Regimen Monograph

Regimen Name | Drug Regimen | Cycle Frequency | Premedication and Supportive Measures | Dose Modifications | Adverse Effects | Interactions | Drug Administration and Special Precautions | Recommended Clinical Monitoring | Administrative Information | References | Other Notes | Disclaimer

A - Regimen Name

ENFO Regimen

Enfortumab vedotin

Disease Site	Genitourinary Bladder / Urothelial
Intent	Palliative
Regimen Category	**Evidence-Informed :** Regimen is considered appropriate as part of the standard care of patients; meaningfully improves outcomes (survival, quality of life), tolerability or costs compared to alternatives (recommended by the Disease Site Team and national consensus body e.g. pan-Canadian Oncology Drug Review, pCODR). Recommendation is based on an appropriately conducted phase III clinical trial relevant to the Canadian context OR (where phase III trials are not feasible) an appropriately sized phase II trial. Regimens where one or more drugs are not approved by Health Canada for any indication will be identified under Rationale and Use.
Rationale and Uses	For the treatment of locally advanced unresectable or metastatic urothelial cancer, in patients who have previously received platinum-containing chemotherapy and a PD-1 or PD-L1 inhibitor, and have good performance status
Supplementary Public Funding	**enfortumab vedotin** New Drug Funding Program (Enfortumab Vedotin - Previously Treated Advanced or Metastatic Urothelial Cancer) (NDFP Website)

back to top

B - Drug Regimen

enfortumab vedotin*	1.25 mg /kg	IV	Days 1, 8, 15

Subsequent doses should NOT be administered less than 1 week apart.

*Dose is capped at a weight of 100 kg.

back to top

C - Cycle Frequency

REPEAT EVERY 28 DAYS

Until disease progression or unacceptable toxicity

back to top

D - Premedication and Supportive Measures

Antiemetic Regimen: Low

- Also refer to CCO Antiemetic Recommendations.

Screen for hepatitis B virus in all cancer patients starting systemic treatment. Refer to the hepatitis B virus screening and management guideline.

Premedication (Prophylaxis for Infusion Reactions):

- Routine premedication is not recommended. No premedication was given for the first dose of enfortumab vedotin during clinical trials.
- Patients who experience an infusion reaction may be premedicated for subsequent infusions. Premedication may include acetaminophen, an antihistamine (e.g., diphenhydramine hydrochloride), and a corticosteroid given 30–60 minutes prior to each infusion. (Powles 2021)

back to top

E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated.

Dosage with toxicity

Dose Level	Enfortumab Vedotin Dose (mg/kg)*
0	1.25
-1	1
-2	0.75
-3	0.5
-4	Discontinue

*For patients ≤ 100 kg. If weight is > 100 kg, dose should be based on 100 kg.

Toxicity	Grade/Severity	Action
Skin Reactions	Grade 1 or 2	Consider topical corticosteroids and antihistamines as needed.
	Grade 3, worsening reactions, or suspected SJS or TEN	Hold*. Consider dermatological referral. Resume at same dose or consider 1 dose level ↓.
	Grade 4, recurrent Grade 3, or confirmed SJS or TEN	Discontinue.
Hyperglycemia	Blood glucose > 13.9 mmol/L	Hold*. Resume at same dose.
Pneumonitis	Grade 2	Hold*. Resume at the same dose or consider 1 dose level ↓.
	Grade 3 or 4	Discontinue.
Peripheral Neuropathy	Grade 2	Hold*. 1st occurrence: resume at same dose. Recurrence: resume at 1 dose level ↓.
	Grade 3 or 4	Discontinue.

Ocular Toxicity	Any	Consider holding or reducing dose. Consider ophthalmology referral if symptoms do not resolve or worsen.
Other Non-hematologic Toxicity	Grade 3	Hold*. Resume at same dose or consider 1 dose level ↓.
	Grade 4	Discontinue.
Hematologic Toxicity	Grade 2 thrombocytopenia	Hold*. Resume at same dose or consider 1 dose level ↓.
	Grade 3	
	Grade 4	Hold*. Resume at 1 dose level ↓ or discontinue.

*Do not restart treatment until blood glucose resolved to ≤ 13.9 mmol/L, and other toxicities ≤ Grade 1.

Hepatic Impairment

MMAE exposure is likely increased in patients with moderate or severe hepatic impairment.

Hepatic Impairment	Enfortumab Vedotin Dose
Child-Pugh A	No adjustment required.
Child-Pugh B	Not studied; avoid use.
Child-Pugh C	

Renal Impairment

No dosage adjustment is required with renal impairment. The effect of end stage renal disease with or without dialysis on the pharmacokinetics of ADC or unconjugated MMAE is unknown.

Dosage in the Elderly

No dose adjustment is required in patients ≥ 65 years of age. No overall differences in efficacy were observed between patients ≥ 65 years and those < 65 years. Patients ≥ 65 years were more like to experience serious adverse events or treatment discontinuation.

back to top

F - Adverse Effects

Refer to enfortumab vedotin drug monograph(s) for additional details of adverse effects.

Very common (≥ 50%)	Common (25-49%)	Less common (10-24%)	Uncommon (< 10%), but may be severe or life-threatening
• Rash (may be severe) • Fatigue • Peripheral neuropathy (may be severe)	• Alopecia • Anorexia, weight loss • Diarrhea • Nausea, vomiting • Constipation • Dysgeusia • Musculoskeletal pain	• Dry eye (may be severe) • Abdominal pain • ↑ LFTs • Myelosuppression ± infection, bleeding (may be severe) • Hyperglycemia (may be severe) • Insomnia	• Tachycardia • Pneumonitis • Extravasation • Epidermal necrosis • Stevens-Johnson syndrome • Toxic epidermal necrolysis • Hand-foot syndrome • Ocular disorders

back to top

G - Interactions

Refer to enfortumab vedotin drug monograph(s) for additional details.

back to top

H - Drug Administration and Special Precautions

Refer to enfortumab vedotin drug monograph(s) for additional details.

Administration

- Reconstitute each vial with Sterile Water for Injection. Swirl gently; do not shake the solution.
- Dilute in D5W, NS, or Ringer's lactate. Invert infusion bag gently to mix.
- Final concentration should be 0.3 mg/mL to 4 mg/mL.
- Administer as an IV infusion over 30 minutes. Do NOT administer as an IV push or bolus.
- Do NOT administer other drugs through the same IV line.
- If extravasation occurs during administration, stop the infusion and monitor for adverse reactions (e.g., skin and soft tissue injury).
- Do not expose the vials or diluted drug to direct sunlight.
- Store unopened vials in a refrigerator at 2-8^{o}C. Do not freeze.

Contraindications/Precautions

- Patients who have a hypersensitivity to this drug or any of its components

Warning/Precautions

- Do NOT start enfortumab vedotin in patients with pre-existing grade ≥ 2 neuropathy, ongoing clinically significant toxicity from previous treatment, active CNS metastases, uncontrolled diabetes, active keratitis or corneal ulcerations.

Pregnancy/Lactation

- This regimen is not recommended for use in pregnancy. Adequate contraception should be used by patients and their partners while on treatment and after the last treatment dose. Recommended methods and duration of contraception may differ depending on the treatment. Refer to the drug monograph(s) for more information.
- Breastfeeding is not recommended during this treatment and after the last treatment dose. Refer to the drug monograph(s) for recommendations after the last treatment dose (if available).
- Fertility effects: Probable

back to top

I - Recommended Clinical Monitoring

Treating physicians may decide to monitor more or less frequently for individual patients but should always consider recommendations from the product monograph.

Refer to the hepatitis B virus screening and management guideline for monitoring during and after treatment.

Recommended Clinical Monitoring

- CBC; Baseline, before each dose, and as clinically indicated
- Liver function tests; Baseline, before each dose, and as clinically indicated
- Blood glucose; Baseline and as clinically indicated (more frequently in patients with or at risk for diabetes mellitus or hyperglycemia)
- Clinical toxicity assessment for infection, bleeding, extravasation, peripheral neuropathy, GI, ocular, respiratory and skin effects; At each visit
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

back to top

J - Administrative Information

Approximate Patient Visit	0.5 to 1 hour
Pharmacy Workload (average time per visit)	23.407 minutes
Nursing Workload (average time per visit)	41.667 minutes

back to top

K - References

CADTH Reimbursement Recommendation: Enfortumab Vedotin (Padcev). Canadian Journal of Health Technologies. January 2022.

Enfortumab vedotin drug monograph. Ontario Health (Cancer Care Ontario).

Powles T, Rosenberg JE, Sonpavde GP, et al. Enfortumab vedotin in previously treated advanced urothelial carcinoma. N Engl J Med 2021;384(12):1125-35. doi: 10.1056/NEJMoa2035807.

March 2024 Updated Dose modifications, Dosage with hepatic impairment, and Pregnancy/lactation sections

back to top

M - Disclaimer

Regimen Abstracts

A Regimen Abstract is an abbreviated version of a Regimen Monograph and contains only top level information on usage, dosing, schedule, cycle length and special notes (if available). It is intended for healthcare providers and is to be used for informational purposes only. It is not intended to constitute or be a substitute for medical advice, and all uses of the Regimen Abstract are subject to clinical judgment. Such information is provided on an "as-is" basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information's quality, accuracy, currency, completeness, or reliability, and Cancer Care Ontario disclaims all liability for the use of this information, and for any claims, actions, demands or suits that arise from such use.

Information in regimen abstracts is accurate to the extent of the ST-QBP regimen master listings, and has not undergone the full review process of a regimen monograph. Full regimen monographs will be published for each ST-QBP regimen as they are developed.

Regimen Monographs

Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.

The information set out in the drug monographs, regimen monographs, appendices and symptom management information (for health professionals) contained in the Drug Formulary (the "Formulary") is intended for healthcare providers and is to be used for informational purposes only. The information is not intended to cover all possible uses, directions, precautions, drug interactions or adverse effects of a particular drug, nor should it be construed to indicate that use of a particular drug is safe, appropriate or effective for a given condition. The information in the Formulary is not intended to constitute or be a substitute for medical advice and should not be relied upon in any such regard. All uses of the Formulary are subject to clinical judgment and actual prescribing patterns may not follow the information provided in the Formulary.

The format and content of the drug monographs, regimen monographs, appendices and symptom management information contained in the Formulary will change as they are reviewed and revised on a periodic basis. The date of last revision will be visible on each page of the monograph and regimen. Since standards of usage are constantly evolving, it is advised that the Formulary not be used as the sole source of information. It is strongly recommended that original references or product monograph be consulted prior to using a chemotherapy regimen for the first time.

Some Formulary documents, such as the medication information sheets, regimen information sheets and symptom management information (for patients), are intended for patients. Patients should always consult with their healthcare provider if they have questions regarding any information set out in the Formulary documents.

While care has been taken in the preparation of the information contained in the Formulary, such information is provided on an "as-is" basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information's quality, accuracy, currency, completeness, or reliability.

CCO and the Formulary's content providers shall have no liability, whether direct, indirect, consequential, contingent, special, or incidental, related to or arising from the information in the Formulary or its use thereof, whether based on breach of contract or tort (including negligence), and even if advised of the possibility thereof. Anyone using the information in the Formulary does so at his or her own risk, and by using such information, agrees to indemnify CCO and its content providers from any and all liability, loss, damages, costs and expenses (including legal fees and expenses) arising from such person's use of the information in the Formulary.

back to top