

Xtandi® (enzalutamide) (Oral)

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I. Length of Authorization

Coverage is provided for 6 months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Xtandi 40 mg capsules: 4 capsules per day
- Xtandi 40 mg tablets: 2 tablets per day
- Xtandi 80 mg tablets: 2 tablets per day

B. Max Units (per dose and over time) [HPCS Unit]:

- 160 mg per day

III. Initial Approval Criteria ¹

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

Universal Criteria ¹

- Patient will receive concurrent treatment with a gonadotropin-releasing hormone (GnRH) analog (e.g., leuprolide, goserelin, triptorelin, histrelin, degarelix, etc.) OR has had a bilateral orchiectomy**; **AND**
- Will not be used in combination with other androgen receptor inhibitors (e.g., darolutamide, apalutamide, etc.); **AND**
- Patient will avoid concomitant therapy with the following, or if therapy is unavoidable, the patient will be monitored closely for adverse reaction and/or dose modifications will be implemented:
 - Coadministration with strong CYP2C8 inhibitors (e.g., gemfibrozil, etc.); **AND**

- Coadministration with strong CYP3A4 inducers (e.g., carbamazepine, rifampin, phenytoin, St. John's Wort, etc.); **AND**

****Note:** Only applies to patients with CRPC or mCSPC. Patients with nmCSPC with high-risk BCR may receive treatment with or without a GnRH analog.

Prostate Cancer †^{1,2,8,9}

- Used as a single agent; **AND**
 - Patient has castration-resistant prostate cancer (CRPC); **OR**
 - Patient has metastatic castration-sensitive prostate cancer (mCSPC); **OR**
 - Patient has non-metastatic castration-sensitive prostate cancer (nmCSPC) with biochemical recurrence at high risk for metastasis (high-risk BCR); **OR**
- Used in combination with talazoparib; **AND**
 - Patient has metastatic castration-resistant prostate cancer (mCRPC); **AND**
 - Patient has homologous recombination repair (HRR) gene-mutated disease as detected by a CLIA-compliant or FDA-approved test❖

❖ If confirmed using an FDA-approved assay – <http://www.fda.gov/companiondiagnostics>

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria¹

Coverage may be renewed based upon the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: seizures, posterior reversible encephalopathy syndrome (PRES), hypersensitivity reactions, ischemic heart disease, falls/fractures, etc.; **AND**

CRPC or mCSPC

- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread

nmCSPC with High-Risk BCR

- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **OR**
- Treatment is being reinitiated after a prior treatment suspension for undetectable Prostate Specific Antigen (PSA) levels (i.e., < 0.2 ng/mL); **AND**
 - PSA has increased to ≥ 2.0 ng/mL in patients who received prior radical prostatectomy; **OR**

- PSA has increased to ≥ 5.0 ng/mL in patients who received prior primary radiation therapy

V. Dosage/Administration ^{1,9}

Indication	Dose
Prostate Cancer	Administer 160 mg (two 80 mg tablets or four 40 mg tablets or four 40 mg capsules) orally once daily

VI. Billing Code/Availability Information

HCPCS Code:

- J8999 – Prescription drug, oral, chemotherapeutic, Not Otherwise Specified

NDC(s):

- Xtandi 40 mg capsule: 00469-0125-xx
- Xtandi 40 mg tablet: 00469-0625-xx
- Xtandi 80 mg tablet: 00469-0725-xx

VII. References

1. Xtandi [package insert]. Northbrook, IL: Astellas Pharma US, Inc.; November 2023. Accessed November 2023.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for enzalutamide. National Comprehensive Cancer Network, 2023. The NCCN Compendium® is a derivative work of the NCCN Guidelines®, NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed November 2023.
3. Scher HI, Fizazi K, Saad F, et al. Increased survival with enzalutamide in prostate cancer after chemotherapy. N Engl J Med. 2012 Sep 27;367(13):1187-97. Epub 2012 Aug 15.
4. Beer TM, Armstrong AJ, Rathkopf DE, et al. Enzalutamide in Metastatic Prostate Cancer before Chemotherapy. N Engl J Med. 2014 Jul 31; 371(5): 424–433.
5. Shore ND, Chowdhury S, Villers A, et al. Efficacy and safety of enzalutamide versus bicalutamide for patients with metastatic prostate cancer (TERRAIN): a randomised, double-blind, phase 2 study. Lancet Oncol. 2016 Feb;17(2):153-163. doi: 10.1016/S1470-2045(15)00518-5. Epub 2016 Jan 14.
6. Hussain M, Fizazi K, Saad F, et al. Enzalutamide in Men with Nonmetastatic, Castration-Resistant Prostate Cancer. N Engl J Med. 2018 Jun 28;378(26):2465-2474. doi: 10.1056/NEJMoa1800536.

7. 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*. 2019 Nov 10;37(32):2974-2986. doi: 10.1200/JCO.19.00799. Epub 2019 Jul 22.
8. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Prostate Cancer, Version 4.2023. National Comprehensive Cancer Network, 2023. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed November 2023.
9. Agarwal N, Azad A, Carles J, et al. TALAPRO-2: Phase 3 study of talazoparib (TALA) + enzalutamide (ENZA) versus placebo (PBO) + ENZA as first-line (1L) treatment in patients (pts) with metastatic castration-resistant prostate cancer (mCRPC). *Journal of Clinical Oncology* 2023 41:6_suppl, LBA17-LBA17. DOI: 10.1200/JCO.2023.41.6_suppl.LBA17.
10. Sridharan S, Shore N, Venugopal B, et al. Enzalutamide or Placebo Plus Leuprolide Acetate and Enzalutamide Monotherapy in Men with High-Risk Biochemically Recurrent Prostate Cancer and Prior Radiotherapy: EMBARK Subgroup Analysis. *International Journal of Radiation Oncology, Biology, Physics*, Volume 117, Issue 4, E4 – E5, November 15, 2023. DOI: <https://doi.org/10.1016/j.ijrobp.2023.08.030>.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C61	Malignant neoplasm of prostate
Z85.46	Personal history of malignant neoplasm of prostate

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: <https://www.cms.gov/medicare-coverage-database/search.aspx>. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/ LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC