BlueCross BlueShield of North Carolina

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Corporate Medical Policy

Enfortumab vedotin-ejfv (Padcev™)

File Name: enfortumab_vedotin_padcev
Origination: 2/2020
Last CAP Review: n/a
Next CAP Review: 11/2020
Last Review: 2/2020

Description of Procedure or Service

Enfortumab vedotin-ejfv (Padcev) is a Nectin-4-directed antibody and microtubule inhibitor conjugate that is indicated 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 in the neoadjuvant/adjuvant, locally advanced or metastatic setting.

Urothelial cancer originates in the portion of the genitourinary system lined by urothelial epithelium (previously referred to as transitional cell epithelium). Most urothelial carcinomas arise in the urinary bladder but may also originate from the urothelial lining of the ureter, urethra or renal pelvis.

Enfortumab vedotin-ejfv (Padcev) was approved by the U.S. Food and Drug Administration (FDA) in December 2019 for the treatment of locally advanced or metastatic urothelial cancer under accelerated approval based on tumor response rate. It is a Nectin-4 directed antibody-drug conjugate that induces cell death through release of monomethyl auristatin E (MMAE) after the complex is internalized by solid tumors expressing the cell adhesion molecule Nectin-4.

Related Medical Policies:
PD-1 Inhibitors
PD-L1 Inhibitors

******Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

Policy

BCBSNC will provide coverage for enfortumab vedotin-ejfv (Padcev™) when it is determined to be medically necessary because the medical criteria and guidelines noted below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Enfortumab vedotin-ejfv (Padcev) is covered

Initial Therapy

Enfortumab vedotin-ejfv (Padcev) is considered medically necessary for the treatment of adult patients with urothelial cancer when the following criteria are met:

- The patient has locally advanced or metastatic disease; and
- The patient has received prior treatment with a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor; and
- The patient has received prior treatment with a platinum-containing chemotherapy in the neoadjuvant/adjuvant, locally advanced or metastatic setting; and
- The patient does not have active central nervous system metastases.

Length of authorization: 12 months

Continuation Therapy

Continuation of treatment with enfortumab vedotin-ejfv (Padcev) beyond 12 months after initiation of therapy, and every 12 months thereafter, is considered medically necessary for the treatment of locally advanced or metastatic urothelial cancer when the following criteria are met:

1. The patient is currently receiving enfortumab vedotin and continues to meet initial criteria; and
2. The patient has continued clinical benefit on enfortumab vedotin therapy as demonstrated by tumor response or lack of disease progression, and an acceptable toxicity profile.

Use of enfortumab vedotin-ejfv (Padcev) may be considered medically necessary for clinical indications not listed above when the drug is prescribed for the treatment of cancer either:

- In accordance with FDA label (when clinical benefit has been established, (see Policy Guidelines); **OR**

- In accordance with specific strong endorsement or support by nationally recognized compendia, when such recommendation is based on strong/high levels of evidence, and/or uniform consensus of clinical appropriateness has been reached.

When Enfortumab vedotin-ejfv (Padcev) is not covered

Enfortumab vedotin-ejfv (Padcev) is considered **investigational** and therefore not covered when the above criteria are not met.

Enfortumab vedotin-ejfv (Padcev) is considered investigational when used for:

1. Non-cancer indications; **OR**

2. When criteria are not met regarding FDA labeling **OR** strong endorsement/support by nationally recognized compendia, as stated under "When Enfortumab vedotin-ejfv (Padcev) is covered."

Policy Guidelines

Details of the clinical trial criteria indicate that tumor origin of urothelial type included bladder, urethra, ureter and renal pelvis. In addition, squamous differentiation or mixed histologies were allowed.

Dosing and Administration

The recommended dose for Padcev is 1.25 mg/kg (up to a maximum of 125 mg for patients ≥100 kg) administered intravenously over 30 minutes on days 1, 8, and 15 of a 28-day cycle until disease progression or unacceptable toxicity.

According to the manufacturer's safety information for Padcev, the most common adverse reactions (≥20% incidence) include fatigue, peripheral neuropathy, decreased appetite, rash, hair loss, nausea, dysgeusia, diarrhea, dry eye, pruritus, and dry skin. Hyperglycemia has occurred in patients treated with Padcev, including death, and diabetic ketoacidosis in those with and without preexisting diabetes mellitus. Peripheral neuropathy (mainly sensory) has also occurred in patients receiving Padcev, and patients should be monitored for new or worsening peripheral neuropathy. Other warnings and precautions observed with Padcev administration include ocular disorders, skin reactions, infusion site extravasation, and embryo-fetal toxicity.

Evidence Summary

The efficacy of enfortumab vedotin was evaluated in a single-arm, multicenter, phase 2 clinical trial (EV-201; NCT03219333) that enrolled 125 patients (≥ 18 years of age) with locally advanced or metastatic urothelial cancer who were previously treated with a PD-1 or PD-L1 inhibitor and platinum-based chemotherapy. Patients with active CNS metastases were excluded from the trial. Ninety percent of patients enrolled in the trial had visceral metastases, including 40% with liver metastases. All tumor biopsy samples taken from 120 patients with adequate tissue for testing demonstrated detectable Nectin-4 expression. The median number of prior systemic therapies at study enrollment was three (range, 1 to 6), and patients with only one prior therapy received platinum and anti-PD-1/L1 therapy in combination. Patients received enfortumab vedotin 1.25 mg/kg intravenously over 30 minutes, up to a maximum dose of 125 mg, given on days 1, 8, and 15 of each 28-day cycle. Treatment continued until disease progression or unacceptable toxicity, with a median follow-up of 10.2 months (range, 0.5 to 16.5 months). The primary efficacy endpoint was confirmed objective response rate (ORR) per Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1, which was 44% (95% CI, 35.1% to 53.2%), including a 12% complete response rate (CR). Other key secondary endpoints included duration of response, progression-free survival, and overall survival. The median duration of response was 7.6 months (range, 0.95 to 11.30+ months; 95% CI, 4.93 to 7.46).

Drugs prescribed for treatment of cancer in accordance with FDA label may be considered medically necessary when clinical benefit has been established, and should not be determined to be investigational as defined in Corporate Medical Policy (CMP), "Investigational (Experimental) Services."

Please refer to CMP "Investigational (Experimental) Services" for a summary of evidence standards from nationally recognized compendia.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: *J9177, S0353, S0354*

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

Astellas Pharma US, Inc. Padcev (enfortumab vedotin-ejfv) for injection, for intravenous use. Highlights of prescribing information. December 2019. Available at: https://astellas.us/docs/PADCEV_label.pdf. Last accessed February 2020.

U.S. Food and Drug Administration. FDA approves new type of therapy to treat advanced urothelial cancer. December 18, 2019. Available at: https://www.fda.gov/news-events/press-announcements/fda-approves-new-type-therapy-treat-advanced-urothelial-cancer. Last accessed February 2020.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Bladder Cancer, version 3.2020. Revised January 17, 2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf. Last accessed February 2020.

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. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6784850/pdf/JCO.19.01140.pdf. Last accessed February 2020.

Medical Director review 2/2020

Policy Implementation/Update Information

2/25/20 New policy developed. Padcev is considered medically necessary for the treatment of adult patients with locally advanced or metastatic urothelial cancer when specified medical criteria and guidelines are met. Added HCPCS codes C9399, J3490, J3590, J9999, S0353, and S0354 to Billing/Coding section. References added. Medical Director review 2/2020. (krc)

6/30/20 Added HCPCS code J9177 to Billing/Coding section effective 7/1/2020 and deleted codes C9399, J3490, J3590, J9999 termed 6/30/2020. (krc)