

# Enfortumab Vedotin

## Nursing perspectives on the management of adverse events in patients with locally advanced or metastatic urothelial carcinoma

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**BACKGROUND:** Many patients with locally advanced or metastatic urothelial carcinoma (mUC) need additional treatment options beyond PD-1 or PD-L1 inhibitors and platinum-based chemotherapies. Enfortumab vedotin-ejfv (EV) is an antibody–drug conjugate directed at Nectin-4 that received accelerated approval for treatment of adults with locally advanced or mUC previously treated with PD-1/PD-L1 inhibitors and platinum-containing chemotherapy in the neoadjuvant/adjunct, locally advanced, or metastatic settings.

**OBJECTIVES:** This article provides practical considerations and recommendations regarding common and potentially treatment-limiting adverse events that may arise with EV therapy.

**METHODS:** The clinical data that supported the approval of EV are reviewed, and supporting safety and management considerations are provided based on the authors' experience.

**FINDINGS:** EV therapy can be optimized through patient and caregiver education, proactive patient monitoring, early identification of adverse events, and timely intervention to alleviate symptoms.

### KEYWORDS

antibody–drug conjugates; enfortumab vedotin; adverse drug event; assessment

### DIGITAL OBJECT IDENTIFIER

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**LOCALLY ADVANCED OR METASTATIC UROTHELIAL CARCINOMA** (mUC) is an aggressive and incurable disease that disproportionately affects older adults, often those with a history of smoking and comorbidities, including cardiovascular disease and diabetes. Safe and effective treatment options are limited. Platinum-based chemotherapy, the standard initial therapy for mUC, is often difficult to tolerate and responses often are short-lived. In the second-line setting, approved programmed cell death protein-1 (PD-1) or programmed cell death-ligand 1 (PD-L1) inhibitor therapies provide meaningful responses in 13%–29% of patients with mUC (Balar et al., 2017; Bristol-Myers Squibb, 2020; EMD Serono, 2019; Merck, 2020; Powles et al., 2017; Rosenberg et al., 2016). Subsequent therapies, including single-agent taxanes, have low objective response rates of only 11%–13% (Bellmunt et al., 2017; Powles et al., 2018). Therefore, a great unmet need for effective treatment options exists throughout the mUC treatment journey.

Enfortumab vedotin-ejfv (EV) received accelerated approval from the U.S. Food and Drug Administration (FDA) in December 2019 for treatment of adults with locally advanced or mUC previously treated with a PD-1 or PD-L1 inhibitor and a platinum-containing chemotherapy in the neoadjuvant/adjunct, locally advanced, or metastatic setting (Astellas Pharma, 2019). EV is an antibody–drug conjugate (ADC) that comprises monomethyl auristatin E (MMAE) as the active anticancer component (Challita-Eid et al., 2016; Doronina et al., 2003; Liu et al., 2020). MMAE induces cell death by disrupting the microtubule apparatus. Unlike other microtubule-disrupting agents, such as taxanes and vinca alkaloids, EV is designed to target the delivery of MMAE to specific cells by using an antibody-delivery mechanism directed against Nectin-4, which is highly expressed in UC and involved in cellular processes associated with oncogenesis (Challita-Eid et al., 2016; Doronina et al., 2003; Liu et al., 2020). EV is administered via IV on days 1, 8, and 15 of each 28-day cycle.

EV-201 (NCT03219333) is a global, phase 2, single-arm study of EV in patients with locally advanced or mUC previously treated with platinum-containing chemotherapy and anti-PD-1/PD-L1 therapy (cohort 1) or anti-PD-1/PD-L1 therapy in patients who are platinum-naïve and cisplatin-ineligible (cohort 2) (Rosenberg et al., 2019). In cohort 1, the basis for the FDA's