Regimen Monograph

A - Regimen Name

AVEL(MNT) Regimen

Avelumab

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
First line maintenance treatment for unresectable, locally advanced or metastatic urothelial cancer, in patients with good performance status, who did not have disease progression with first-line platinum-based induction chemotherapy (e.g. 4-6 cycles of CISPGEMC or CRBPGEMC)

Supplementary Public Funding
avelumab
New Drug Funding Program (Avelumab - Maintenance Treatment for Unresectable Locally Advanced or Metastatic Urothelial Carcinoma) (NDFP Website)

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B - Drug Regimen

avelumab*	10 mg /kg	IV	Day 1

*Maximum 800 mg per dose

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C - Cycle Frequency

REPEAT EVERY 14 DAYS

Until disease progression or unacceptable toxicity, whichever comes first

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D - Premedication and Supportive Measures

Antiemetic Regimen: Minimal

Other Supportive Care:

Also refer to CCO Antiemetic Recommendations.

Premedication with an antihistamine and acetaminophen prior to the first 4 infusions is recommended. Consider for subsequent infusions based on clinical judgement and prior infusion reactions.

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E - Dose Modifications

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

Avoid the use of corticosteroids or immunosuppressants before starting treatment.

Dosage with toxicity

Healthcare professionals should also consult the most recent avelumab product monograph for additional information.

Dose reductions are not recommended for avelumab. Doses may be delayed or discontinued based on toxicity.

Summary of Principles of Management of Immune-Related Adverse Effects (irAEs):

- Immune-related adverse effects (irAEs) are different in their presentation, onset and duration compared to conventional chemotherapy. Patient and provider education is essential.
- Initial irAE presentation can occur months after completion of treatment and affect multiple organs.
- Dose escalation or reduction is not recommended.
- If no other cause can be identified (such as infection), any new symptom should be considered immune-related and prompt treatment initiated.
- Organ-specific system-based toxicity management is recommended.

Refer to CCO's Immune Checkpoint Inhibitor Toxicity Management Guideline for detailed descriptions of Immune-related toxicities and their management.

Infusion-related reactions:

Toxicity Grade	Action
1	Slow infusion rate by 50%
2	Interrupt infusion until ≤ grade 1; restart at 50% lower infusion rate.
≥3	Discontinue

Hepatic Impairment

Refer to CCO's Immune Checkpoint Inhibitor Toxicity Management Guideline for detailed descriptions for immune-related hepatic toxicity management.

Hepatic impairment	Avelumab dose
Mild (bilirubin ≤ ULN and AST > ULN OR bilirubin 1-1.5 x ULN)	no change
Moderate (bilirubin 1.5-3 x ULN)	
Severe (bilirubin > 3 x ULN)	no data

Renal Impairment

Refer to CCO's Immune Checkpoint Inhibitor Toxicity Management Guideline for detailed descriptions for immune-related renal toxicity management.

Creatinine clearance (ml/min)	Avelumab dose
≥ 60	no change
30-59	
15-29	

Dosage in the Elderly

No overall differences in safety or efficacy were reported between elderly patients and younger patients. There is limited safety data in patients ≥ 75 years of age in maintenance treatment after first-line platinum-based chemotherapy.

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F - Adverse Effects

Refer to avelumab drug monograph(s) for additional details of adverse effects

Common (25-49%)	Less common (10-24%)	Uncommon (< 10%), but may be severe or life-threatening
• Fatigue	• Musculoskeletal pain • Rash, pruritus • Urinary tract infection • Diarrhea (may be severe) • Anemia • Constipation • Nausea, vomiting • Fever/chills • Anorexia, weight loss • Cough, dyspnea • Edema • Abdominal pain • Hypothyroidism • Infusion-related reaction (may be severe) • Hypertension	• Hyperthyroidism • Hypersensitivity • Adrenal insufficiency • Pneumonitis • Myocarditis • Hepatitis • Nephrotoxicity, nephritis • Diabetes mellitus • Myositis • Rheumatoid arthritis • Myasthenia gravis • Guillain-Barre syndrome • Uveitis • Erythema multiforme

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G - Interactions

Refer to avelumab drug monograph(s) for additional details

No formal pharmacokinetic drug-drug interaction studies have been conducted. Avelumab is mainly metabolized through catabolic pathways; it is not expected that avelumab will have drug-drug interactions with other medications.

Use of systemic corticosteroids or immunosuppressants should be avoided prior to starting avelumab because of the potential for interference with avelumab's efficacy. They can be used to treat immune-mediated reactions after starting the drug.

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H - Drug Administration and Special Precautions

Refer to avelumab drug monograph(s) for additional details

Administration

- DO NOT administer as an IV push or bolus.
- Dilute avelumab with 0.9% or 0.45% saline solution (preferably 250 mL) prior to infusion. It must not be mixed with other products or diluents.
- Mix the diluted solution by gentle inversion; do not shake.
- Infuse over 60 minutes using a sterile, non-pyrogenic, low-protein binding 0.2 micrometer in-line or add-on filter.
- Do not co-administer with other drugs through the same IV line; flush the line with 0.9% or 0.45% saline after administration.
- Avelumab is compatible with polyethylene, polypropylene and ethylene vinyl acetate infusion bags, glass bottles, polyvinyl chloride infusion sets and in-line filters with polyethersulfone membranes and pore sizes of 0.2 micrometer.
- Avelumab vials should be stored at 2-8^{o}C; do not freeze.
- Store in the original container and protect from light.

Contraindications/Precautions

- Patients who have a hypersensitivity to this drug or any components of the formulation.

Warnings/Precautions

- Use with caution and monitor closely in patients with pre-existing conditions such as colitis, hepatic impairment, respiratory or endocrine disorders, such as hypo or hyperthyroidism or diabetes mellitus.
- Avelumab may cause fatigue; patients should be advised not to drive or operate machinery/tools until they are sure of feeling well.

Pregnancy / Lactation

- Avelumab may cause fetal harm and is not recommended for use in pregnancy. Adequate contraception should be used by both sexes during treatment, and for at least **1 month** after the last dose.
- Breastfeeding is not recommended during treatment and for at least **1 month** after the last dose.
- Fertility effects: Unknown

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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.

Recommended Clinical Monitoring

- CBC; Baseline, before each dose and as clinically indicated
- Liver function tests; Baseline, before each dose and as clinically indicated; frequent with severe toxicity
- Renal function tests; Baseline, periodically during treatment and as clinically indicated; frequent with severe toxicity
- Thyroid function tests; Baseline and before each dose, or at least once monthly
- Blood glucose; Baseline, periodically during treatment and as clinically indicated
- Clinical toxicity assessment for infusion-related reactions, fatigue, immune-mediated reactions, including GI, skin, respiratory, neurologic, cardiac, ophthalmic and endocrine toxicities; At each visit and as clinically indicated
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

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J - Administrative Information

Approximate Patient Visit	1.5 to 2 hours
Pharmacy Workload (average time per visit)	20.1 minutes
Nursing Workload (average time per visit)	44.167 minutes

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K - References

Avelumab drug monograph, Ontario Health (Cancer Care Ontario).

pCODR expert review committee final recommendation: Avelumab (Bavencio) for urothelial carcinoma. March 23, 2021.

Powles T, Park SH, Voog E, et al. Avelumab maintenance therapy for advanced or metastatic urothelial carcinoma. N Engl J Med . 2020 Sep 24;383(13):1218-1230. doi: 10.1056/NEJMoa2002788.

PEBC Advice Documents or Guidelines

- Systemic Therapy for Metastatic Urothelial Cancer: Endorsement of a Portion of the European Association of Urology Guideline on Muscle-Invasive and Metastatic Bladder Cancer

September 2023 Updated the "Administrative Information" section with pharmacy and nursing workload.

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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.

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