

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 2012 for the treatment of castration-resistant prostate cancer. It gained approval for metastatic castration-sensitive prostate cancer in 2019. The efficacy in patients with either castration-sensitive or castration-resistant prostate cancer was demonstrated in 5 major clinical trials: AFFIRM², PREVAIL³, TERRAIN⁴, PROSPER⁵, ARCHES.⁶ Enzalutamide therapy in mCSPC is recommended both by NCCN (Category 1)⁷ and American Urological Association (Strong Recommendation; Evidence Level: Grade A).⁸ 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
 - Ensure orders for gonadotropin-releasing hormone (GnRH) analog or 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 and blood pressure at baseline and periodically throughout duration of 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)
- Review concomitant anticoagulation medications and adjust accordingly⁹

Patient Centered Activities:

- Provide [Oral Chemotherapy Education \(OCE\)](#) Sheet
- Review side effect of fatigue and strategies to mitigate
- Can be taken with or without food at the same time once daily and swallow whole
- Store at room temperature in the original bottle; do not remove desiccant from bottle

References:

1. [Xtandi® \(enzalutamide\) \[prescribing information\]](#).
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. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Prostate Cancer.
8. Lowrance WT, Breau RH, Chou R et al: Advanced Prostate Cancer: AUA/ASTRO/SUO Guideline PART I. *J Urol* 2021; 205: 14
9. 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.

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