Drug Policy:

Xtandi™ (enzalutamide)

POLICY NUMBER UM ONC_1228	SUBJECT Xtandi™ (enzalutamide)		DEPT/PROGRAM UM Dept	PAGE 1 OF 4
DATES COMMITTEE REVIEWED 11/07/12, 04/09/14, 12/01/15, 12/21/16, 10/31/17, 11/08/17, 09/21/18, 08/14/19, 12/11/19, 04/08/20, 07/08/20, 08/12/20, 08/11/21, 09/08/21, 11/15/21, 05/11/22, 08/10/22, 11/09/22, 07/12/23, 8/9/23,10/11/23, 01/10/24, 02/14/24	**APPROVAL DATE** February 14, 2024	**EFFECTIVE DATE** February 23, 2024	**COMMITTEE APPROVAL DATES** 11/07/12, 04/09/14, 12/01/15, 12/21/16, 10/31/17, 11/08/17, 09/21/18, 08/14/19, 12/11/19, 04/08/20, 07/08/20, 08/12/20, 08/11/21, 09/08/21, 11/15/21, 05/11/22, 08/10/22, 11/09/22, 07/12/23, 8/9/23, 10/11/23, 01/10/24, 02/14/24	
PRIMARY BUSINESS OWNER: UM		**COMMITTEE/BOARD APPROVAL** Utilization Management Committee		
NCQA STANDARDS UM 2		**ADDITIONAL AREAS OF IMPACT**		
CMS REQUIREMENTS	**STATE/FEDERAL REQUIREMENTS**		**APPLICABLE LINES OF BUSINESS** Commercial, Exchange, Medicaid	

I. PURPOSE

To define and describe the accepted indications for Xtandi (enzalutamide) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

II. INDICATIONS FOR USE/INCLUSION CRITERIA

A. **Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided:**

1. The requested medication was used within the last year, AND
2. The member has not experienced disease progression and/or no intolerance to the requested medication, AND
3. Additional medication(s) are not being added to the continuation request.

B. **Prostate Cancer**

1. Xtandi (enzalutamide) may be used in combination with an LHRH analog or after orchiectomy (ADT- Androgen Deprivation Therapy) for ANY of the following clinical settings:

a. In members with non-metastatic castration resistant prostate cancer, M0 disease with no visible metastases on conventional imaging, AND a PSA Doubling Time of less than or equal to 10 months OR

b. In members with metastatic castration sensitive/resistant prostate cancer.

2. Xtandi (enzalutamide) may be used in members with non-metastatic castration-sensitive prostate cancer (nmCSPC) with biochemical recurrence at high risk for metastasis (high-risk BCR).

    a. nmCSPC is defined as:

        i. PSA doubling time ≤ 9 months

        ii. PSA ≥ 1 ng/mL(post-RP)

        iii. PSA ≥ 2 ng/mL above the nadir (post-RT)

        iv. Testosterone level ≥ 150 ng/mL

    b. Members receiving Xtandi (enzalutamide) for nmCSPC may be treated with or without a GnRH analog concurrently.

3. Xtandi (enzalutamide) may be used with Talzenna (talazoparib) for homologous recombination repair (HRR) gene-mutated metastatic castration-resistant prostate cancer (mCRPC) with the exception of BRCA 1 and 2 mutation positive mCRPC. Enzalutamide may be used with talazoparib for mCRPC that is positive for any one of following: ATM, ATR, BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCA, FANCL, MLH1, MREL11A, NBN, PALB2, RAD51B, RAD51C, RAD51D, or RAF54L

    The above policy position is based on the lack of Level 1 evidence (randomized trials and/or meta-analyses) to show superior outcomes for patients with BRCA1/2 mutation positive prostate cancer using talazoparib and enzalumatide in comparison to the recommended alternatives listed below. The alternative regimens supported by Evolent Policies are: 1) niraparib and abiraterone acetate with prednisone, 2) Akeega (niraparib and abiraterone acetate) with prednisone, and 3) olaparib and abiraterone acetate with prednisone.

4. Patients receiving enzalutamide and talazoparib should also receive a GnRH analog concurrently or should have had bilateral orchiectomy.

III. EXCLUSION CRITERIA

A. The member has disease progression while on or after taking Xtandi (enzalutamide), or a similar Androgen Receptor Signaling Inhibitor such as Erleada (apalutamide) OR Nubeqa (darolutamide).

B. The member has BRCA 1 and 2 positive mCRPC.

C. Xtandi (enzalutamide) is being used concurrently with other anti-cancer therapy including abiraterone, cabazitaxel, docetaxel, or sipuleucel-T, apalutamide, or darolutamide.

D. Dosing exceeds single dose limit of Xtandi (enzalutamide) of 160 mg.

E. Treatment with Xtandi (enzalutamide) exceeds the maximum limit of 120 (40 mg) capsules, 120 (40 mg) tablets, or 60 (80 mg) tablets per month.

F. Investigational use of Xtandi (enzalutamide) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:

1. Whether the clinical characteristics of the patient and the cancer are adequately represented in

the published evidence.

2. Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
3. Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definitions of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
4. Whether the experimental design, considering the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
5. That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
6. That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
7. That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

IV. MEDICATION MANAGEMENT

A. Please refer to the FDA label/package insert for details regarding these topics.

V. APPROVAL AUTHORITY

A. Review – Utilization Management Department

B. Final Approval – Utilization Management Committee

VI. ATTACHMENTS

A. None

VII. REFERENCES

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C. Freedland SJ, et al. Improved Outcomes with Enzalutamide in Biochemically Recurrent Prostate Cancer. N Engl J Med 2023; 389:1453-1465 DOI: 10.1056/NEJMoa2303974

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E. Xtandi prescribing information. Astellas Pharmaceutical Inc. Northbrook IL 2023.

F. Clinical Pharmacology Elsevier Gold Standard 2023.

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I. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2023.

J. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. J Clin Oncol. 2014 Apr 20;32(12):1277-80.

K. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf.