Canada's Drug Agency
L'Agence des médicaments du Canada

Enzalutamide

Formulary Management Expert Committee Responses to Questions From the Drug Programs

Table 1: Response Summary

Drug program implementation questions	Clinical expert response	FMEC response
Considerations for relevant comparators		
The EMBARK trial compared enzalutamide-leuprolide vs. enzalutamide alone vs. leuprolide alone. The EMBARK trial used leuprolide as the ADT of choice in the study. There are currently a number of different ADTs available in Canada, with varying administration schedules. Are they all considered interchangeable?	As per the clinical expert, all LHRH antagonists and agonists can be considered interchangeable in terms of efficacy.	FMEC defers to the clinical experts.
If the enzalutamide-ADT combination is considered a treatment option in this review, as the EMBARK study only looked at using enzalutamide with leuprolide, confirmation is needed that enzalutamide can be used with any ADT on the Canadian market.	As per the clinical expert, it is appropriate to use enzalutamide in combination with any form of ADT (which includes any form of chemical or surgical castration), not just leuprolide.	FMEC defers to the clinical experts.
The project scope posted for this nonsponsored reimbursement review included abiraterone as a comparator which may not be relevant as public funding for abiraterone was not established for the same population. In a previous review about abiraterone in patients with high-risk nonmetastatic prostate cancer, the recommendation excluded a subpopulation (< 5% of enrolled patients) with BCR after previous primary treatment.	The clinical expert noted that abiraterone was approved for curative intent in patients with high-risk, localized prostate cancer with no BCR, making it an unsuitable comparator for this review.	FMEC defers to the clinical experts. FMEC discussed that while abiraterone-prednisone (a non-ADT drug) is a treatment option in the nmCSPC setting, the evidence for supporting this regimen is limited in patients with BCR, with less than 5% included in the studied population. In some jurisdictions, patients with BCR will not qualify for funding of abiraterone-

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		prednisone. Thus, there remains an unmet need for patients with BCR.
Special implementation issues		
Is the definition of high-risk disease that was used in the clinical trial consistent with how high-risk nonmetastatic prostate cancer is defined and used in clinical practice?	As per the clinical expert, the definition used in the EMBARK trial aligns with that in clinical practice.	FMEC defers to the clinical experts.
The trial included patients with ECOG 0 to 1. Should patients with ECOG > 2 be considered?	As per the clinical expert, treatment eligibility should be determined by the care team and on overall patient fitness, irrespective of ECOG status.	FMEC defers to the clinical experts.
Is there a role for re-treatment with enzalutamide when a patient's disease progresses to a more advanced stage (e.g., metastatic CRPC)?	As per the clinical expert, re-challenging with the same ARPi in advanced stages after use in nmCSPC is not standard practice.	FMEC defers to the clinical experts.
Should there be time-limited funding considerations to allow enzalutamide to be added for existing patients with nmCSPC who recently initiated therapy with ADT (within the last 6 months)?	As per the clinical expert, a 6-month period is considered reasonable.	FMEC defers to the clinical experts.
If a patient is treated with enzalutamide or enzalutamide + ADT in the nmCSPC setting, what are the options for nonmetastatic castration-resistant setting and in the metastatic castration-resistant setting?	As per the clinical expert, if a patient has previously received enzalutamide for nmCSPC and then progresses, treatment options become limited. Other ARPIs, such as darolutamide or apalutamide, are not recommended due to their chemical similarity to enzalutamide. For patients progressing to nonmetastatic CRPC, options are also limited, as most data in this setting involve patients without prior ARPI exposure. However, this may represent a small subset of patients, especially with the increasing use of PSMA PET in such scenarios.	FMEC defers to the clinical experts.
System and economic issues		
The EMBARK study used conventional imaging (CT or MRI) for the assessment of prostate cancer status during the study.	As per the clinical expert, institutional approaches vary regarding conflicting PSMA and conventional imaging results. The expert suggests treating	FMEC defers to the clinical experts.

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With PSMA PET being available for eligible patients, how will this affect disease assessment?	patients as having metastatic CSPC if PSMA PET shows metastatic disease, though practices may evolve over the coming years with the increasing availability of PSMA PET.	
Given the potential update, a budget impact tool would be helpful. Generic versions are currently under review at Health Canada and not yet marketed in Canada.	The clinical expert had no insight or comment on this issue.	Potential generic versions are included in the costing in this review.

ADT = androgen deprivation therapy; ARPI = androgen receptor pathway inhibitor; BCR = biochemical recurrence; CRPC = castrate-resistant prostate cancer; ECOG = Eastern Cooperative Oncology Group; FMEC = Formulary Management Expert Committee; LHRH = luteinizing hormone-releasing hormone; nmCSPC = nonmetastatic castrate-sensitive prostate cancer; PSA = prostate-specific antigen; PSMA PET = prostate-specific membrane antigen positron emission tomography; vs. = versus.