Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Enfortumab vedotin-ejfv (Padcev®)	MP-RX-FP-70-23	☒ MMM MA ☒ MMM Multihealth

Service Category

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

Service Description

This document addresses the use of Enfortumab vedotin-ejfv (Padcev®), a Nectin-4-directed antibody and microtubule inhibitor conjugate approved by the Food and Drug Administration (FDA) for the treatment of certain patients with locally advanced or metastatic urothelial cancer.

Background Information

The FDA approved indications for Padcev are for the treatment of adults with locally advanced or metastatic urothelial cancer who have previously received a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor, and a platinum containing chemotherapy or in those who are ineligible for cisplatin-containing chemotherapy and have previously received one or more prior lines of therapy in the neoadjuvant/adjuvant, locally advanced, or metastatic setting. Padcev was approved under the FDA accelerated program based on tumor response rate. Continued approval is contingent upon confirmatory trials.

The National Comprehensive Cancer Network recommends Padcev as subsequent-line systemic therapy for locally advanced or metastatic disease (2A category) based on the same pivotal trial that helped to gain FDA approval.

Padcev has a black box warning for severe and fatal cutaneous adverse reactions, including Stevens-Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN).

Definitions and Measures

- Adjuvant therapy: Treatment given after the primary treatment to increase the chances of a cure; may include chemotherapy, radiation, hormone or biological therapy.
- Chemotherapy: Medical treatment of a disease, particularly cancer, with drugs or other chemicals. Disease Progression: Cancer that continues to grow or spread.
- ECOG or Eastern Cooperative Oncology Group Performance Status: A scale and criteria used by doctors and researchers to assess how an individual's disease is progressing, assess how the disease affects the daily living abilities of the individual, and determine appropriate treatment and prognosis. This scale may also be referred to as the WHO (World Health Organization) or Zubrod score which is based on the following scale:
    - 0 = Fully active, able to carry on all pre-disease performance without restriction
    - 1 = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, for example, light housework, office work

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- 2 = Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours
- 3 = Capable of only limited self-care, confined to bed or chair more than 50% of waking hours
- 4 = Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair
- 5 = Dead

- Immune checkpoint inhibitor: A type of drug that blocks certain proteins made by some types of immune system cells, such as T cells, and some cancer cells. When these proteins are blocked, the "brakes" on the immune system are released and T cells are able to kill cancer cells better. Examples of checkpoint proteins found on T cells or cancer cells include programmed death (PD)-1, PD-ligand 1 (PD-L1), and cytotoxic T-lymphocyte–associated antigen (CTLA)-4/B7-1/B7-2.
- Locally advanced cancer: Cancer that has spread only to nearby tissues or lymph nodes.
- Metastasis: The spread of cancer from one part of the body to another; a metastatic tumor contains cells that are like those in the original (primary) tumor and have spread.
- 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.
- Neoadjuvant therapy: Treatment given as a first step to shrink a tumor before the main treatment, which is usually surgery, is given. Examples of neoadjuvant therapy include chemotherapy, radiation therapy, and hormone therapy. It is a type of induction therapy.
- Programmed death (PD)-1 proteins: PD-1 proteins are found on T-cells and attach to PD ligands (PD-L1) found on normal (and cancer) cells (see immune checkpoint inhibitor above). Normally, this process keeps T-cells from attacking other cells in the body. However, this can also prevent T-cells from attacking cancer cells in the body. Examples of FDA approved anti-PD-1 agents include Keytruda (pembrolizumab), Opdivo (nivolumab), and Libtayo (cemiplimab).
- Programmed death ligand (PD-L)-1: The ligands found on normal (and cancer) cells to which the PD-1 proteins attach (see immune checkpoint inhibitor above). Cancer cells can have large amounts of PD-L1 on their surface, which helps them to avoid immune attacks. Examples of FDA approved anti-PD-L1 agents include Bavencio (avelumab), Tecentriq (atezolizumab), and Imfinzi (durvalumab).
- Urothelial carcinoma: A type of bladder cancer which occurs in the urinary tract system.

Approved Indications

PADCEV FDA approved indications include;

- As a single agent for the treatment of adult patients with locally advanced or metastatic urothelial cancer who:
  - Have previously received a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor and platinum- containing chemotherapy, or
  - Are ineligible for cisplatin-containing chemotherapy and have previously received one or more prior lines of therapy.

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- In combination with pembrolizumab for the treatment of adult patients with locally advanced or metastatic urothelial cancer who are not eligible for cisplatin-containing chemotherapy. The approval for this indication has been granted through accelerated approval, which relies on factors such as tumor response rate and the duration of the response. Ongoing approval for this particular use may depend on the confirmation and detailed description of clinical benefits as determined in subsequent trials.

Other Uses

None

Applicable Codes

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.

HCPCS	Description
J9177	Injection, enfortumab vedotin-ejfv, 0.25 mg (Padcev)

ICD-10	Description
C67.1-C67.9	Malignant neoplasm of bladder
C79.11-C79.19	Secondary malignant neoplasm of other urinary organs
Z92.21	Personal history of antineoplastic chemotherapy
Z92.22	Personal history of monoclonal drug therapy

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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.

Enfortumab vedotin-ejfv (Padcev®)

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 locally advanced or metastatic urothelial cancer; **AND**
ii. Individual is using as a single agent for subsequent therapy after progression in one of the following ways:
    A. Anti-PD-1 or anti-PD-L1 agent and platinum-containing chemotherapy; OR
    B. Individual is ineligible for cisplatin-containing chemotherapy and have previously received one or more prior lines of therapy; **AND**
iii. Individual as a current ECOG performance status of 0-2.

B. Criteria For Continuation of Therapy

i. MMM considers continuation of Enfortumab vedotin-ejfv (Padcev®) 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. 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.
    B. Current imaging studies and other objective measures, as appropriate, showing no progression of disease when compared with previous results.

C. Authorization Duration

i. Initial Approval Duration: Up to 6 months
ii. Reauthorization Approval Duration: Up to 6 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. Individuals with moderate or severe hepatic impairment (Child-Pugh B or C); **OR**
ii. When the above criteria (Section A: Criteria for Initial Approval) are not met and for all other indications.

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Limits or Restrictions

A. 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	Recommended Dosing Regimen	Recommended Treatment Duration
Enfortumab vedotin-ejfv (Padcev®) as a single agent	1.25 mg/kg (up to a **maximum of 125 mg for patients ≥100 kg**) i.v. administered on Days 1, 8 and 15 of a 28-day cycle	Until disease progression or unacceptable toxicity.
Enfortumab vedotin-ejfv (Padcev®) in combination with pembrolizumab	1.25 mg/kg (up to a **maximum of 125 mg for patients ≥100 kg**) i.v. administered on Days 1 and 8 of a 21-day cycle	Until disease progression or unacceptable toxicity.
Exceptions		
None		

Reference Information

1. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2023. URL: http://www.clinicalpharmacology.com. Updated periodically.
2. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: January 12, 2023.
3. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
4. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2023; Updated periodically.
5. NCCN Clinical Practice Guidelines in Oncology™. © 2023 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on January 12, 2023.
    a. Bladder Cancer. V3.2022. Revised December 21, 2022.
6. Powles T, Rosenberg JE, Sonpavde GP, et al. Enfortumab vedotin in previously treated advanced urothelial carcinoma. N Engl J Med 2021; 384:1125-1135
7. Yu EY, Petrylak DP, O'Donnell PH, et al. Enfortumab vedotin after PD-1 or PD-L1 inhibitors in cisplatin-ineligible patients with advanced urothelial carcinoma (EV-201): a multicenter, single-arm, phase 2 trial. Lancet Oncol 2021; 22:872-882.

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Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

Policy History

Revision Type	Summary of Changes	P&T Approval Date	MPCC Approval Date
Policy Adoption	Elevance Health's Medical Policy adoption.	N/A	11/30/2023
Select 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

Revised: 11/11/2023