumab vedotin plus rituximab in patients with relapsed or refractory non-Hodgkin lymphoma: final results from a phase 2 randomised study (ROMULUS). Lancet Haematol. 2019 May;6(5):e254-e265. doi: 10.1016/S2352-3026(19)30026-2. Epub 2019 Mar 29.
6. Sehn LH, Herrera AF, Flowers CR, et al. Polatuzumab Vedotin in Relapsed or Refractory Diffuse Lage B-Cell Lymphoma. J Clin Oncol 2020; 38:155-165.
7. NCCN Clinical Practice Guidelines in Oncology™. © 2021 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed March 26, 2024.
    a. B-cell Lymphomas. V1.2026. Revised February 18, 2026.
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Polatuzumab vedotin-piiq (Polivy)	MP-RX-FP-73-23	☒ MMM MA ☒ MMM MultiHealth	11/30/2023	5/6/2026
			Last Review Date: 5/6/2026	Frequently Revision: Annual

Policy History:

Type of Review	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Annual Review	Updated Background section to reflect current NCCN recommendations and expanded clinical uses, including additional combination regimens and CAR T-cell therapy pathways. Added clarification to include histologic transformation of indolent lymphoma to diffuse large B-cell lymphoma (DLBCL) or high-grade B-cell lymphoma within the relapsed/refractory DLBCL criteria, consistent with NCCN 2A recommendations.. Revised NCCN category for Pola-R-CHP regimen from NCCN 2B to NCCN 1 to align with current NCCN B-Cell Lymphomas guidelines; Revised CAR T-cell therapy pathway language to clarify use of polatuzumab vedotin-piiq as preapheresis holding therapy (therapy administered prior to leukapheresis for CAR T-cell manufacturing) and as postpheresis bridging therapy, including guidance to delay bendamustine administration until after leukapheresis when clinically appropriate, consistent with NCCN 2A recommendations for relapsed/refractory diffuse large B-cell lymphoma and high-grade B-cell lymphomas; Revised Pola-R-CHP criteria to include monomorphic and systemic polymorphic post-transplant lymphoproliferative disorder (B-cell type) within the eligible diagnoses, consistent with NCCN 2A recommendations for first- and second-line therapy in post-transplant lymphoproliferative disorders; Added NCCN 2A recommendation for Mantle Cell Lymphoma for relapsed/refractory disease (relapse #2 or greater) in combination with mosunetuzumab-axgb following prior second-line therapy including ncBTKi, CAR T-cell therapy, or other continuous/fixed-duration regimens. Updated Background section to align with current NCCN recommendations. Revised language to clarify supported B-cell lymphoma subtypes and expanded combination regimens, including GemOx plus rituximab, mosunetuzumab-axgb, and cellular therapy bridging strategies. Removed reference to follicular lymphoma as a standalone indication to ensure consistency with coverage criteria. No changes to coverage requirements.Coding Reviewed: Added C83.80–C83.89 and C85.80–C85.89 to capture additional specified B-cell lymphoma subtypes, including certain HIV-related and rare variants. No changes to billing code J9309.	5/1/2026	5/6/2026
Annual Review	Added: Non-Candidates for CAR T-Cell Therapy, Polatuzumab vedotin-piiq + mosunetuzumab-axgb (category 2A) and No Intention to Proceed to Transplant, Polatuzumab vedotin-piiq + mosunetuzumab-axgb (category 2A) per NCCN guidelines (B-Cell Lymphomas Version 2.2025)	7/17/2025	8/8/2025

Policy Name: Polatuzumab vedotin-piiq (Polivy)	Policy Number: MP-RX-FP-73-23	Scope: ☒ MMM MA ☒ MMM MultiHealth	Origination Date: 11/30/2023	Effective Date: 5/6/2026
			Last Review Date: 5/6/2026	Frequently Revision: Annual

Annual Review	Remove duplicative criteria and clarify criteria for Pola-R-CHP regimen. Coding Reviewed: No Changes; Add additional types of B-cell lymphoma per NCCN; add option for single agent use or combination with rituximab or bendamustine only per NCCN. Coding Reviewed: Added ICD-10-CM B20, D47.Z1.	3/14/2025	4/2/2025
Annual Review	Update statement for criteria for initial approval: Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met all approval criteria.	3/25/2024	5/9/2024
Policy Inception	Elevance Health's Medical Policy adoption. 08/18/2023	N/A	11/30/2023