

This resource has been developed in collaboration with Professor Alison Birtle, Consultant Clinical Oncologist, Rosemere Cancer Centre, Lancashire Teaching Hospitals; Professor Simon Crabb, Professor of Experimental Cancer Therapeutics, University of Southampton; and Dr Samantha Strumeier, Uro-Oncology Clinical Nurse Specialist and Advanced Practice Nurse, Barts Health. Their views are their own, based upon their clinical experience and are not necessarily representative of their institutions.

Expert considerations: Implementing KEYTRUDA® (pembrolizumab) + enfortumab vedotin▼ as first-line treatment for unresectable or metastatic urothelial carcinoma (u/mUC)

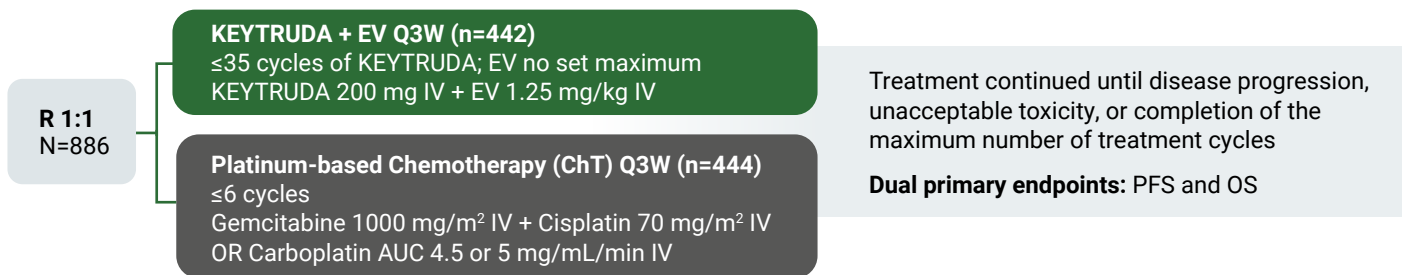
KEYTRUDA is licensed in combination with enfortumab vedotin (EV) for the first-line treatment of u/mUC in adults. Before prescribing, please consult the SmPC and Risk Management Materials.¹

PURPOSE OF THIS RESOURCE

This resource supports integration of the KEYTRUDA + EV regimen into NHS pathways and should be used in conjunction with published guidance and recommendations, where available. The flow chart and content on page 2 reflect the insights and experience of the consulted clinicians. Responsibility for treatment decisions remains with the treating healthcare professional(s).

OVERVIEW OF DATA FROM THE KEYNOTE-A39/EV-302 TRIAL¹⁻³

KEYNOTE-A39 is a randomised, open-label, phase 3 trial in patients with previously untreated, unresectable locally advanced or mUC.



Median follow-up: 17.2 months	Progression-free survival (PFS)			Overall survival (OS)		
	Median PFS (95% CI)	Events, n (%)	HR (95% CI)	Median OS (95% CI)	Events, n (%)	HR (95% CI)
KEYTRUDA + EV	12.5 months (10.4–16.6)	223 (50.5%)	0.45 (0.38–0.54); p<0.001	31.5 months (25.4–NR)	133 (30.1%)	0.47 (0.38–0.58); p<0.001
Platinum-based ChT	6.3 months (6.2–6.5)	307 (69.1%)		16.1 months (13.9–18.3)	226 (50.9%)	

Adapted from Powles T, et al. Ann Oncol 2024.

Safety summary

- The **most common TRAEs of any grade** with KEYTRUDA + EV were peripheral sensory neuropathy (50.0%), pruritus (39.8%), alopecia (33.2%), and maculo-papular rash (32.7%); and with ChT were anaemia (56.6%), neutropenia (41.6%), and nausea (38.8%)
- TRAEs of grade ≥3 occurred** in 55.9% of patients in the KEYTRUDA + EV arm and in 69.5% of patients in the ChT arm
- In the KEYTRUDA + EV arm, the **most common TEAEs of special interest of grade ≥3** that have been previously associated with KEYTRUDA were severe skin reactions (11.8%), pneumonitis (3.6%), and hepatitis (1.8%). The **most common TRAEs of special interest of grade ≥3** that have been previously associated with EV were skin reactions (15.5%), peripheral neuropathy (6.8%), and hyperglycaemia (6.1%). Refer to the SmPC for the full list of AEs

Adverse events should be reported. Reporting information can be found at <https://yellowcard.mhra.gov.uk> or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Merck Sharp & Dohme (UK) Limited (Tel: 0208 154 8000).

Abbreviations:

AE, adverse event; AUC, area under the curve; ChT, chemotherapy; CI, confidence interval; EV, enfortumab vedotin; HR, hazard ratio; IV, intravenous; MHRA, Medicines and Healthcare products Regulatory Agency; mUC, metastatic urothelial carcinoma; NHS, National Health Service; NR, not reached; OS, overall survival; PFS, progression-free survival; Q3W, every three weeks; R, randomised; SmPC, summary of product characteristics; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event; u/mUC, unresectable or metastatic urothelial carcinoma.

[Click here to access UK prescribing information](#)

How to use this page: The left side presents detailed expert considerations for each stage of the patient pathway; the right summarises the pathway as a visual flow, highlighting new steps to guide decision-making and delivery in practice



UROLOGY CLINIC

Consider what information may be helpful for patients in preparation for onward referral to oncology:

- What happens next, how will the referral be communicated, and who will patients see at the referral?
- Explain that the oncologist will discuss potential treatment options, engaging patients in shared decision-making to agree on the best course of action

MDT

- Confirm the **availability of key clinical information** (including fitness assessments, comorbidities and treatment suitability)
- Ensure the **KEYTRUDA + enfortumab vedotin protocol** has been developed, approved and implemented in the hospital formulary

ONCOLOGY CLINIC

Consider multidisciplinary collaboration and pre-emptive AE monitoring plans:

- **Collaborate with experienced teams** (e.g., clinical investigators) for treatment guidance
- **Share insights on the patient experience of this indication** (e.g., AE onset timing and feedback) with the MDT to support awareness and learning
- **Complete team training** on managing expected and serious AEs
- Adhere to treatment protocols, and **regularly review AE patterns** and clinical experiences

Develop AE monitoring plan from initiation of treatment:

- **Identify opportunities, resources and tools** to detect early asymptomatic AEs (e.g., importance of day 8 visit, use of tuning forks or tendon hammers for neurological and musculoskeletal examinations)
- **Define questions** to help patients identify and report early asymptomatic AEs
- **Proactively engage relevant disciplines** (e.g., dermatology, neurology) to support AE management
- Agree on **parameters and escalation process** for early/asymptomatic onset

CONSENT

Confirm the patients:

- Understand the treatment plan and potential benefits/risks
- Have received appropriate supporting written information
- Have had the chance to ask questions and provide informed consent before treatment

TREATMENT INITIATION

Review and ensure team readiness to deliver KEYTRUDA + enfortumab vedotin:

- Are all **Nursing, Treatment Suite, AOS and Pharmacy teams** aware of the treatment protocol and do they require training?
- Confirm which additional teams need notification of the new treatment protocol (e.g., **out-of-hours helpline, acute oncology teams, and emergency teams**)
- Arrange patient discussion with the dedicated nurse (e.g., **Uro-Oncology CNS, Urology CNS, Advanced Nurse Practitioner**) to discuss and share treatment support information
- **Review and monitor early treatment experience** with the combination and ensure access to both the KEYTRUDA and enfortumab vedotin SmPCs

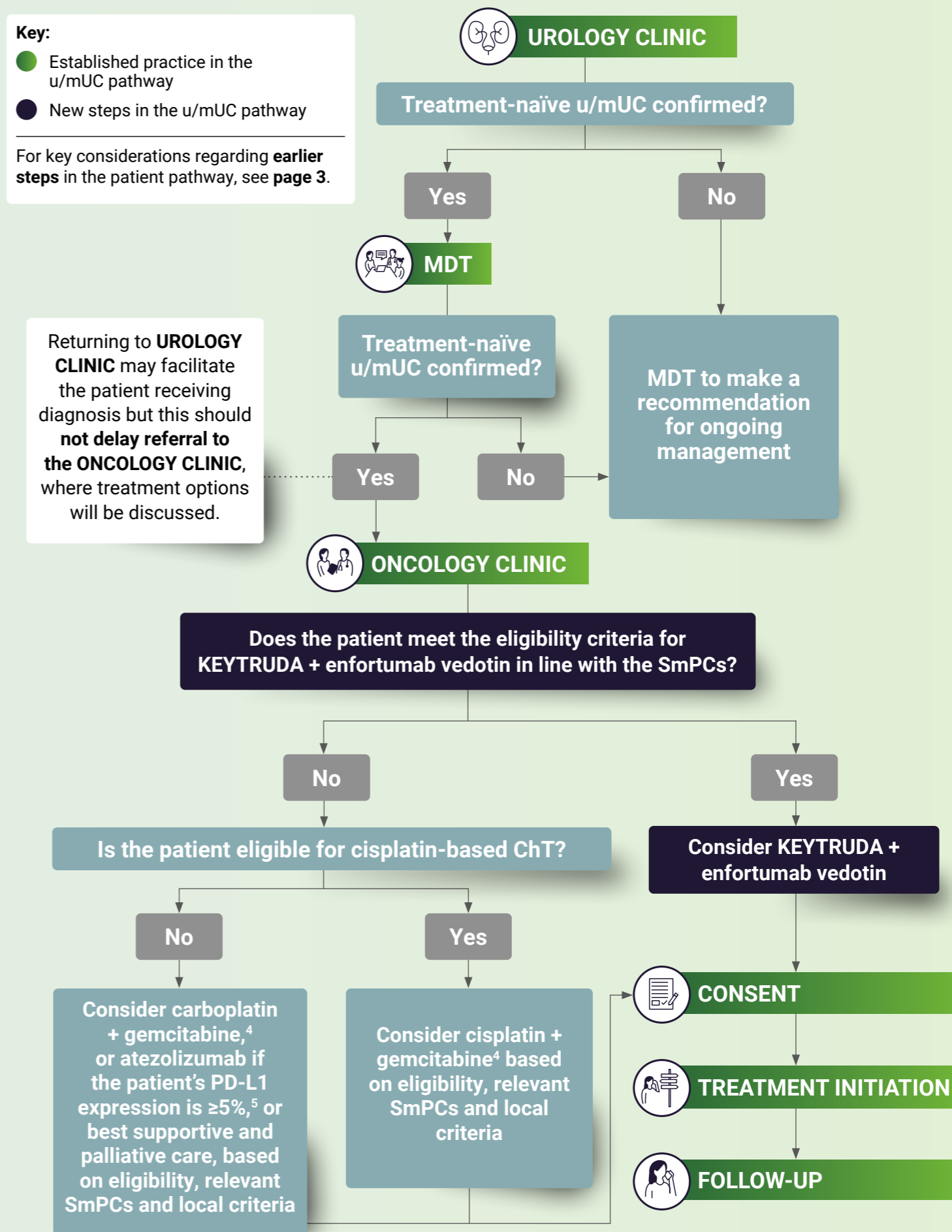
FOLLOW-UP

- Document a clear **follow-up schedule** (e.g., per protocol, AE monitoring, bloods/imaging) and share with relevant team members
- **Ensure patients know who their named CNS is and how to contact them** and also have the AOS contact details. This should include out-of-hours contact details

Key:

- Established practice in the u/mUC pathway
- New steps in the u/mUC pathway

For key considerations regarding **earlier steps** in the patient pathway, see **page 3**.



Returning to **UROLOGY CLINIC** may facilitate the patient receiving diagnosis but this should **not delay referral to the ONCOLOGY CLINIC**, where treatment options will be discussed.

Abbreviations: 1L, first-line; AE, adverse event; AOS, acute oncology services; ChT, chemotherapy; CNS, cancer nurse specialist; MDT, multidisciplinary team; SmPC, summary of product characteristics; u/mUC, unresectable or metastatic urothelial carcinoma.

Expert considerations: Pathway readiness for KEYTRUDA + enfortumab vedotin in u/mUC

This resource focuses on treatment decision-making, initiation and management. The following expert considerations support the implementation of best practice bladder cancer pathways, to streamline clinical decision-making and reduce delays for MDT discussion:



PRE-DIAGNOSIS

- Have any symptoms (e.g., haematuria) been misattributed to benign causes (e.g., UTI)?
- Have all atypical presentations (e.g., recurrent UTIs in women) been fully investigated for malignancy?



UROLOGY REFERRAL

- Has the two-week wait referral been made promptly, where appropriate?
- Have any non-typical symptoms or non-GP referral pathways been appropriately prioritised?



IMAGING AND STAGING

- Has initial imaging (e.g., CT TAP) provided complete staging information?
- Have follow-up scans been requested early to avoid any delays?



TURBT

- Do you have the necessary tissue sample(s) to diagnose u/mUC?

[Click here to send an email to request further information on this indication from your local MSD representative](#)

This link will open an email window with pre-populated contact information

[Click here to access MSD Connect which includes promotional resources on the KEYNOTE-A39 trial and management of u/mUC patients](#)

This link will direct you to an MSD promotional website

Abbreviations:

CT TAP, computed tomography scan of the thorax, abdomen and pelvis; **GP**, general practitioner; **MDT**, multidisciplinary team; **TURBT**, transurethral resection of bladder tumour; **u/mUC**, unresectable or metastatic urothelial carcinoma; **UTI**, urinary tract infection.

References:

1. KEYTRUDA Summary of Product Characteristics.
2. Powles T, et al. *N Engl J Med*. 2024;390(10):875–888.
3. Powles T, et al. *Ann Oncol*. 2024;35(6):485–490.
4. NICE. Guideline NG2. 2015. Available from: <https://www.nice.org.uk/guidance/ng2> (last accessed: September 2025).
5. Tecentriq (atezolizumab) Summary of Product Characteristics.

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