POLICY NUMBER UM_1362	**SUBJECT** Polivy™ (polatuzumab vedotin)		**DEPT/PROGRAM** UM Dept	**PAGE 1 OF 4**
DATE REVIEWED 07/09/19	**APPROVAL DATE** July 10, 2019	**EFFECTIVE DATE** July 10, 2019	**REVISION DATES** (latest version listed last)	
PRIMARY BUSINESS OWNER: **APPROVED BY:** Dr. Andrew Hertler		**COMMITTEE/BOARD APPROVAL** Utilization Management Committee		
URAC STANDARDS HUM 1		**ADDITIONAL AREAS OF IMPACT**		
CMS REQUIREMENTS	**STATE/FEDERAL REQUIREMENTS**		**APPLICABLE LINES OF BUSINESS** Oncology	

I. PURPOSE

To define and describe the accepted indications for Polivy (polatuzumab vedotin) usage in the treatment of cancer.

II. DEFINITIONS

Polivy (polatuzumab vedotin): is a CD79b-directed antibody-drug conjugate (ADC) consisting of 3 components including the humanized IgG1 monoclonal antibody specific for human CD79b; the small molecule anti-mitotic agent monomethyl auristatin E (MMAE); and a protease-cleavable linker, maleimidocaproyl-valine-citrulline-p-aminobenzyloxycarbonyl (mc-vc-PAB), that covalently attaches MMAE to the polatuzumab antibody. The anticancer activity of polatuzumab vedotin is due to the binding of the ADC to CD79b expressing B-cells followed by the internalization of the ADC-CD79b complex, and the release of MMAE via selective proteolytic cleavage. MMAE inhibits cell division and induces apoptosis in rapidly dividing cells by binding to microtubules.

Polivy (polatuzumab vedotin) is FDA approved in combination with bendamustine and a rituximab product for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma following at least 2 prior therapies.

Polivy (polatuzumab vedotin) is available in 140 mg as a lyophilized powder in a single-dose vial.

III. POLICY

New Century Health is responsible for processing all medication requests from network ordering providers. Medications not authorized by New Century Health may be deemed as not approvable and therefore not reimbursable. Treatment request outside the approved FDA manufacturer labeling or CMS approved compendia must follow CMS Medicare Benefit Policy Manual Chapter 15. If references are not produced, delays may occur to the processing of such request.

Inclusion Criteria: Polivy (polatuzumab vedotin) may be considered medically necessary when any of the following selection criteria are met:

1. **Diffuse Large B-Cell Lymphoma (DLBCL)**
    - **a.** The member has relapsed/refractory DLBCL and Polivy (polatuzumab vedotin) is being used in combination with bendamustine and rituximab **AND**
    - **b.** Member is not eligible for stem cell transplant or has relapsed after transplant **AND**
    - c. Has failed at least 2 prior therapies, including ALL of the following:
        - **i.** R-CHOP/R-CEPP/R-CDOP/R-CEOP/R-EPOCH/R-GCVP **AND**

ii. R-ESHAP/RDHAP **OR**

iii. Gemcitabine containing regimen (i.e. GDP)

Exclusion Criteria: Polivy (polatuzumab vedotin) is not considered medically necessary when any of the following selection criteria are met:

1. Polivy (polatuzumab vedotin) is being used after disease progression with the same regimen or prior bendamustine unless response was greater than 1 year.
2. Dosing exceeds single dose limit of Polivy (polatuzumab vedotin) 1.8 mg/kg.
3. Treatment exceeds the maximum months duration limit of 6 cycles.
4. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature may be deemed as not approvable and therefore not reimbursable.

IV. PROCEDURE

Requests for Polivy (polatuzumab vedotin) shall be reviewed for appropriateness per FDA approved product labeling, the National Comprehensive Cancer Network (NCCN) and American Society of Clinical Oncology (ASCO) clinical guidelines, or CMS approved compendia.

1. **Dosage and Administration:** 1.8 mg/kg as an intravenous infusion over 90 minutes every 21 days for 6 cycles in combination with bendamustine and a rituximab product. Subsequent infusions may be administered over 30 minutes if the previous infusion is tolerated. Premedicate with an antihistamine and antipyretic before Polivy. Administer Pneumocystis jiroveci pneumonia and herpes prophylaxis during polatuzumab vedotin therapy. Consider prophylactic granulocyte colony-stimulating factor use.
2. **Dosage Adjustments:**
    a. Hepatic impairment (mild; bilirubin greater than ULN to 1.5 times ULN or AST greater than ULN): No adjustment needed to the starting dose.
    b. Hepatic impairment (moderate or severe; bilirubin greater than 1.5 times ULN): Avoid use.
    c. Infusion Reaction (Grade 1 to 3): Interrupt infusion and give supportive treatment; permanently discontinue for the first instance of Grade 3 wheezing, bronchospasm, or generalized urticaria, for recurrent Grade 2 wheezing or urticaria, or for recurrence of any Grade 3 symptoms; upon complete resolution of symptoms, infusion may be resumed at 50% of the rate achieved prior to interruption; in the absence of infusion related symptoms, the rate of infusion may be escalated in increments of 50 mg/hr every 30 minutes; for the next cycle, infuse over 90 minutes, and if no infusion-related reaction occurs, subsequent infusions may be administered over 30 minutes.
    d. Infusion Reaction (Grade 4): Immediately stop infusion immediately, give supportive treatment and permanently discontinue therapy.
    e. Neutropenia (Grade 3 or 4, on day 1 of any cycle): Hold until absolute neutrophil count (ANC) recovers to greater than 1000/mcL; if ANC recovers to greater than 1000/mcL on or before day 7, resume all treatment without any additional dose reductions; consider granulocyte colony stimulating factor prophylaxis for subsequent cycles; if ANC recovers to greater than 1000/mcL after day 7, restart all treatment and consider granulocyte colony stimulating factor prophylaxis for subsequent cycles; if prophylaxis was given, consider dose reduction of bendamustine; if dose reduction of bendamustine has already occurred,

consider dose reduction of polatuzumab vedotin-piiq to 1.4 mg/kg; if primary cause of neutropenia is due to lymphoma, dose delay or reduction may not be needed.

f. Peripheral neuropathy (Grade 2 or 3): Hold dosing until improvement to Grade 1 or lower; if recovered to Grade 1 or lower on or before day 14, restart with the next cycle at a permanently reduced dose of 1.4 mg/kg; discontinue therapy if a prior dose reduction to 1.4 mg/kg has occurred or if not recovered to Grade 1 or lower on or before day 14.

g. Peripheral neuropathy (Grade 4): Discontinue therapy.

h. Thrombocytopenia (Grade 3 or 4, on day 1 of any cycle): Hold until platelets recover to greater than 75,000/mcL; if platelets recover to greater than 75,000/mcL on or before day 7, resume all treatment without any additional dose reductions; if platelets recover to greater than 75,000/mcL after day 7, restart all treatment, with dose reduction of bendamustine; if dose reduction of bendamustine has already occurred, consider dose reduction of polatuzumab vedotin-piiq to 1.4 mg/kg; if primary cause of neutropenia is due to lymphoma, dose delay or reduction may not be needed.

3. **Monitoring**

a. Resolution or improvement of disease-related signs (PET-CT with bone marrow confirmation, recovery of blood counts) may indicate efficacy.

b. Pregnancy status: Prior to initiation of therapy in females of reproductive potential.

c. Tumor lysis syndrome in patients with high tumor burden or rapidly proliferative tumors

d. Complete blood counts, including differential

e. Liver enzymes and bilirubin

f. Infusion-related reactions: During infusion (90 or 30 minutes) and for a time period following completion of infusion that is at least equivalent to the duration of infusion (90 or 30 additional minutes).

g. Symptoms of peripheral neuropathy, including hypoesthesia, hyperesthesia, paresthesia, dysesthesia, neuropathic pain, burning sensation, weakness, or gait disturbance.

h. Signs of developing bacterial, fungal, and viral infections.

i. New or worsening neurological, cognitive, or behavioral changes.

V. APPROVAL AUTHORITY

1. Review – UM Department
2. Final Approval – UM Committee

VI. ATTACHMENTS

None

VII. REFERENCES

1. Polivy PI prescribing information. Genentech, Inc. South San Francisco, 2019.
2. Clinical Pharmacology Elsevier Gold Standard. 2019.
3. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, Co. 2019.

4. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium. 2019.
5. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD. 2019.