**Regimen Monograph**



## A - Regimen Name

# BICAGOSE Regimen

**Bicalutamide-Goserelin**

**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** **goserelin**
ODB - General Benefit (ODB Formulary )

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

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## B - Drug Regimen

**goserelin**

| | | |
|---|---|---|
| 3.6mg | SC depot | EVERY 4 WEEKS |
| **OR** | | |
| 10.8mg | SC depot | EVERY 3 MONTHS (Q 13 weeks) |

(Outpatient prescription in fixed-dose injection kits of 3.6mg and 10.8mg)

| | | | |
|---|---|---|---|
| **bicalutamide** | 50 mg | PO | Daily |

(Outpatient prescription in multiples of 50mg tablets)

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## 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

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## D - Premedication and Supportive Measures

**Antiemetic Regimen:** Not applicable

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## 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**

Goserelin
Dosage with myelosuppression: No adjustment required.

Bicalutamide:

| Toxicity | Action |
|---|---|
| Myelosuppression | No adjustment required |
| Pneumonitis | Hold; investigate. If confirmed, discontinue. |
| Cardiac failure, arterial or venous thromboembolism | Discontinue |
| Grade 3 or 4 LFT increases | Discontinue |

**Hepatic Impairment**

Goserelin: No adjustment required.

Bicalutamide: No adjustment required in the presence of mild hepatic impairment. Caution should be exercised in moderate to severe hepatic impairment, as bicalutamide is extensively metabolized in the liver. Elimination is lower in subjects with severe hepatic impairment, leading to increased accumulation.

**Renal Impairment**

Goserelin: No adjustment required. (Although half-life is longer in patients with CrCl < 20 mL/min, it is not likely to cause drug accumulation.)

Bicalutamide: No adjustment required.

**Dosage in the elderly:**

Goserelin: No adjustment required.

Bicalutamide: No adjustment required.

**Children:**

Goserelin: Safety and efficacy not established.

Bicalutamide: Do not use.

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## F - Adverse Effects

Refer to goserelin, 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<br>• Myelosuppression (mild)<br>• Musculoskeletal pain<br>• Diarrhea / constipation<br>• Fatigue<br>• Nausea/vomiting<br>• Cough, dyspnea (may be severe)<br>• Edema<br>• Abdominal pain<br>• Infection<br>• Urinary symptoms<br>• Dizziness<br>• Osteoporosis<br>• ↓ Glucose tolerance | • Cardiotoxicity, arrhythmia<br>• Arterial thromboembolism<br>• Venous thromboembolism<br>• GI obstruction/hemorrhage<br>• Hypersensitivity<br>• ↑ LFTs<br>• Pneumonitis<br>• Pituitary hemorrhage<br>• Injection site injury/vascular injury |

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## G - Interactions

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

Goserelin:

- Caution with concomitant QT-prolonging drugs, as androgen deprivation can have an additive QT-prolonging effect.

Bicalutamide:

- Bicalutamide inhibits CYP3A4 (and 2C9, 2C19, 2D6 to a lesser extent); exercise caution when using drugs metabolized by CYP enzymes, especially those with a narrow therapeutic index.
- Bicalutamide displaces warfarin from protein binding, and can increase prothrombin time.
- Monitor when used with concomitant QT-prolonging drugs, as bicalutamide and goserelin (see above) can have an additive QT-prolonging effect.

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## H - Drug Administration and Special Precautions

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

### Administration:

Goserelin:

- Subcutaneous injection of the depot into the anterior abdominal wall, below the naval line. Injection usually given at the Cancer Centre or physician's office. Should be administered by a healthcare professional experienced in administering deep subcutaneous injections under the supervision of a physician. Drug supplied by outpatient prescription.
- Store in original packaging between 2ºC and 25ºC. Protect from light and moisture.

Bicalutamide:

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

### Contraindications:

Goserelin:

- In patients who have a hypersensitivity to this drug or any of its components.
- In females with undiagnosed abnormal vaginal bleeding.

Bicalutamide:

- In patients with hypersensitivity to the drug or any of its components.
- In localized prostate cancer undergoing "watchful waiting"
- In females and children.

**Other Warnings/Precautions:**

Goserelin:

- 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.
- Patients who experience anaphylaxis/anaphylactoid shock while on goserelin may require removal of the implant. If implant removal is necessary, it may be located by ultrasound.
- Goserelin required administration by deep subcutaneous injection and is not recommended in patients with low body mass index (BMI <18.5) or in patients who are fully anticoagulated (INR >2).

Bicalutamide:

- Bicalutamide 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.
- It contains lactose; use should be carefully considered in patients with hereditary galactose intolerance, severe lactase deficiency or glucose-galactose malabsorption.

**Pregnancy and Lactation:**

Goserelin:

- Genotoxicity: No
- Embryotoxicity: Yes
- Fetotoxicity: Yes
  Not recommended for use in pregnancy. Adequate non-hormonal contraception must be used by both sexes during treatment and for at least 6 months after goserelin cessation (general recommendation).
- Breastfeeding: Not recommended.
  Goserelin is secreted into milk in animals.
- Fertilitiy effects: Fertility may be affected in males and females, but may be reversible.

Bicalutamide:

- Bicalutamide has shown to be non-genotoxic, but is fetotoxic and is contraindicated in pregnancy and nursing.
- It effects on long-term fertility have not been established.
- Bicalutamide may lead to inhibition of spermatogenesis.

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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

- Liver function tests; baseline and regular
- Clinical assessment of disease flare, pneumonitis, androgen withdrawal symptoms, osteoporosis, injection site reactions, hepatic, lung or cardiovascular effects, hyperglycemia, thromboembolism, signs of abdominal hemorrhage
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

Suggested Clinical Monitoring

- Hemoglobin; baseline and periodic

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## J - Administrative Information

Outpatient prescription; Goserelin to be injected at Cancer Centre or physician's office

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## K - References

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: 2006 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.

**October 2016** updated adverse effects, added interactions, administration and precautions

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## M - Disclaimer

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