Enfortumab vedotin Monotherapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved reimbursement status*
For the treatment of adult patients with locally advanced or metastatic urothelial carcinoma (UC) who have previously received a platinum-containing chemotherapy and a programmed death receptor 1 (PD-1) or programmed death ligand 1 inhibitor (PD-L1).	C65, C66, C67, C68	00846a	ODMS 01/12/2023

*This is for post 2012 indications only

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.

Enfortumab vedotin is administered on Days 1, 8 and 15 of a 28-day cycle. Treatment should be continued until disease progression or unacceptable toxicity.

Facilities to treat anaphylaxis MUST be present when systemic anti-cancer therapy (SACT) is administered.

Day	Drug	Dose	Route	Diluent & Rate	Cycle
1, 8, 15	Enfortumab vedotin	1.25mg/kg	IV infusion	50mL 0.9% NaCl over 30 minutes	Every 28 days
For patient weight ≥100kg, the dose calculation should use 100kg (maximum dose=125mg).					
Final concentration of enfortumab vedotin should be 0.3-4mg/mL.					
In-line filters or syringe filters of pore size: 0.2-1.2 µm are recommended to be used during administration.					
Glucose 5% or Compound Sodium Lactate (Hartmann's Solution) may also be used as diluent.					

ELIGIBILITY:

- Indication as above
- Adequate haematological and organ function
- ECOG status 0-2

EXCLUSIONS:

- Hypersensitivity to enfortumab vedotin or to any of the excipients
- Pregnancy / breastfeeding

CAUTIONS:

- Active CNS metastases
- Uncontrolled diabetes mellitus
- Pre-existing ≥ Grade 2 sensory or motor neuropathy
- Active keratitis or corneal ulcerations

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist

TESTS:

Baseline tests:

- FBC, renal, liver profile and blood glucose
- Lipase, phosphate, HbA1c
- Assessment of pre-existing neuropathy
- Ophthalmology assessment if clinically indicated
- Skin assessment

Regular tests:

- FBC, renal, liver profile and blood glucose on Day 1, 8 and 15 of Cycle 1, then on Day 1 of each subsequent cycle
- Phosphate on day 1
- Lipase and HbA1c, on day 1 if clinically indicated
- Ophthalmology assessment if clinically indicated
- Skin assessment should be carried out throughout treatment

Disease monitoring:

Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant
- Recommended dose reductions for enfortumab vedotin are outlined in Table 1
- Dose interruption, reduction and discontinuation recommendations for enfortumab vedotin are outlined in Tables 2, 3 and 4

Table 1: Recommended dose reductions for enfortumab vedotin for adverse reactions

	Dose level
Starting dose	1.25 mg/kg up to 125 mg
First dose reduction	1.0 mg/kg up to 100 mg
Second dose reduction	0.75 mg/kg up to 75 mg
Third dose reduction	0.5 mg/kg up to 50 mg

Haematological:

Table 2: Dose modification of enfortumab vedotin in haematological toxicity

ANC ($x10^9$/L)		**Platelets ($x10^9$/L)**	**Dose**
≥1.5	and	≥75	100% dose
1.0–1.49	or	50-74	100% dose, except: If platelets 50-74 x 10^9/L, withhold dose until platelets ≥75 $x10^9$/L or have returned to baseline, then resume treatment at the same dose level.
0.5-0.99	or	25-49	Withhold dose until ANC ≥ 1.5 x 10^9/L and platelets ≥75 x 10^9/L or returned to baseline, then resume treatment at the same dose level or consider dose reduction by 1 dose level*.
<0.5	or	<25	Withhold dose until ANC ≥ 1.5 x 10^9/L and platelets ≥75 x 10^9/L or returned to baseline, then reduce dose by 1 dose level and resume treatment* or consider discontinuation. For anaemia, treatment discontinuation should be strongly considered
* Use of transfusions or growth factors may be considered **(Refer to local policy).**			

Renal and Hepatic Impairment:

Table 3: Dose modification of enfortumab vedotin in renal and hepatic impairment

Renal Impairment		**Hepatic Impairment**	
CrCl (mL/minute)	**Dose**	**Severity**	**Dose**
≥ 15	No dose adjustment is needed	**Mild**	No dose adjustment is needed
< 15	No need for dose adjustment is expected	**Moderate/Severe**	Not recommended
Haemodialysis	No need for dose adjustment is expected		

Management of adverse events:

Table 4: Dose interruption, reduction and discontinuation recommendations for enfortumab vedotin for non-haematological toxicity

Adverse reaction	Severity*	Dose modification*
Skin reactions	Suspected Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN) or bullous lesions	• Immediately withhold and refer to specialised care.
	Confirmed SJS or TEN; Grade 4 or recurrent Grade 3	• Permanently discontinue.
	Grade 2 worsening or Grade 2 with fever or Grade 3	• Withhold until Grade ≤1 • Referral to specialised care should be considered • Resume at the same dose level or consider dose reduction by one dose level (see Table 1)
Hyperglycaemia	Blood glucose >13.9 mmol/L (>250 mg/dL)	• Withhold until elevated blood glucose has improved to ≤13.9 mmol/L (≤250 mg/dL) • Resume treatment at the same dose level
Pneumonitis/ interstitial lung disease (ILD)	Grade 2	• Withhold until Grade ≤1, then resume at the same dose or consider dose reduction by one dose level (see Table 1)
	Grade ≥3	• Permanently discontinue.
Peripheral neuropathy	Grade 2	• Withhold until Grade ≤1 • For first occurrence, resume treatment at the same dose level • For a recurrence, withhold until Grade ≤1, then resume treatment reduced by one dose level (see Table 1)
	Grade ≥3	• Permanently discontinue.
*Toxicity was graded per National Cancer Institute Common Terminology Criteria for Adverse Events Version 5.0 (NCI-CTCAE v5.0) where Grade 1 is mild, Grade 2 is moderate, Grade 3 is severe and Grade 4 is life-threatening		

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL

- As outlined in NCCP Classification Document for Systemic Anti Cancer Therapy (SACT) Induced Nausea and Vomiting - Available on the NCCP website

Low **(Refer to local policy).**

For information:
Within NCIS regimens, antiemetics have been standardised by Medical Oncologists and Haemato-oncologists and information is available in the following documents:

- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Medical Oncology) -Available on the NCCP website
- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Haemato-oncology) - Available on the NCCP website

PREMEDICATIONS:

- For patients who have experienced a prior infusion reaction, premedication consisting of an oral anti-pyretic, antihistamine and IV corticosteroid should be administered 30 minutes prior to subsequent infusions of enfortumab vedotin **(Refer to local policy)**

OTHER SUPPORTIVE CARE:

- Consider artificial tears for prophylaxis of dry eye **(Refer to local policy)**
- Consider topical corticosteroids and antihistamines for mild to moderate skin reactions **(Refer to local policy)**

ADVERSE EFFECTS:

- Please refer to the relevant Summary of Product Characteristics (SmPC) for details.

DRUG INTERACTIONS:

- Consult current drug interaction databases and relevant SmPC for details.

COMPANY SUPPORT RESOURCES/Useful Links:

Please note that this is for information only and does not constitute endorsement by the NCCP

Patient Card
https://assets.hpra.ie/products/Human/38097/7e581f21-f008-485c-9528-f7993cb75a3e.pdf

REFERENCES:

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2. Giraud EL, de Lijster B, Krens SD, Desar IME, Boerrigter E, van Erp NP. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment: an update. Lancet Oncol 2023; 24: e229. Available at: https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(23)00216-4/fulltext
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4. Enfortumab vedotin (Padcev®) SmPC. Last updated: 27/09/2024. Accessed: October 2024. Available at: https://www.ema.europa.eu/en/documents/product-information/padcev-epar-product-information_en.pdf

Version	Date	Amendment	Approved By
1	01/12/2023		Prof Maccon Keane
2	15/12/2023	Addition of skin assessment to baseline and regular tests	Prof Maccon Keane

3	25/03/2025	Reviewed. Updated exclusions and cautions sections. Updated regimen in line with NCCP standardisation.	Prof Maccon Keane
3a	08/05/2025	Update to ICD10 code.	NCCP

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.