Regimen Monograph

A - Regimen Name

DURV Regimen

Durvalumab

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	Treatment of patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy

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B - Drug Regimen

durvalumab*	10 mg /kg	IV	Every 2 weeks

(This drug is not currently publicly funded for this regimen and intent)

OR

durvalumab	1500 mg	IV	Every 4 weeks

(This drug is not currently publicly funded for this regimen and intent)

Patients with weight ≤ 30 kg must receive 10mg/kg every 2 weeks weight-based dosing, until weight increases to > 30 kg.

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C - Cycle Frequency

10 mg/kg dosing: Repeat every 2 weeks

1500 mg dosing: Repeat every 4 weeks

Until disease progression or unacceptable toxicity

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D - Premedication and Supportive Measures

Antiemetic Regimen: Minimal

- 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):

- Consider pre-medication in patients with prior infusion related 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 durvalumab product monograph for additional information.
- Dose reductions are not recommended for durvalumab . Doses may be delayed or discontinued based on toxicity.
- Hold durvalumab for severe infections; manage symptoms and treat with anti-infectives.

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.**

Non-immune-related toxicity

Severity	Action
Grade 2 or 3	Hold until ≤ Grade 1 or baseline
Grade 4	Discontinue*

*Decision to discontinue for lab abnormalities should be based on signs/ symptoms and clinical judgement.

Management of Infusion related Reactions

Severity	Action
Grade 1 or 2	Interrupt or slow the rate of infusion by 50%. Consider pre-medications prior to subsequent infusions.
Grade 3 or 4	Discontinue

Hepatic Impairment

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

Hepatic Impairment	Durvalumab Dose
Mild (bilirubin ≤ ULN and AST > ULN or bilirubin >1 to 1.5 x ULN and any AST)	No dosage adjustment is required
Moderate (bilirubin >1.5 to 3 x ULN and any AST)	
Severe (bilirubin >3 x ULN and any AST)	No data

Renal Impairment

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

Creatinine Clearance (mL/min)	Durvalumab Dose
≥ 30	No dosage adjustment is required
< 30	No data

Dosage in the Elderly

No dosage adjustment is required for patients aged 65 and older. No overall differences in safety or efficacy were reported between patients ≥ 65 years of age and younger patients.

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F - Adverse Effects

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

Less common (10-24%)	Uncommon (< 10%), but may be severe or life-threatening
• Fatigue • Rash/pruritus (may be severe) • Diarrhea (may be severe - colitis) • Infection • Anorexia • Hypothyroidism • Constipation • Cough • Musculoskeletal pain • Headache • Abdominal pain • Insomnia	• Hepatitis • Creatinine increased / nephritis • Pneumonitis • Hyperthyroidism • Infusion related reaction • Adrenal insufficiency • Hypophysitis • Thyroiditis • Type 1 diabetes mellitus • Immune thrombocytopenic purpura • Myositis • Rhabdomyolysis • Myasthenia gravis • Guillain-Barre syndrome • Aseptic meningitis • Myocarditis • Uveitis • Pancreatitis • Stevens-Johnson syndrome • Toxic epidermal necrolysis

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G - Interactions

Refer to durvalumab drug monograph(s) for additional details.

No formal pharmacokinetic drug-drug interaction studies have been conducted.

Use of systemic corticosteroids or immunosuppressants should be avoided prior to starting durvalumab because of potential interference with 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 durvalumab drug monograph(s) for additional details.

Administration

- Administer by IV infusion over 60 minutes using a sterile, low-protein binding 0.2-0.22 micron in-line filter.
- Durvalumab is supplied as a single-use, preservative-free vial.
- Visually inspect the vial for particulates and discolouration prior to dilution. Undiluted solution should be clear to opalescent and colorless to slightly yellow.
- Using aseptic technique, withdraw the required drug volume and transfer to an IV bag of NS or D5W to a final concentration of 1 to 15 mg/mL.
- Mix by gentle inversion; do not shake.
- Do not co-administer with other drugs; flush line after each dose.
- Store unopened drug vials under refrigeration (2-8^{o}C) in the original package.
- Protect from light and do not freeze.

Contraindications

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

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.
- Some clinical trials excluded patients with a history of immunodeficiency; medical conditions that required systemic immunosuppression; history of severe immune-mediated adverse reactions; history of allogeneic organ transplantation; prior exposure to immune checkpoint inhibitors; history of chest radiation therapy; untreated CNS metastases; HIV; active tuberculosis, hepatitis B or C infection, or patients who received live attenuated vaccine(s) within 30 days before or after starting durvalumab.
- Use caution when driving or operating machinery as patients may experience adverse effects affecting their ability to concentrate or react.

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 and Q3-6 weeks, or as clinically indicated
- Liver function tests; Baseline and Q3-6 weeks, or as clinically indicated
- Renal function tests, urine protein; Baseline and Q3-6 weeks, or as clinically indicated
- Thyroid function tests; Baseline, and as clinically indicated
- Blood glucose; Baseline, and as clinically indicated
- Clinical toxicity assessment for infection, fatigue, infusion reactions, immune-mediated reactions, including GI, skin, ocular, respiratory, neurologic, cardiac, musculoskeletal, hematologic 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 hours
Pharmacy Workload (average time per visit)	18.6 minutes
Nursing Workload (average time per visit)	40.75 minutes

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K - References

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

Powles T, O'Donnell PH, Massard C, et al. Efficacy and safety of durvalumab in locally advanced or metastatic urothelial carcinoma: updated results from a phase 1/2 open-label study. JAMA Oncol 2017;3(9):e172411.

Sonpavde GP, Sternberg CN, Loriot Y, et al. Primary results of STRONG: An open-label, multicenter, phase 3b study of fixed-dose durvalumab monotherapy in previously treated patients with urinary tract carcinoma. Eur J Cancer. 2022 Mar;163:55-65.

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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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