Canada's Drug and
Health Technology Agency

CADTH Reimbursement Recommendation

Abiraterone Acetate and Prednisone

Reimbursement request: Abiraterone acetate in combination with prednisone, with or without enzalutamide, for the treatment of patients with high-risk nonmetastatic prostate cancer who are starting long-term androgen deprivation therapy

Final recommendation: Reimburse with conditions.

Summary of CADTH Recommendation

The CADTH Formulary Management Expert Committee (FMEC) concluded there is an unmet need for a clinically meaningful therapy in the high-risk nonmetastatic prostate cancer (nmPC) setting, where there are currently no reimbursed options.

Metastasis-free survival (the length of time after treatment that a patient lives without any signs or symptoms of cancer spreading to other parts of the body) was identified as an outcome of interest to both patients and clinicians.

Abiraterone acetate and prednisone represent a new systemic therapy in this setting. Evidence in high-risk nmPC based on the STAMPEDE trial showed adding these drugs to standard therapy (androgen deprivation therapy) improved MFS in a clinically meaningful way.

Enzalutamide, when added to abiraterone acetate and prednisone, did not appear to add clinically meaningful benefit and it increased toxicity and cost.

What Is High-Risk nmPC?

Prostate cancer (PC) can be categorized as nonmetastatic (nm) when localized to the prostate or metastatic when it spreads to other parts of the body. nmPC is the earliest diagnosis of PC; if detected early, the treatment goal of nmPC is cure and the 5-year survival rate is 91%. PC is the third-leading cause of death from cancer in Canada among males.

What Did We Hear From Patients?

nmPC negatively affects work, relationships, mental health, and the ability to focus or exercise. Access, cost, and side effects are challenges with current therapies. Abiraterone acetate cost is a concern, but side effects are tolerable, at-home drugs are of value, and patients credit abiraterone acetate with managing their cancer.

Refer to Patient Group Input section of the CADTH report.

What Did We Hear From Clinicians?

Clinicians noted that the treatment goals for nmPC are to delay disease recurrence and prolong life. They also noted that limited systemic therapies are approved in high-risk nmPC and emphasized the need for better treatment options beyond androgen deprivation therapy alone.

Refer to Clinician Input section of the CADTH report.

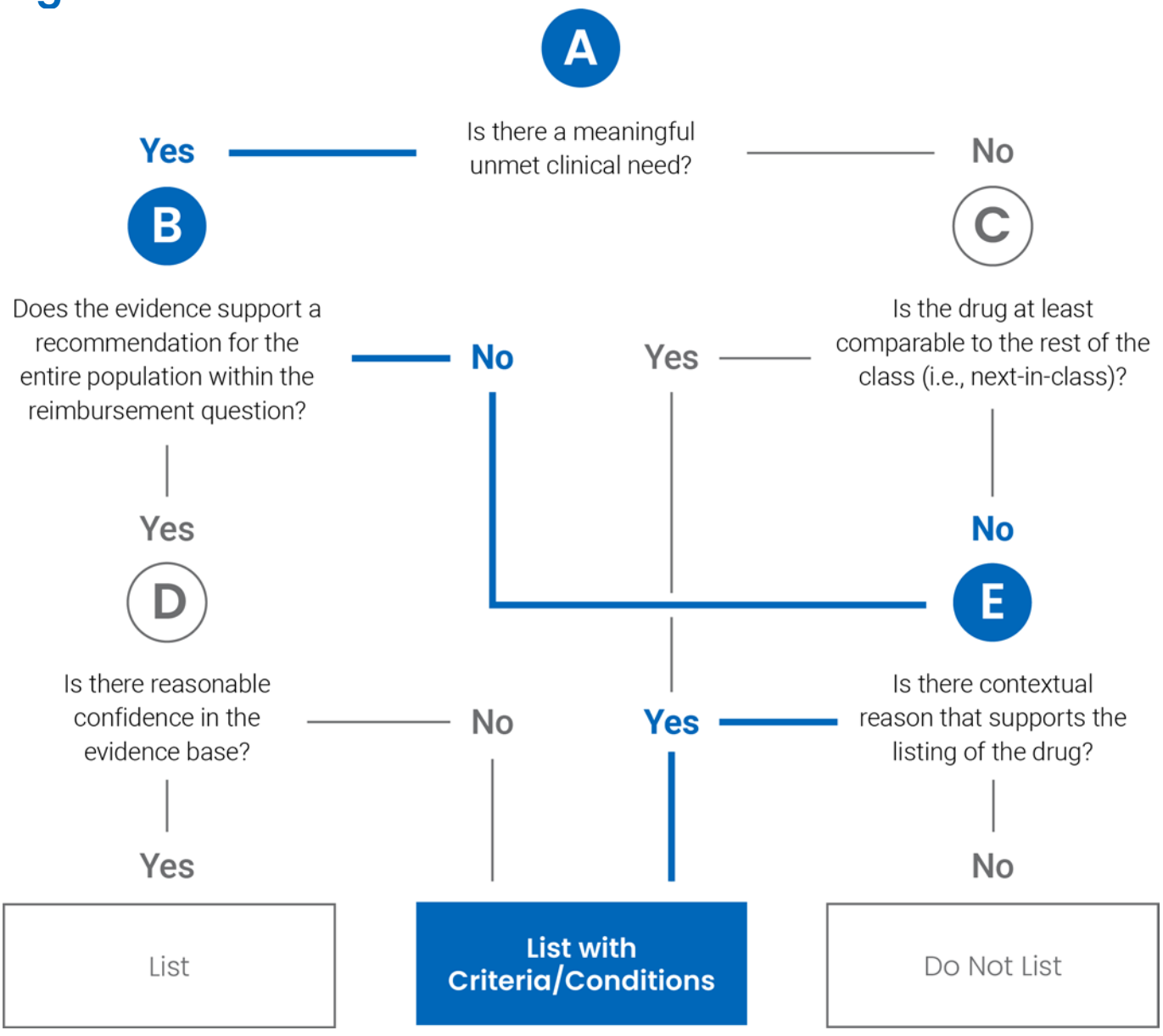
What Did We Hear From the Pharmaceutical Industry and Public Drug Programs?

Industry highlighted that the definition of risk should align with the National Comprehensive Cancer Network definition of very high-risk localized PC. Drug plans questioned the definition of high-risk nmPC, re-treatment eligibility, appropriate time to initiate therapy, treatment algorithms, and concerns with resource requirements.

Refer to Industry Input and Drug Plan Input sections of the CADTH report.

Deliberative Framework

Figure 1: Decision Path



Decision Summary

Table 1: Why Did FMEC Make This Recommendation?

Decision node	Vote	Reason
(A) Is there a meaningful unmet clinical need?	Yes (8)	• Standard of care for patients with high-risk nmPC is an ADT and local therapy of PC (radiation). Based on the STAMPEDE trial, the addition of abiraterone acetate and prednisone shows a convincing and clinically meaningful benefit in terms of MFS and represents a new systemic therapy in the first-line setting. • MFS was identified by both clinical experts and patients as an outcome of importance. • Other important end points in the STAMPEDE trial, such as overall survival, PC-specific survival, and progression free survival also showed a consistent benefit. • FMEC considered that median MFS was not available in either treatment arm of the STAMPEDE trial and that multiplicity of comparisons may not have been controlled for. FMEC concluded that the consistency in results across multiple end points in the STAMPEDE trial provided confidence in the trials' conclusions.
	No (0)	—
(B) Does the evidence support a recommendation for the entire population under consideration for reimbursement? Population under consideration for reimbursement: Newly diagnosed patients with high-risk nmPC who are starting long-term ADT for the first time	Yes (0)	—
	No (8)	• In the STAMPEDE trial, the inclusion criteria used for high-risk nmPC differs from what is used in the Canadian clinical context. Therefore, clinically important trial end points, such as MFS, are only available for those patients who would be characterized as very high risk in the Canadian clinical context. • FMEC guest specialists noted that, in a Canadian context, patients with very high-risk nmPC could represent a limited proportion of the overall nmPC population (estimated at approximately 20%). • FMEC noted that trials for additional drugs in the wider population of patients with localized high-risk PC setting are anticipated to be available soon. Therefore, FMEC did not consider greater allowance for uncertainty in the evidence beyond the STAMPEDE trial population of patients with high-risk nmPC.
(E) Is there a subpopulation or contextual reason that supports the reimbursement of the drug?	Yes (8)	• Very high-risk nmPC ◦ Based on the STAMPEDE trial, the addition of abiraterone acetate and prednisone to ADT shows a convincing and clinically meaningful benefit for MFS in patients with nmPC at the very highest risk. • Biochemical recurrence: ◦ The STAMPEDE trial also included patients with high-risk nmPC in the biochemical recurrent population after previous primary treatment (< 5% of patients enrolled in the trial). FMEC noted that extrapolating the results of the STAMPEDE trial to patients in the biochemical recurrent population would be based on limited evidence, so FMEC did not include this population in the reimbursement recommendation. Furthermore, the FMEC clinical experts noted that the goals of treatment in these patients would not be the same as those of high-risk localized PC patients for whom the treatment goal is cure.

Decision node	Vote	Reason
		• Receiving radiation therapy ◦ In the STAMPEDE trial population, 85% of patients enrolled received radiation therapy. The FMEC clinical experts noted that, in patients who are not receiving localized therapy, the goals of treatment are no longer cure, and other androgen receptor pathway inhibitors would be used in this setting. FMEC highlighted that there is not a similar unmet need for abiraterone acetate and prednisone in populations of patients that do not receive radiation therapy. • Combination use with enzalutamide ◦ Based on the STAMPEDE trial, FMEC considered the addition of enzalutamide to ADT, abiraterone acetate, and prednisone. FMEC concluded that a lack of observed benefit of add-on enzalutamide therapy in the STAMPEDE trial, combined with the added harms and cost, does not justify reimbursement of abiraterone acetate and prednisone combined with enzalutamide. • FMEC noted that the generic price of abiraterone acetate is less expensive than the brand price in most jurisdictions other than Ontario.
	No (0)	—

ADT = androgen deprivation therapy; FMEC = CADTH Formulary Management Expert Committee; MFS = metastasis-free survival; nmPC = nonmetastatic prostate cancer; PC = prostate cancer.

Full Recommendation

FMEC recommends that abiraterone acetate in combination with prednisone be reimbursed for patients with high-risk nmPC who are starting long-term ADT if the conditions in Table 2 are met.

Table 2: Conditions, Reasons, and Guidance

Reimbursement condition	Reason	Implementation guidance
Initiation		
1. Abiraterone acetate and prednisone should be reimbursed in patients with very high-risk nmPC who meet all the following criteria: 1.1. node positive or node negative with 2 of the following: • clinical tumour stage T3 or T4 • Gleason sum score 8 to 10 • PSA ≥ 40 ng/mL 1.2. no prior systemic therapy for PC 1.3. good performance status.	The initiation criteria align with the STAMPEDE trial inclusion criteria. In the STAMPEDE trial, 39% of patients were node positive, 79% had a Gleason score sum of 8 to 10, and 92% had a tumour stage T3 or T4. The definition of high-risk nmPC in the STAMPEDE trial differs from that used in Canadian clinical practice, which would be more consistent with very high-risk nmPC. Therefore, the initiation criteria are restricted to the very high-risk subpopulation of nmPC.	In the STAMPEDE trial, 85% of the patient population received radiation therapy. FMEC notes that patients should continue this therapy for up to 2 years provided they do not have intolerable toxicity and have not had progression of their cancer.

Reimbursement condition	Reason	Implementation guidance
2. Abiraterone acetate and prednisone should not be reimbursed in combination with enzalutamide.	The treatment arm that included enzalutamide in the STAMPEDE trial did not show an added benefit and it was associated with an increase in toxicity.	—
3. Abiraterone acetate and prednisone should not be reimbursed in patients who have biochemical recurrence.	The biochemical recurrent population is not included in the initiation criteria because < 5% of patients were biochemically recurrent in the STAMPEDE trial. FMEC clinical experts noted that the goals of treatment in these patients would not be the same as high-risk localized PC patients for whom the treatment goal is cure.	—
Discontinuation		
4. Abiraterone acetate and prednisone should be discontinued if the patient has any of the following: 4.1. completed 2 years of therapy 4.2. significant intolerance of the therapy 4.3. progression of the cancer.	The STAMPEDE trial investigated the addition of abiraterone acetate to ADT for 2 years. FMEC clinical experts also noted that this aligns with Canadian clinical practice.	FMEC clinical experts note that there is heterogeneity in clinical definitions of progression of PC.
Prescribing		
5. Abiraterone acetate and prednisone should be prescribed by clinicians familiar with the treatment of PC and knowledgeable in the management of therapy toxicities.	The prescribing condition is to ensure that abiraterone acetate and prednisone are prescribed only for appropriate patients and adverse events are managed in an optimized and timely manner.	—
Pricing		
6. Abiraterone acetate should be priced no more than the cheapest generic price.	—	—

ADT = androgen deprivation therapy; FMEC = CADTH Formulary Management Expert Committee; nmPC = nonmetastatic prostate cancer; PC = prostate cancer.

Feedback on Draft Recommendation

CADTH received feedback on the draft recommendation by the British Columbia Cancer Genitourinary Tumour Group and Vancouver Prostate Centre, Ontario Health (Cancer Care Ontario) Genitourinary Cancer Drug Advisory Committee, and Janssen Inc. This feedback was reviewed in conjunction with CADTH's Provincial Advisory Group (PAG); a request for reconsideration of the draft FMEC recommendation was not received from PAG.

FMEC Information

Members of the committee: Dr. Emily Reynen (Chair), Dr. Alun Edwards, Ms. Valerie McDonald, Dr. Jim Silvius, Dr. Marianne Taylor, Dr. Maureen Trudeau, Dr. Dominika Wranik

Guest specialists: Dr. Peter Chung (guest specialist), Dr. Robyn Macfarlane (guest specialist)

Meeting date: June 29, 2023

Conflicts of interest: None

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