Regimen Monograph

A - Regimen Name

BICALPRL Regimen

Bicalutamide-Leuprolide

Disease Site

Genitourinary - Prostate

Intent

Neoadjuvant
Adjuvant
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 cytoreduction before brachytherapy
- in combination with radiotherapy for the treatment of high-risk localized prostate cancer
- for palliative treatment of recurrent, progressive or metastatic prostate cancer

Supplementary Public Funding

leuprolide
ODB - General Benefit (leuprolide - long-acting formulation) (ODB Formulary)

bicalutamide
ODB - General Benefit (bicalutamide) (ODB Formulary)

back to top

B - Drug Regimen

leuprolide

(Various dosage strengths and dose schedules available.)

Leuprolide*

7.5 mg	EVERY MONTH
or	
22.5mg	EVERY 3 MONTHS
or	
30mg	EVERY 4 MONTHS
or	
45mg	EVERY 6 MONTHS

(Outpatient prescription in fixed-dose injection kits of 7.5mg, 22.5mg, 30mg, 45mg)

*Route of administration depends on product brand and formulation. Refer to the leuprolide drug monograph.

AND

bicalutamide	50 mg	PO	Daily

(Outpatient prescription in multiples of 50mg tablets)

back to top

C - Cycle Frequency

Duration of therapy is dependent on the indication.

- Neoadjuvant - Generally up to 6 months in duration
- Adjuvant - Generally up to 3 years
- Palliative - Continue until disease progression

back to top

E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated. The following recommendations have been adapted from clinical trials or product monographs and could be considered.

Dosage with toxicity

Toxicity	Bicalutamide	Leuprolide
Myelosuppression	No adjustment required	
Pneumonitis	Discontinue	
Cardiotoxicity, arterial or venous thromboembolism	Discontinue	
Grade 3 or 4 LFT increases	Discontinue	Hold until recovery then restart. If recurs consider discontinuing
Pituitary apoplexy	No adjustment required	Discontinue

Hepatic Impairment

Leuprolide: No adjustment required. See table above for management of drug-related hepatotoxicity.

Bicalutamide:

	Bicalutamide
Mild	No adjustment needed
Moderate	Caution
Severe	Caution

Renal Impairment

Bicalutamide and leuprolide: No adjustment required

back to top

F - Adverse Effects

Refer to leuprolide, bicalutamide drug monograph(s) for additional details of adverse effects

Most Common Side Effects	Less Common Side Effects, but may be Severe or Life Threatening
• Androgen withdrawal symptoms • Constipation/diarrhea, abdominal pain • Fatigue • Disease flare (may be severe) • Osteopenia/osteoporosis • Urinary Symptoms • Edema • Musculoskeletal pain, headache • Injection site reactions • Cough/dyspnea (may be severe) • Rash • Glucose intolerance	• Pneumonitis • Arterial thromboembolism • Venous thromboembolism • GI obstruction/hemorrhage • Arrhythmia • Cardiotoxicity • Hypersensitivity • ↑ LFTs • Pituitary apoplexy • Seizures • ↑ QTc • Depression (may be severe) • Hepatotoxicity

back to top

G - Interactions

Refer to leuprolide, bicalutamide drug monograph(s) for additional details

back to top

H - Drug Administration and Special Precautions

Refer to leuprolide, bicalutamide drug monograph(s) for additional details

Administration (leuprolide):

- Outpatient prescription; administer in Cancer Centre or physician's office
- Vary injection site
- For long-acting preparations, reconstitute with supplied diluent immediately before injection as directed (see product monograph).
- Do not give multiple monthly injections together to make up a q3 or q4 month dose, as the release characteristics are different

Lupron Depot® 7.5mg, 22.5mg and 30mg:

- For Intramuscular use only.
- Usual sites of injection include the anterior thigh, gluteal area or deltoid. Vary injection sites.
- Store at room temperature.

Eligard® 7.5mg, 22.5mg, 30mg, and 45mg:

- For Subcutaneous use only. Choose an injection site on the abdomen, upper buttocks, or anywhere with adequate amounts of subcutaneous tissue.
- Keep refrigerated, or may be stored at room temperature in original packaging for a period of 8 weeks before administration.
- Allow product to reach room temperature before using.

Administration (bicalutamide):

- Outpatient prescription for home administration
- May be taken with or without food

Warnings/precautions:

Leuprolide:

- contraindicated **i**n patients with hypersensitivity to the drug, its components or similar nonapeptides
- contains benzyl alcohol and may cause local reactions.
- Use with caution in patients with osteoporosis (or risk factors for osteoporosis), diabetes, risk factors for QT prolongation, history of depression, cardiovascular disease, metastatic vertebral lesions and/or urinary tract obstruction due to the risk of disease flare, and in patients at risk of convulsions

Bicalutamide:

- contraindicated in patients with hypersensitivity to the drug or any of its components, in

localized prostate cancer undergoing ”watchful waiting”, in females and children.
- results in fluid retention and should be used with caution in patients with cardiac disease as well as in patients at risk for prolonged QTc.
- contains lactose; use should be carefully considered in patients with hereditary galactose intolerance, severe lactase deficiency or glucose-galactose malabsorption.
- effects on long-term **fertility** have not been established; may lead to inhibition of spermatogenesis.

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.

Recommended Clinical Monitoring

- Blood glucose/HbA1c; baseline and periodic, especially in diabetic patients
- EKG, Electrolytes (including K, Ca, Mg); baseline, also regular for patients at risk of electrolyte abnormality and QT prolongation
- Liver function tests; baseline and regular
- PSA; baseline and periodic
- Clinical assessment for disease flare, osteoporosis, injection site reactions, fluid retention, pneumonitis, androgen withdrawal effects, psychiatric, cardiovascular, hepatic effects and thromboembolism; at each visit

- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

Suggested Clinical Monitoring

- Hemoglobin; baseline and periodic

back to top

J - Administrative Information

Outpatient prescription; Leuprolide drug administration at Cancer Centre or physician's office

back to top

K - References

Bicalutamide and leuprolide drug monographs, Cancer Care Ontario.

Crook JM, O'Callaghan CJ, Duncan G, et al. Intermittent androgen suppression for rising PSA levels after radiotherapy. N Engl J Med 2012;367:895-903.

Denham JW, Steigler A, Lamb DS, et al. Short-term neoadjuvant androgen deprivation and radiotherapy for locally advanced prostate cancer: 10-year data from the TROG 96.01 randomised trial. Lancet Oncol 2011;12(5):451-9.

Heidenreich A, Bellmunt J, Bolla M, et al. EAU Guidelines on Prostate Cancer. Part 1: Screening, Diagnosis, and Treatment of Clinically Localised Disease. European Urology 2011;59:61-71.

Loblaw DA, Virgo KS, Nam R, et al. Initial Hormonal Management of Androgen-Sensitive Metastatic, Recurrent, or Progressive Prostate Cancer: 2007 Update of an American Society of Clinical Oncology Practice Guideline. J Clin Oncol 2007; 25: 1596-605.

Mottet N, Bellmunt J, Bolla M, et al EAU guidelines on prostate cancer. Part II: Treatment of advanced, relapsing, and castration resistant prostate cancer. European Urology 2011:59;572-83.

June 2017 Aligned dosing with ST-QBP, modified drug administration and special precautions section

back to top

M - Disclaimer

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

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back to top