Xtandi® (enzalutamide) – Expanded indication

- On November 17, 2023, Astellas and Pfizer announced the FDA approval of Xtandi (enzalutamide), for the treatment of patients with non-metastatic castration-sensitive prostate cancer (nmCSPC) with biochemical recurrence at high risk for metastasis (high-risk BCR).

- Xtandi is also approved for treatment of castration-resistant prostate cancer (CRPC) and metastatic castration-sensitive prostate cancer (mCSPC).

- The approval of Xtandi for the expanded indication was based on EMBARK, a randomized, double-blind, placebo-controlled study in 1,068 patients with nmCSPC with high-risk BCR. Patients were randomized to receive Xtandi concurrently with leuprolide, Xtandi as open-label as a single agent, or placebo concurrently with leuprolide. The major efficacy measure was metastasis-free survival (MFS) in patients randomized to receive Xtandi plus leuprolide compared to patients randomized to receive placebo plus leuprolide. MFS in patients randomized to receive Xtandi as a single agent compared to patients randomized to receive placebo plus leuprolide and overall survival (OS) were additional efficacy measures.

    - A statistically significant improvement in MFS was demonstrated in patients randomized to receive Xtandi plus leuprolide compared with patients randomized to receive placebo plus leuprolide. A statistically significant improvement in MFS was also demonstrated in patients randomized to receive Xtandi as a single agent compared with patients randomized to receive placebo plus leuprolide (see table below).
    - OS data were not mature at the time of MFS analysis (12.2% deaths across the overall population of 1,068 patients).

	Xtandi + leuprolide	Placebo + leuprolide	Xtandi
MFS			
Number of events (%)	45 (12.7)	92 (25.7)	63 (17.7)
Median, months (95% CI)	NR (NR, NR)	NR (85.1, NR)	NR (NR, NR)
Hazard ratio relative to placebo plus leuprolide (95% CI)	0.42 (0.30, 0.61)	--	0.63 (0.46, 0.87)
P-value for comparison to placebo + leuprolide	$p < 0.0001$	--	$p = 0.0049$

NR = Not reached

- The recommended dosage of Xtandi is 160 mg administered orally once daily with or without food until disease progression or unacceptable toxicity.

    - Patients with nmCSPC with high-risk BCR may be treated with Xtandi with or without a gonadotropic-releasing hormone (GnRH) analog.

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— For patients who receive Xtandi with or without a GnRH analog, treatment can be suspended if Prostate Specific Antigen (PSA) is undetectable (< 0.2 ng/mL) after 36 weeks of therapy. Treatment should be reinitiated when PSA has increased to ≥ 2.0 ng/mL for patients who had prior radical prostatectomy or ≥ 5.0 ng/mL for patients who had prior primary radiation therapy.