

Positive Quality Intervention: Enzalutamide (Xtandi®) In Castration-Resistant Prostate Cancer or Metastatic Castration-Sensitive Prostate Cancer

Description: The purpose of this PQI is a summary of process for initiating and monitoring enzalutamide therapy in patients with either castration-resistant prostate cancer or metastatic castration-sensitive prostate cancer (mCSPC).¹

Background: Enzalutamide is a pure androgen receptor inhibitor approved in August of 2012 for the treatment of castration-resistant prostate cancer. It gained approval for metastatic castration-sensitive prostate cancer in December of 2019. The efficacy in patients with either castration-sensitive or castration-resistant prostate cancer was demonstrated in 5 major clinical trials: AFFIRM, PREVAIL, TERRAIN, PROSPER, ARCHES (see *Supplemental Information* section). Enzalutamide therapy in mCSPC is recommended both by National Comprehensive Cancer Network (Category 1)⁹ and American Urological Association Guidelines (Strong Recommendation; Evidence Level: Grade A)⁸ however is underutilized among new patients both in oncology and urology settings. Enzalutamide use in mCSPC should be considered as a potential and evidence-based option.

PQI Process: Identify patients of CRPC and mCSPC and evaluate eligibility for second-generation anti-androgens such as enzalutamide. Upon receipt of a new prescription for enzalutamide for prostate cancer:

- Initial dosing for all indications is 160 mg once daily
 - Available as 40 mg tablets, 40 mg capsules, or 80 mg tablets
 - Swallow capsules or tablets whole
 - Patients should also receive a gonadotropin-releasing hormone (GnRH) analog concurrently or should have had bilateral orchiectomy
 - Reduce enzalutamide dose accordingly if co-administered with:
 - Strong CYP2C8 inhibitors – 80 mg daily
 - Strong CYP3A4 inducers – 160 mg to 240 mg once daily
- Monitor LFTs at baseline and periodically throughout duration of therapy
- Monitor blood pressure at baseline and throughout therapy
- Dose modifications
 - Grade ≥ 3 toxicity or intolerable side effects, withhold dosing for 1 week or until symptoms improve to \leq Grade 2, then resume at the same dose or a reduced dose (120 mg or 80 mg), if warranted
- Review concomitant anticoagulation medications and adjust accordingly⁷

Patient Centered Activities:

- Provide [Oral Chemotherapy Education \(OCE\)](#) Sheet
- Administration: Can be taken with or without food at the same time once daily
- Review baseline labs and chronic medications – dose adjustment needed with concomitant CYP3A4 inducers or CYP2C8 inhibitors
- Storage: Store at room temperature in the original bottle; do not remove desiccant from bottle

Important notice: NCODA has developed this Positive Quality Intervention platform. This platform represents a brief summary of medication uses and therapy options derived from information provided by the drug manufacturer and other resources. This platform is intended as an educational aid and does not provide individual medical advice and does not substitute for the advice of a qualified healthcare professional. This platform does not cover all existing information related to the possible uses, directions, doses, precautions, warning, interactions, adverse effects, or risks associated with the medication discussed in the platform and is not intended as a substitute for the advice of a qualified healthcare professional. The materials contained in this platform are for informational purposes only and do not constitute or imply endorsement, recommendation, or favoring of this medication by NCODA, which assumes no liability for and does not ensure the accuracy of the information presented. NCODA does not make any representations with respect to the medications whatsoever, and any and all decisions, with respect to such medications, are at the sole risk of the individual consuming the medication. All decisions related to taking this medication should be made with the guidance and under the direction of a qualified healthcare professional.

References:

1. Xtandi® (enzalutamide) [prescribing information]. New York, NY: Astellas Pharma US, Inc; 2020.
2. Fizazi K, Scher HI, Miller K, Basch E, Sternberg CN, Cella D, Forer D, Hirmand M, de Bono JS. Effect of enzalutamide on time to first skeletal-related event, pain, and quality of life in men with castration-resistant prostate cancer: results from the randomised, phase 3 AFFIRM trial. *Lancet Oncol*. 2014 Sep;15(10):1147-56. doi: 10.1016/S1470-2045(14)70303-1. Epub 2014 Aug 4. Erratum in: *Lancet Oncol*. 2014 Oct;15(11):e475. PMID: 25104109.
3. Beer TM, Armstrong AJ, Rathkopf D, et al. Enzalutamide in men with chemotherapy-naïve metastatic castration-resistant prostate cancer: extended analysis of the phase 3 PREVAIL study. *Eur Urol* 2017;71(2):151-4.
4. Shore ND, Chowdhury S, Villers A, et al. Efficacy and safety of enzalutamide versus bicalutamide for patients with metastatic prostate cancer (TERRAIN): a randomized, double-blind, phase 2 study. *Lancet Oncol* 2016;17(2):153-63.
5. Hussain M, Fizazi K, Saad F, et al. Enzalutamide in men with nonmetastatic, castration-resistant prostate cancer. *N Engl J Med* 2018;378(26):2465-74.
6. Armstrong AJ, Szmulewitz RZ, Petrylak DP, et al: ARCHES: A randomized, phase III study of androgen-deprivation therapy with enzalutamide or placebo in men with metastatic hormone-sensitive prostate cancer. *J Clin Oncol* 37:2974-2986, 2019
7. Shatzel JJ, Daughety MM, Olson SR, et al. Management of Anticoagulation in Patients With Prostate Cancer Receiving Enzalutamide. *J Onco Prac* 2017;13(11):720-728.
8. Lowrance WT, Breau RH, Chou R et al: Advanced Prostate Cancer: AUA/ASTRO/SUO Guideline PART I. *J Urol* 2021; 205: 14
9. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Prostate Cancer V.2.2021. © National Comprehensive Cancer Network, Inc. 2020. All rights reserved.

Supplemental Information:

Xtandi® Support Solutions®: Patient Support program

- Enroll [online](#) or by calling 1-855-8XTANDI (1-855-898-2634)
- Benefits Verification
- Prior Authorization and Denial Appeals Assistance
- XTANDI® Quick Start+® Program
- XTANDI® Patient Savings Program
- Astellas Patient Assistance Program
- Financial Assistance Information for Medicare Patients

	AFFIRM²	PREVAIL³	TERRAIN⁴	PROSPER⁵	ARCHES⁶
Patient Population	mCRPC	mCRPC	mCRPC	nmCRPC	mCSPC
Study Design	Enzalutamide + LHRH therapy (n=800) vs placebo LHRH therapy (n=399)	Enzalutamide + LHRH therapy (n=872) vs placebo LHRH therapy (n=845)	Enzalutamide + LHRH therapy (n=184) Vs. bicalutamide + LHRH therapy (n=191)	Enzalutamide + LHRH therapy (n=933) vs placebo LHRH therapy (n=468)	Enzalutamide + LHRH therapy (n=574) vs placebo LHRH therapy
Outcomes	<i>Median time to first skeletal event:</i> Enzalutamide 16.7 months vs placebo 13.3 months <i>Pain progression at week 13:</i> Enzalutamide 28% vs. placebo 39%	<i>Median overall survival:</i> Enzalutamide 35.3 months vs placebo 31.3 months <i>Median radiographic progression-free survival:</i> Not reached with enzalutamide + LHRH therapy vs 3.7 months with placebo + LHRH therapy	<i>Median radiographic progression-free survival:</i> Enzalutamide group 19.5 months vs bicalutamide group 13.4 months <i>Median progression-free survival:</i> Enzalutamide patients 15.7 months and bicalutamide patients 5.8 months	<i>Median metastasis-free survival:</i> 3 years with enzalutamide therapy vs 14.7 months with placebo First use of subsequent prostate cancer therapy was delayed by: Median of 3 years with enzalutamide + LHRH therapy vs. 17.7 months with placebo + LHRH therapy	<i>Risk of radiographic disease progression or death:</i> 61% reduction with enzalutamide + LHRH therapy vs placebo + LHRH therapy <i>Risk of starting a new antineoplastic therapy:</i> 72% reduction with enzalutamide + LHRH therapy vs placebo + LHRH therapy

*mCRPC-metastatic castration-resistant prostate cancer, LHRH-luteinizing hormone-releasing hormone, CRPC-castration-resistant prostate cancer, mCSPC - metastatic castration-sensitive prostate cancer, nmCRPC-non-metastatic castration-resistant prostate cancer

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