09-J3000-59

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Reviewed: 05/10/23

Revised: 03/15/24

Subject: Enfortumab Vedotin (Padcev™) IV

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

Dosage/ Administration	Position Statement	Billing/Coding	Reimbursement	Program Exceptions	Definitions
Related Guidelines	Other	References	Updates		

DESCRIPTION:

Enfortumab vedotin-ejfv (Padcev™) is Food and Drug Administration (FDA) approved 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 a platinum-containing chemotherapy in the locally advanced or metastatic setting. It is also FDA-approved for locally advanced or metastatic urothelial cancer in patients who are ineligible for cisplatin-containing chemotherapy and have previously received one or more lines of therapy. The FDA most recently approved enfortumab vedotin in combination with pembrolizumab for the treatment of adult patients with locally advanced or metastatic urothelial cancer.. Enfortumab vedotin-ejfv is an antibody-drug conjugate that works by binding to the adhesion protein Nectin-4 on the surface of cancer cells. The downstream effect results in release of a microtubule disrupting agent within the cell that causes cell cycle arrest and apoptotic cell death.

The efficacy of enfortumab vedotin-ejfv was evaluated in a multicenter trial in 608 patients with locally advanced or metastatic urothelial carcinoma. Patients who received prior treatment with a PD-1 or PD-L1 inhibitor and platinum-based chemotherapy were included. The major efficacy outcome was overall survival (OS), progression free survival (PRS) and overall response rate (ORR) between the enfortumab vedotin and investigator‘s choice of chemotherapy. The OS was significantly improved in the enfortumab treatment arm as compared those who received chemotherapy (12.9 months vs 9 months). The PFS was significantly improved with enfortumab as compared to chemotherapy (5.6 months vs 3.4 months). The ORR which included both complete and partial responders was significantly improved for the enfortumab treatment arm as compared to chemotherapy (40.6 % vs 17.9%). The most common adverse reactions were rash (54%), fatigue (50%), peripheral neuropathy (50%), alopecia (47%), decreased appetite (41%), diarrhea (35%), and pruritus (34%).

The National Comprehensive Cancer Network (NCCN) guidelines for the treatment of bladder cancer recommend the use of enfortumab vedotin-ejfv.

POSITION STATEMENT:

Initiation of enfortumab vedotin-ejfv (Padcev™) **meets the definition of medical necessity** when used for **ONE** of the following and all of the indication specific criteria are met:

1. Bladder cancer (also includes cancer of the urethra, upper genitourinary tract and prostate)
    A. Member is diagnosed with locally advanced or metastatic urothelial carcinoma
    B. **ONE** of the following (i, ii, or iii):
        i. **ALL** of the following (a,b, and c):
            a. Member has previously received a platinum-containing regimen (i.e.,cisplatin or carboplatin)
            b. Member has previously received a PD-1 or PD-L1 inhibitor (i.e., pembrolizumab, nivolumab, atezolizumab, avelumab, or durvalumab)
            c. Enfortumab vedotin will be given as a single agent
        ii. **ALL** of the following (a,b, and c):
            a. Member is ineligible for cisplatin-containing chemotherapy
            b. Member has previously received one or more lines of therapy
            c. Enfortumab vedotin will be given as a single agent
        iii. Will be used in combination with pembrolizumab
    C. The dose does not exceed **ONE** of the following;
        i. Single agent: 1.25 mg/kg (maximum 125 mg) administered on day 1, 8 , and 15 of a 28 day cycle
        ii. In combination with pembrolizumab: 1.25 mg/kg (maximum 125 mg) administered on day 1 and 8 of a 21 day cycle
2. Other FDA-approved or NCCN-supported diagnosis (not previously listed)
    A. **ONE** of the following is met:
        i. Member is diagnosed with a condition that is consistent with an indication listed in the product's FDA-approved prescribing information (or package insert) **AND** member meets any additional requirements listed in the "Indications and Usage" section of the FDA-approved prescribing information (or package insert)
        ii. Indication AND usage is recognized in NCCN Drugs and Biologics Compendium as a Category 1 or 2A recommendation
    B. Dose does not exceed the maximum FDA-approved dosing

Approval duration: 6 months

Continuation of enfortumab vedotin-ejfv (Padcev™) **meets the definition of medical necessity** for the treatment of bladder cancer or other FDA-approved or NCCN supported diagnosis when **ALL** of the following criteria are met:

1. An authorization or reauthorization for enfortumab vedotin-ejfv has been previously approved by Florida Blue or another health plan in the past 2 years, **OR** the member has previously met **ALL** indication-specific criteria.
2. The member's disease has not progressed while receiving treatment with enfortumab vedotin-ejfv
3. The dose does not exceed **ONE** of the following:
    a. Single agent: 1.25 mg/kg (maximum 125 mg) administered on day 1, 8 , and 15 of a 28 day cycle
    b. In combination with pembrolizumab: 1.25 mg/kg (maximum 125 mg) administered on day 1 and 8 of a 21 day cycle

Approval duration: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- For the treatment of adult patients with locally advanced or metastatic urothelial cancer who:
    - When used as a single agent and have previously received a programmed death recptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor, and a platinum-containing chemotherapy, or
    - When used as a single agent and are ineligible for cisplatin-containing chemotherapy and have previously received one or more prior lines of therapy
    - When used in combination with pembrolizumab
- Administer as an IV infusion only.
    - Single agent dose: 1.25 mg/kg (up to a maximum of 125 mg for patients greater than or equal to 100 kg) over 30 min on Days 1,8, and 15 of a 28-day cycle until disease progression or unacceptable toxicity.
    - In combination with pembrolizumab: 1.25 mg/kg (maximum 125 mg) administered on day 1 and 8 of a 21 day cycle until disease progression or unacceptable toxicity.

Dose Adjustments

- Avoid use in patients with moderate or severe hepatic impairment.
- See prescribing information for dose adjustment and discontinuation for adverse reactions.

Drug Availability

- 20 mg and 30 mg powder in a single-dose vial for reconstitution.

PRECAUTIONS:

Boxed Warning

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

Contraindications

- none

Precautions/Warnings

- Hyperglycemia: Diabetic ketoacidosis may occur. Closely monitor blood glucose levels in patients with, or at risk for, diabetes mellitus or hyperglycemia. Withhold if blood glucose > 250 mg/dL.
- Pneumonitis: Severe, life-threatening or fatal pneumonitis may occur. Withhold for persistent or recurrent Grade 2 pneumonitis and consider dose reduction. Permanently discontinue for Grade 3 or 4 pneumonitis.
- Peripheral neuropathy: Monitor patients for new or worsening peripheral neuropathy and consider dose interruption, adjustment or discontinuation.
- Ocular disorders: Vision changes may occur. Monitor for ocular disorders and consider prophylactic artificial tears for dry eyes and treatment with ophthalmic topical steroids after an ophthalmic exam. Consider dose interruption, adjustment or discontinuation when ocular disorders occur.
- Skin reactions: See boxed warning regarding fatal skin reactions. If severe, withhold until improvement or resolution and closely monitor patients. Consider topical corticosteroids and antihistamines.
- Infusion site extravasation: Ensure adequate venous access prior to administration, monitor the infusion site and stop immediately for suspected extravasation.
- Embryo-fetal toxicity: May cause fetal harm; advise of the risk to a fetus and use contraception.

BILLING/CODING INFORMATION:

HCPCS Coding

J9177	Injection, enfortumab vedotin-ejfv, 0.25 mg

ICD-10 Diagnosis Codes That Support Medical Necessity

C61	Malignant neoplasm of prostate
C65.1 – C65.9	Malignant neoplasm of renal pelvis

C66.1 – C66.9	Malignant neoplasm of ureter
C67.0 – C67.9	Malignant neoplasm of bladder
C68.0	Malignant neoplasm of urethra
C68.8	Malignant neoplasm of overlapping sites of urinary organs

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

DEFINITIONS:

None applicable.

RELATED GUIDELINES:

None applicable.

OTHER:

None applicable.

REFERENCES:

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7. Padcev [prescribing information]. Astellas Pharmaceuticals US, Inc. Northbrook, Illinois. Dec 2024.
8. Rosenberg JE, O'Donnell PH, Balar AV et al. Pivotal trial of enfortumab vedotin in urothelial carcinoma after platinum and anti-programmed death 1/programmed death ligand 1 therapy. *J Clin Oncol.* 2019. 37 (29): 2592-2600.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 05/10/23.

GUIDELINE UPDATE INFORMATION:

03/15/20	New Medical Coverage Guideline.
07/01/20	Revision: Added HCPCS code J9177 and deleted code J3590.
04/15/21	Review and revision to guideline; consisting of updating references.
08/15/21	Revision to guideline; consisting of updating the position statement, description, dosing, warnings, coding and references.
04/15/22	Review and revision to guideline; consisting of updating the references.
06/15/23	Review and revision to guideline; consisting of updating the position statement to include use in combination with pembrolizumab.
03/15/24	Revision to guideline; consisting of updating the position statement for treatment with pembrolizumab.