BlueCross BlueShield
Federal Employee Program

PADCEV
(enfortumab vedotin-ejfv)

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Padcev (enfortumab vedotin-ejfv) is a Nectin-4-directed antibody-drug conjugate (ADC) and microtubule inhibitor conjugate. The anticancer activity of Padcev is thought to be due to the binding of the ADC to Nectin-4-expressing cells, followed by internalization of the ADC-Nectin-4 complex, and the release of monomethyl auristatin E (MMAE) via proteolytic cleavage. Release of MMAE is thought to disrupt the microtubule network within the cell, subsequently inducing cell cycle arrest and apoptotic cell death (1).

Regulatory Status

FDA-approved indications: Padcev is a Nectin-4-directed antibody and microtubule inhibitor conjugate indicated: (1)

- In combination with pembrolizumab for the treatment of adult patients with locally advanced or metastatic urothelial cancer.
- 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.

Padcev has a boxed warning regarding the risk of severe and fatal cutaneous adverse reactions, including Stevens-Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN). Due to these risks, patients should be closely monitored for skin reactions. If severe skin reactions, SJS or TEN is suspected, Padcev should be withheld immediately and a referral for specialized care should be considered. In confirmed cases of SJS or TEN that are Grade 4 or recurrent Grade 3 skin reactions, Padcev should be permanently discontinued (1).

Hyperglycemia has occurred in patients treated with Padcev, including death, and diabetic ketoacidosis (DKA) in those with and without pre-existing diabetes mellitus. Blood glucose levels should be monitored closely in patients with, or at risk for, diabetes mellitus or hyperglycemia. If blood glucose is elevated (>250 mg/dL), Padcev should be withheld (1).

Peripheral neuropathy, predominantly sensory, has occurred in patients treated with Padcev.

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Patients should be monitored for symptoms of new or worsening peripheral neuropathy and dose interruption or dose reduction should be considered when peripheral neuropathy occurs. Padcev should be permanently discontinued in patients that develop Grade ≥3 peripheral neuropathy (1).

Padcev can cause fetal harm when administered to a pregnant woman. Female patients of reproductive potential should be advised to use effective contraception during treatment with Padcev and for 2 months after the last dose. Male patients with female partners of reproductive potential should be advised to use effective contraception during treatment with Padcev and for 4 months after the last dose (1).

The safety and effectiveness of Padcev in pediatric patients less than 18 years of age have not been established (1).

Summary

Padcev (enfortumab vedotin-ejfv) is a Nectin-4-directed antibody-drug conjugate (ADC) and microtubule inhibitor conjugate indicated for the treatment of patients with locally advanced or metastatic urothelial cancer. The anticancer activity of Padcev is thought to be due to the binding of the ADC to Nectin-4-expressing cells, followed by internalization of the ADC-Nectin-4 complex, and the release of monomethyl auristatin E (MMAE) via proteolytic cleavage. Release of MMAE is thought to disrupt the microtubule network within the cell, subsequently inducing cell cycle arrest and apoptotic cell death. Padcev carries a boxed warning for the risk of severe cutaneous skin reactions including SJS and TEN. The safety and effectiveness of Padcev in pediatric patients less than 18 years of age have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Padcev while maintaining optimal therapeutic outcomes.

References

1. Padcev [package insert]. Bothell, WA: Astellas Pharma US, Inc.; December 2023.
2. NCCN Drugs & Biologics Compendium® Enfortumab vedotin-ejfv 2024. National Comprehensive Cancer Network, Inc. Accessed on October 3, 2024.