STATE OF IOWA DEPARTMENT OF
Health AND Human
SERVICES

Padcev (enfortumab vedotin-efjv)
PAM-041

Iowa Medicaid Program:	Prior Authorization	**Effective Date:**	01/21/2021
Revision Number:	3	**Last Rev Date:**	10/20/2023
Reviewed By:	Medicaid Medical Director	**Next Rev Date:**	10/18/2024
Approved By:	Medicaid Clinical Advisory Committee	**Approved Date:**	10/15/2021

Overview

Medication: [1]	enfortumab vedotin-efjv
Brand Name:	Padcev®
Pharmacologic Category:	Nectin-4 directed antibody-drug conjugate (ADC)
FDA-Approved Indication(s):	1. Indicated for the treatment of adult patients with locally advanced or metastatic urothelial cancer (mUC) 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. 2. Indicated, in combination with pembrolizumab, for the treatment of adult patients who are not eligible for cisplatin-containing therapy. ➢ Accelerated Approval: This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials. ➢ **NEW Indication:** FDA-approved April 3, 2023
How Supplied:	Single-dose vial, containing 20 mg or 30 mg of enfortumab vedotin-efjv.
Dosage and Administration:	• Intravenous (IV) infusion; as a **single agent**: ○ 1.25 mg/kg (up to a maximum of 125 mg for patients ≥100 kg) on Days 1, 8 and 15 of a 28-day cycle until disease progression or unacceptable toxicity. • IV infusion; **in combination with pembrolizumab**: ○ 1.25 mg/kg (up to a maximum of 125 mg for patients ≥100 kg) on Days 1 and 8 of a 21-day cycle until disease progression or unacceptable toxicity (refer to pembrolizumab's prescribing information for recommended dosing).
Benefit Category:	Medical

BOXED WARNING: Serious Skin Reactions

- Padcev® can cause severe and fatal cutaneous adverse reactions including Stevens-Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN), which occurred predominantly during the first cycle of treatment, but may occur later. Closely monitor patients for skin reactions.
- Immediately withhold Padcev® and consider referral for specialized care for suspected SJS or TEN or severe skin reactions. Permanently discontinue with confirmed SJS or TEN; or Grade 4 or recurrent Grade 3 skin reactions.

Descriptive Narrative

Bladder cancer is the most common malignancy involving the urinary system. Urothelial (transitional cell) carcinoma is the predominant histologic type in the United States.[2] In 2023, the United States is expected to see 82,290 new cases of bladder cancer with an estimated 16,710 deaths.[3]

About 90 percent of patients with bladder cancer are over the age of 55 years, with an average age of 73 years at the time of diagnosis. Overall, the chance that men will develop this cancer in their lifetime is about 1 in 28 men. For women, the chance is about 1 in 91. Urothelial cancer is strongly associated with smoking and increased dietary fat. Because these are also factors that predispose to other medical conditions, including cardiovascular, cerebrovascular, and pulmonary disease, patients with urothelial cancer often have significant comorbidities.[4]

Guidelines

As new and emerging therapies are rapidly coming to market, oncology treatment recommendations and guidelines are constantly changing. To keep up with these changes, the National Comprehensive Cancer Network (NCCN) publishes guidelines which are developed and updated by 60 individual panels, comprising over 1,660 clinicians and oncology researchers from the 31 NCCN Member Institutions.[5]

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

The information referenced at the time of this policy writing/revision is from:

- NCCN Guidelines for Bladder Cancer (Version 3.2023 – May 25, 2023)[6]

NCCN Guidelines® Recommendation(s) for enfortumab vedotin-efjv (Padcev®) in bladder cancer
(1) First-line systemic therapy for locally advanced or metastatic disease (Stage IV) A. Cisplatin ineligible i. Pembrolizumab and enfortumab vedotin-ejfv: Category 2A, preferred regimen (2) Second-line systemic therapy for locally advanced or metastatic disease (Stage IV) A. Post-platinum or other chemotherapy [a, b] i. Pembrolizumab and enfortumab vedotin-ejfv: Category 2B, other recommended regimen ii. Enfortumab vedotin-ejfv: Category 2A, alternative preferred regimen [c] B. Post-checkpoint inhibitor [b] i. Enfortumab vedotin-ejfv: Category 2A, preferred regimen for cisplatin ineligible, chemotherapy naïve (3) Subsequent-line systemic therapy for locally advanced or metastatic disease (Stage IV) [d, e] A. Enfortumab vedotin-ejfv: Category 1, preferred regimen
[a] If progression-free survival >12 months after platinum (e.g., cisplatin or carboplatin), consider re-treatment with platinum if the patient is still platinum eligible. [b] Participation in clinical trials of new agents is recommended. [c] Indicated for cisplatin ineligible patients who have received one or more prior lines of therapy. [d] Patient should have already received platinum and a checkpoint inhibitor, if eligible. [e] Appropriate for patients who received a first-line platinum-containing chemotherapy followed by avelumab maintenance therapy.

NCCN Categories of Evidence and Consensus (all recommendations are category 2A unless otherwise indicated)	
Category 1	Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A	Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B	Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3	Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

NCCN Categories of Preference (all recommendations are considered appropriate)	
Preferred intervention	Interventions that are based on superior efficacy, safety, and evidence; and, when appropriate, affordability.
Other recommended intervention	Other interventions that may be somewhat less efficacious, more toxic, or based on less mature data; or significantly less affordable for similar outcomes.
Useful in certain circumstances	Other interventions that may be used for select patient populations (defined with recommendation).

Eastern Cooperative Oncology Group (ECOG) Performance Status[7]

Developed by the Eastern Cooperative Oncology Group (ECOG), now part of the ECOG-ACRIN Cancer Research Group, and published in 1982, the ECOG Performance Status Scale describes a patient's level of functioning in terms of their ability to care for themself, daily activity, and physical ability (walking, working, etc.). It is used by doctors and researchers to assess how a patient's disease is progressing, how the disease affects the daily living abilities of the patient and determine appropriate treatment and prognosis.

GRADE	ECOG PERFORMANCE STATUS [Synonyms: WHO/Zubrod score]
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, e.g., light house work, office work.
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.

Criteria

Examples of Therapies Mentioned in Criteria *(for reference only, not a complete list)*		
Platinum-containing regimens	Programmed death receptor-1 (PD-1) inhibitor	Programmed death-ligand 1 (PD-L1) inhibitor
• DDMVAC (dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin) • Gemcitabine and cisplatin • CMV (cisplatin, methotrexate, and vinblastine)	• cemiplimab (Libtayo)* • nivolumab (Opdivo)# • pembrolizumab (Keytruda)*	• atezolizumab (Tecentriq)* • avelumab (Bavencio)* • durvalumab (Imfinzi)*

* Iowa Medicaid program: prior authorization # Iowa Medicaid program: claims prepay

Prior authorization is required.

Padcev® is considered medically necessary when **ALL** of the following are met:

1. Diagnosis of locally advanced or metastatic urothelial cancer (mUC); **AND**
2. Member is 18 years of age or older; **AND**
3. Member meets one of the following (a, b, or c):
    a. Has received previous treatment with a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor and platinum-containing chemotherapy; **OR**
    b. Is ineligible for cisplatin-containing chemotherapy and has previously received one or more prior lines or therapy; **OR**
    c. Is ineligible for cisplatin-containing chemotherapy and Padcev® is prescribed in combination with pembrolizumab (Keytruda®); **AND**
4. Member has a current Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 2; **AND**
5. Prescribed by, or in consultation with, a hematologist or oncologist; **AND**
6. Request meets one of the following (a, b, or c):
    a. Padcev® is prescribed as a single agent at a dosage of 1.25 mg/kg (up to a maximum of 125 mg for patients ≥ 100 kg) on days 1, 8, and 15 of a 28-day cycle; OR
    b. Padcev® is prescribed in combination with Keytruda® at a dosage of 1.25 mg/kg (up to a maximum of 125 mg for patients ≥ 100 kg) on days 1 and 8 of a 21-day cycle; OR
    c. Regimen is supported by clinical practice guidelines. Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Padcev® is considered medically necessary for continuation of therapy when **ALL** of the following are met:

1. Member is currently receiving medication through the Iowa Medicaid benefit or has previously met initial approval criteria; **AND**
2. Documentation of positive clinical response to therapy, as demonstrated by tumor response or lack of disease progression, and an acceptable toxicity profile; **AND**
3. Prescribed by, or in consultation with, a hematologist or oncologist; **AND**
4. Request meets one of the following (a, b, or c):
    a. Padcev® is prescribed as a single agent at a dosage of 1.25 mg/kg (up to a maximum of 125 mg for patients ≥ 100 kg) on days 1, 8, and 15 of a 28-day cycle; OR
    b. Padcev® is prescribed in combination with Keytruda® at a dosage of 1.25 mg/kg (up to a maximum of 125 mg for patients ≥ 100 kg) on days 1 and 8 of a 21-day cycle; OR
    c. Regimen is supported by clinical practice guidelines. Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Approval Duration and Quantity Limits

	Initial Authorization	Subsequent Authorization(s)
Approval Duration	6 months	12 months
Quantity Limits	• Single agent (28-day treatment cycle) ○ 1.25 mg/kg/day (maximum of 125 mg per day for patients ≥ 100 kg) ○ Maximum of 3 days per treatment cycle (days 1, 8, and 15 of a 28-day cycle)	
	• In combination with Keytruda (21-day treatment cycle) ○ 1.25 mg/kg/day (maximum of 125 mg per day for patients ≥ 100 kg) ○ Maximum of 2 days per treatment cycle (days 1 and 8 of a 21-day cycle)	

Coding and Product Information

The following list(s) of codes and product information are provided for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment, nor does the exclusion of a code imply that its association to the HCPCS code is inappropriate.

HCPCS	Description
J9177	Injection, enfortumab vedotin-ejfv, 0.25 mg

ICD-10	Description
C64.1-C64.9	Malignant neoplasm of kidney
C65.1-C65.9	Malignant neoplasm of renal pelvis
C66.1-C66.9	Malignant neoplasm of right ureter
C67.0-C67.9	Malignant neoplasm of bladder
C68.0-C68.9	Malignant neoplasm of urethra, paraurethral glands, overlapping sites of urinary organs, and urinary system not otherwise specified (NOS)

NDC	Labeler	Dosage	Pkg Size	Pkg Qty	Units/Pkg
51144-0020-01	Seagen, Inc.	0.25 mg	1	EA	80
51144-0030-01	Seagen, Inc.	0.25 mg	1	EA	120

Compliance

1. Should conflict exist between this policy and applicable statute, the applicable statute shall supersede.
2. Federal and State law, as well as contract language, including definitions and specific contract provisions or exclusions, take precedence over medical policy and must be considered first in determining eligibility for coverage.
3. Medical technology is constantly evolving, and Iowa Medicaid reserves the right to review and update medical policy on an annual or as-needed basis.

Medical necessity guidelines have been developed for determining coverage for member benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. Medical necessity guidelines are developed for selected physician administered medications found to be safe and proven to be effective in a limited, defined

population or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. Criteria are revised and updated annually, or more frequently if new evidence becomes available that suggests needed revisions.

References

[1] Padcev prescribing information (04/2023). Seagen Inc.: Bothell, WA Available online at www.padcev.com/hcp. Accessed August 24, 2023.

[2] Bellmunt J. Treatment of metastatic urothelial cancer of the bladder and urinary tract. Shah SP, ed. UptoDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed October 13, 2023.

[3] SEER Cancer Stat Facts: Bladder Cancer. National Cancer Institute. Bethesda, MD. Available online at seer.cancer.gov. Accessed October 8, 2023.

[4] American Cancer Society. Key Statistics for Bladder Cancer. Available online at www.cancer.org/cancer/bladder-cancer/about/key-statistics.html. Accessed October 8, 2023.

[5] National Comprehensive Cancer Network (NCCN). Development and Update of Guidelines. Available online at www.nccn.org. Accessed October 11, 2023.

[6] Referenced from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Bladder Cancer V.3.2023 – May 25, 2023. Accessed October 12, 2023. The NCCN Guidelines are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version of the guideline, go online to NCCN.org.

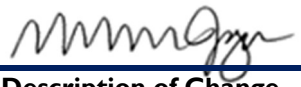
[7] Oken M, Creech R, Tormey D, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol. 1982;5:649-655.

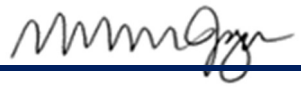
Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

Criteria Change History

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		
Signature			

Change Date	Changed By	Description of Change	Version
10/20/2023	CAC	Annual review. Updated Overview section (new indication FDA-approved 4/3/2023: in combination with pembrolizumab, for the treatment of adult patients with locally advanced or metastatic urothelial cancer who are not eligible for cisplatin-containing therapy; and added boxed warning regarding serious skin reactions). Updated Descriptive Overview to include 2023 statistics. Updated NCCN Guidelines. Added criteria for new indication. Updated Quantity Limits section to include dosing for new indication. Updated labeler name to Seagen in Coding section.	3
Signature			
William (Bill) Jagiello, DO			

Change Date	Changed By	Description of Change	Version
10/21/2022	CAC	Annual review. Updated annual cancer statistics and NCCN guideline references (no changes to actual guidelines noted). Added standard language to continuation criteria: "1. Member is currently receiving medication through the Iowa Medicaid benefit or has previously met initial approval criteria." Formatting.	2
Signature			
William (Bill) Jagiello, DO			

Change Date	Changed By	Description of Change	Version
10/15/2021	CAC	Criteria implementation.	1
Signature			
William (Bill) Jagiello, DO			

CAC = Medicaid Clinical Advisory Committee