Medical Drug Clinical Criteria

Subject:	Padcev (enfortumab vedotin-ejfv)		
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Table of Contents

Overview

This document addresses the use of Padcev (enfortumab vedotin). Padcev is a Nectin-4-directed antibody and microtubule inhibitor conjugate indicated for adults with urothelial cancer.

The FDA approved indications for Padcev is 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 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

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.

Clinical Criteria

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.

Padcev (enfortumab vedotin-ejfv)

Requests for Padcev (enfortumab vedotin-ejfv) may be approved if the following criteria are met (Label, NCCN 1, 2A):

I. Individual has a diagnosis of locally advanced or metastatic urothelial cancer; **AND**
   A. Individual is using in one of the following ways:
      1. In combination with pembrolizumab as first-line systemic therapy; **OR**
      ~~II.~~2. Individual is using as a single agent for subsequent therapy after progression in one of the following ways:
         ~~A.~~a. Anti-PD-1 or anti-PD-L1 agent and platinum-containing chemotherapy; **OR**
         ~~B.~~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.~~

Padcev (enfortumab vedotin-ejfv) may not be approved for the following:

I. Individuals with moderate or severe hepatic impairment (Child-Pugh B or C); **OR**
II. When the above criteria are not met and for all other indications.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

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

ICD-10 Diagnosis

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

Document History

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Revised: 02/23/2024
Document History:

- 02/23/2024 – Annual Review: Update criteria with FDA label updates for use in combination with pembrolizumab. Remove ECOG requirements. Wording and formatting updates. Coding Reviewed: No changes.
- 02/24/2023 – Annual Review: No changes. Coding Reviewed: No changes.
- 02/25/2022 – Annual Review: Update criteria with FDA indication updates. Update references. Coding Reviewed: Added ICD-10-CM Z92.21-Z92.22.
- 02/19/2021 – Annual Review: Update criteria to clarify use as single agent per NCCN and clinical trials. Coding Reviewed: Added ICD-10-CM C79.11-C79.19.
- 02/21/2020 – Annual Review: Add new clinical criteria document for Padcev (enfortumab vedotin-eifv). Coding Reviewed: Added HCPCS C9399,J3490, J9999, ICD-10 C67.1-C67.9 Coding Review 7/1/2020: Added HCPCS J9177 (Effective 7/1/2020), Delete J3490, J9999, C9399 6/30/2020

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