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

AVEL Regimen

Avelumab

Disease Site	Skin Merkel Cell
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 metastatic Merkel cell carcinoma (MCC) in previously treated adults or adults ineligible for treatment with chemotherapy.
Supplementary Public Funding	**avelumab** New Drug Funding Program (Avelumab - Metastatic Merkel Cell Carcinoma) (NDFP Website)

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B - Drug Regimen

avelumab	10 mg /kg	IV	Day 1

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C - Cycle Frequency

REPEAT EVERY 14 DAYS

Until disease progression or unacceptable toxicity

Note: NDFP funds a maximum of 12 months after confirmation of complete response.

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D - Premedication and Supportive Measures

Antiemetic Regimen: Minimal

Other Supportive Care:

- 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 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

Differences in safety or efficacy between patients aged 65 and older compared to younger patients have not been evaluated.

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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 • 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 • Sarcoidosis

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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

- Patients with pre-existing autoimmune disease (AID) were excluded from clinical trials. Data from post-marketing suggest that there are risks of immune-related reactions in patients with pre-existing AID. Consider the risks versus the benefit of giving avelumab in these patients.
- 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

- 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: 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.

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; 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).

D'Angelo SP, Lebbé C, Mortier L, et al. First-line avelumab in a cohort of 116 patients with metastatic Merkel cell carcinoma (JAVELIN Merkel 200): primary and biomarker analyses of a phase II study. J Immunother Cancer 2021 Jul;9(7):e002646.

Kaufman HL, Russell J, Hamid O, et al. Avelumab in patients with chemotherapy-refractory metastatic Merkel cell carcinoma: a multicentre, single-group, open-label, phase 2 trial. Lancet Oncol 2016;17(10):1374-85.

January 2025 Updated Adverse effects and Warnings sections

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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.

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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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