Regimen Monograph

A - Regimen Name

ABIRDEXA Regimen

Abiraterone-Dexamethasone

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 treatment of metastatic castrate-resistant prostate cancer, as an alternative in patients who cannot tolerate prednisone in ABIRPRED.
Supplementary Public Funding	**abiraterone** Exceptional Access Program (abiraterone - Metastatic castrate-resistant prostate cancer, according to specific criteria) (EAP Website) **dexamethasone** ODB - General Benefit (dexamethasone) (ODB Formulary)

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B - Drug Regimen

abiraterone	1000 mg	PO	once daily
dexamethasone	0.5 mg	PO	once daily

Patients should continue to receive a GnRH agonist during abiraterone treatment unless they have had a prior orchiectomy.

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C - Cycle Frequency

CONTINUOUS TREATMENT

Until disease progression or unacceptable toxicity

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D - Premedication and Supportive Measures

Control hypertension and correct hypokalemia before treatment.

Patients may require increased corticosteroid dosage before, during and after periods of unusual stress such as surgery or trauma.

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E - Dose Modifications

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

Dosage with toxicity

Toxicity	Abiraterone Dose	Dexamethasone Dose
ALT or AST >5 x ULN OR Total bilirubin >3 x ULN	Hold; monitor liver function closely until recovery to baseline then restart at 500 mg once daily. Discontinue at recurrence.	No change.
ALT or AST >20 x ULN	Discontinue permanently.	
ALT or AST >3 x ULN AND Total bilirubin >2 x ULN (in the absence of biliary obstruction or other causes)		
Myopathy/rhabdomyolysis		
Confirmed pneumonitis/allergic alveolitis		

Hepatic Impairment

Increased exposure and half-life have been observed in patients taking abiraterone with hepatic impairment at baseline.

Hepatic Impairment (at baseline)	Abiraterone Dose	Dexamethasone Dose
Mild (Child-Pugh Class A)	No dose adjustment required	No dose adjustment required
Moderate (Child-Pugh Class B)	Do not use abiraterone	
Severe (Child-Pugh Class C)		

Renal Impairment

No adjustment required for dexamethasone or abiraterone.

Dosage in the Elderly

No overall differences in effectiveness or adverse effects were seen between elderly and younger patients.

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F - Adverse Effects

Refer to abiraterone, dexamethasone 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
• Increased LFTs (may be severe) • Fatigue • Musculoskeletal pain • Edema	• Constipation • Diarrhea • Androgen deprivation symptoms • ↓ K / mineralocorticoid effects • Hypertension • Cough, dyspnea • Insomnia • Nausea, vomiting • Infection (URTI, UTI) • Dyspepsia • Anemia • Urinary symptoms • Steroid effects (weight gain, hyperglycemia, insomnia, myopathy, cataracts, osteoporosis)	• Arrhythmia • QT prolongation • Cardiotoxicity • Adrenal insufficiency • Pneumonitis/allergic alveolitis • Rhabdomyolysis • Hypersensitivity • Falls/fracture

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G - Interactions

Refer to abiraterone, dexamethasone drug monograph(s) for additional details

- Avoid co-administration with CYP2D6 substrates with narrow therapeutic range due to increased risk of toxicity. If must co-administer, consider dose reduction of 2D6 substrate.
- Avoid strong CYP3A4 inducers due to risk of reduced abiraterone efficacy.
- Avoid spironolactone as this may stimulate disease progression.
- Avoid use with radium 223 dichloride due to increased risk of fractures and mortality.
- Caution when co-administered with drugs that increase risk of myopathy/rhabdomyolysis.
- Use with caution in patients with diabetes as isolated cases of hypoglycemia has been reported post marketing, particularly in patients receiving concomitant therapy with pioglitazone or repaglinide.

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H - Drug Administration and Special Precautions

Refer to abiraterone, dexamethasone drug monograph(s) for additional details.

Administration

Abiraterone

- Abiraterone must be taken on an empty stomach. No solid or liquid food should be eaten for at least 2 hours before and at least 1 hour after the dose.
- The tablets should be swallowed whole with a glass of water.
- If an abiraterone dose is missed, the dose should be skipped and the next dose taken as scheduled. Patients should not double the dose to make up for the missed one.
- Since abiraterone may harm the fetus, women who are pregnant or who may become pregnant should handle abiraterone with protection (e.g. gloves).
- Store at 15-30°C.

Contraindications

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

Other Warnings/Precautions

- Patients with pre-existing moderate or severe hepatic impairment should not receive abiraterone. Patients with moderate to severe hepatic impairment, active hepatitis, chronic liver disease or ascites were excluded from clinical trials.
- Use with caution in patients with cardiovascular disease as they were not included in clinical trials. Increased mineralocorticoid levels from CYP17 inhibition may cause hypertension, hypokalemia and fluid retention. Use with caution in patients whose underlying medical conditions may be affected by these effects.
- Caution is advised if patients need to be withdrawn from prednisone. Monitoring for adrenocortical insufficiency should occur.
- Adrenal insufficiency has been reported in patients taking abiraterone and prednisone. Increased corticosteroid dosage may be required before, during and after the stressful situation.
- Contains lactose and should not be used in patients with hereditary galactose intolerance, severe lactase deficiency or glucose-galactose malabsorption.
- Efficacy may be lower in patients who have been treated previously with ketoconazole for their prostate cancer.
- The safety and efficacy of combination abiraterone and cytotoxic chemotherapy use has not been established.

Pregnancy/Lactation

- Abiraterone is **contraindicated and not for use in women**. Adequate contraception should be used by both sexes during treatment, and for at least **1 week** after the last dose. Barrier contraception (including condoms) should be used.
- Breastfeeding is not recommended.
- Fertility Effects: Observed in animal studies (may be reversible)

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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

- Blood pressure, serum potassium, fluid retention; Baseline and monthly
- Liver function tests, bilirubin; Baseline, every 2 weeks for the first 3 months and monthly thereafter, or as clinically indicated
- Monitor for adrenal insufficiency; As clinically indicated when prednisone is withdrawn, or during periods of infection/stress
- Monitor for mineralocorticoid excess; As clinically indicated if patient continues on abiraterone after stopping prednisone
- Blood glucose levels in patients with pre-existing diabetes receiving concomitant pioglitazone or repaglinide; Baseline and as clinically indicated
- Clinical toxicity assessment for infection, hot flashes, steroid side effects, gastrointestinal, dermatological, musculoskeletal, urinary, cardiac and respiratory effects; At each visit
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

Suggested Clinical Monitoring

- Cholesterol and triglycerides; Baseline, every 2 to 3 months and as clinically indicated

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K - References

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

de Bono JS., Logothetis CJ, Molina A, et al. Abiraterone and increased survival in metastatic prostate cancer. N Engl J Med 2011;364:1995-2005.

Ryan CJ, Smith MR, de Bono JS, et al. Abiraterone in metastatic prostate cancer without previous chemotherapy. N Engl J Med 2013;368(2):138-48.

Venkitaraman R et al. A randomised phase 2 trial of dexamethasone versus prednisolone in castration-resistant prostate cancer. Eur Urol. 2015 Apr; 67(4)673-9.

June 2021 Updated Dose Modifications, Adverse Effects, Interactions, Other Warnings/Precautions and Monitoring 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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