

Regimen Monograph

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A - Regimen Name

DARO Regimen

Darolutamide

Disease Site Genitourinary
 Prostate

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 high risk non-metastatic castration resistant prostate cancer (nmCRPC), in patients with ECOG status ≤ 2

(Refer to EAP for full details of funding criteria and exclusions)

Supplementary Public Funding [darolutamide](#)
Exceptional Access Program (darolutamide - For the treatment of high risk non-metastatic castration resistant prostate cancer (nmCRPC) according to clinical criteria) ([EAP Website](#))

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B - Drug Regimen[darolutamide](#)

600 mg

PO

BID

Patients should also receive a gonadotropin-releasing hormone (GnRH) analog unless they have had a bilateral orchiectomy.

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Until disease progression or unacceptable toxicity

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Antiemetic Regimen: Not applicable

Other Supportive Care:

- Optimize management of cardiovascular risk factors (e.g., hypertension, diabetes, or dyslipidemia).

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

Dosage with toxicity

Dose Level	Darolutamide Dose
0	600 mg BID
-1	300 mg BID
-2	Discontinue

Toxicity	Action
Intolerable or \geq grade 3	Hold or \downarrow 1 dose level until symptoms improve. Then may resume at previous dose.
Drug-induced liver injury (DILI)	Discontinue.
Seizure	Consider discontinuing.

Hepatic Impairment

During a pharmacokinetic (PK) study, patients with moderate hepatic impairment had a 1.9-fold higher darolutamide exposure.

Hepatic Impairment	Darolutamide Dose
Mild (Child-Pugh class A)	No dose adjustment necessary
Moderate (Child-Pugh class B)	300 mg BID
Severe (Child-Pugh class C)	Not studied

Renal Impairment

During PK studies, patients with mild, moderate and severe renal impairment had a 1.1-, 1.3- and 1.5-fold higher darolutamide exposure, respectively.

Creatinine Clearance (mL/min)	Darolutamide Dose
≥ 30	No dose adjustment necessary
15 - 29*	300 mg BID (limited data)
$< 15^{**}$	Not studied

*Not on hemodialysis

**Including patients with ESRD on dialysis

Dosage in the Elderly

No clinically relevant differences in safety or efficacy in patients ≥ 65 years of age. Compared to patients < 65 years of age, patients > 85 years of age had a 1.6-fold higher darolutamide exposure without associated greater toxicity.

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F - Adverse Effects

Refer to [darolutamide](#) drug monograph(s) for additional details of adverse effects.

Less common (10-24%)	Uncommon (< 10%), but may be severe or life-threatening
<ul style="list-style-type: none"> • \uparrow LFTs • Fatigue 	<ul style="list-style-type: none"> • Cardiac ischemia • Heart failure • Thromboembolism • Drug-induced liver injury • Fractures • Seizure • Urinary retention, hematuria

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G - Interactions

Refer to [darolutamide](#) drug monograph(s) for additional details.

- Avoid concomitant use when possible with **combined** P-gp and strong CYP3A4 inducers (e.g. rifampin) due to \downarrow darolutamide concentration.
- Consider an alternative with less inhibition to **combined** P-gp, BCRP, and strong CYP3A4 inhibitors (e.g. itraconazole) due to \uparrow risk of darolutamide toxicity. If co-administered, monitor closely.

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- Avoid concomitant use when possible with BCRP substrates (e.g. rosuvastatin) due to ↑ risk of substrate toxicity. If co-administered, monitor closely; consider substrate dose reduction.
 - Caution with concomitant use of OATP1B1 or OATP1B3 substrates (e.g. rosuvastatin) due to ↑ risk of substrate toxicity. Monitor for toxicity and consider substrate dose reduction.

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H - Drug Administration and Special Precautions

Refer to [darolutamide](#) drug monograph(s) for additional details.

Administration

- Administer darolutamide with food.
- Tablets should be swallowed whole.
- If a dose is missed, patient may take as soon as possible. If it is close to the next dose, patient should not double the dose to make up for the missed dose.
- Store at room temperature (15°C to 30°C). Keep bottle tightly closed after opening. Once bottle is opened, darolutamide is stable for 3 months.

Contraindications

- Patients who are hypersensitive to this drug or any of its components.

Warnings/Precautions

- Patients with uncontrolled hypertension, recent stroke, myocardial infarction, severe/unstable angina pectoris, coronary/peripheral artery bypass graft or CHF NYHA Class III or IV were excluded in clinical trials.
- Tablets contain lactose; carefully consider use in patients with hereditary galactose intolerance, severe lactase deficiency or glucose-galactose malabsorption.

Pregnancy/Lactation

- Darolutamide is **not indicated for use in females**. It may cause harm to a developing fetus or lead to loss of pregnancy. Adequate contraception should be used by patients and their partners during treatment, and for **3 months** after the last dose.

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- Patients who produce sperm should use a condom and not donate sperm during treatment, and for **3 months** after the last dose.
 - Excretion into breast milk: Unknown
 - Fertility Effects: Probable

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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 and as clinically indicated
- Liver function tests; Baseline and as clinically indicated
- Renal function tests; Baseline and as clinically indicated
- PSA and radiographic disease progression; Baseline and as clinically indicated
- Clinical toxicity assessment for fatigue, seizures, musculoskeletal, dermatologic, GI and cardiovascular effects; At each visit
- Grade toxicity using the current [NCI-CTCAE \(Common Terminology Criteria for Adverse Events\) version](#)

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K - References

Darolutamide drug monograph. Ontario Health (Cancer Care Ontario).

Fizazi K, Shore N, Tammela TL, et al. Darolutamide in nonmetastatic, castration-resistant prostate cancer. *N Engl J Med* 2019;380:1235-46.

Fizazi K, Shore N, Tammela TL, et al. Nonmetastatic, Castration-Resistant Prostate Cancer and Survival with Darolutamide. *N Engl J Med*. 2020 Sep 10;383(11):1040-1049.

March 2024 Updated Dose modifications section

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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.

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