PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Xtandi Prior Authorization Policy
- Xtandi® (enzalutamide capsules and tablets – Astellas/Pfizer)

REVIEW DATE: 03/26/2025

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Xtandi is an androgen receptor inhibitor indicated for the treatment of patients with **castration-resistant prostate cancer (CRPC), metastatic castration-sensitive prostate cancer (mCSPC)**, and **non-metastatic castration-sensitive prostate cancer (nmCSPC)** with biochemical recurrence at high risk for metastasis (high-risk biochemical recurrence [high-risk BCR]).[1] For CRPC and mCSPC, patients should receive Xtandi with a concurrent gonadotropin-releasing hormone (GnRH) analog or should have had a bilateral orchiectomy. Patients with nmCSPC with high-risk BCR may be treated with or without a GnRH analog.

Guidelines

According to the National Comprehensive Cancer Network (NCCN) guidelines on prostate cancer (version 1.2025 – December 4, 2024), all patients with metastatic CRPC should continue androgen deprivation therapy to maintain castrate levels of serum testosterone (< 50 ng/dL).

- For patients with non-metastatic CRPC, if the prostate specific antigen doubling time is ≤ 10 months, Xtandi, Erleada® (apalutamide tablets), and Nubeqa® (darolutamide tablets) are all preferred category 1 recommended options.
- For patients with mCRPC adenocarcinoma, therapies are based on prior docetaxel or prior novel hormone therapy use.

    - No prior docetaxel and no prior novel hormone therapy: the preferred regimens are Xtandi (category 1), abiraterone (category 1 only if no visceral metastases), and docetaxel (category 1). Talzenna® (talazoparib capsules) + Xtandi is recommended for homologous recombination repair (HRR) mutation (category 1).
    - Prior docetaxel, but no prior novel hormone therapy: the preferred regimens include Xtandi or abiraterone (both category 1), and Jevtana® (cabazitaxel intravenous infusion) [category 2A]. Talzenna + Xtandi for HRR mutation is a category 2A recommendation.
    - Prior novel hormone therapy but no prior docetaxel: Xtandi, abiraterone, and abiraterone + dexamethasone are "other recommended regimens" (both category 2A). Talzenna + Xtandi for HRR mutation is a category 2B recommendation in this setting.
    - Prior docetaxel and prior novel hormone therapy: All systemic therapies are category 2B if visceral metastases are present. Preferred regimens are Jevtana (category 1) and docetaxel rechallenge. Xtandi, abiraterone, and other secondary hormone therapy are "other recommended regimens" (all category 2A).
- For progressive non-metastatic CSPC after maximal pelvic therapy, Xtandi ± leuprolide is recommended as "useful in certain circumstances" (category 2A). It is recommended in patients who have the following high-risk criteria: non-metastatic by conventional imaging; prostate-specific antigen (PSA) doubling time (PSADT) ≤ 9 month; PSA ≥ 2 ng/mL above nadir after radiotherapy or ≥ 1 ng/mL after radiotherapy with or without postoperative radiotherapy; and not considered a candidate for pelvic-directed therapy. Xtandi is also recommended in combination with docetaxel or external beam radiation therapy (category 2B).
- For mCSPC androgen deprivation therapy in combination with Xtandi, abiraterone + steroid, Erleada, and docetaxel are all category 1 recommended preferred options. Yonsa® (abiraterone acetate) with methylprednisolone is a category 2B recommendation.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Xtandi. All approvals are provided for the duration noted below.

- **Xtandi® (enzalutamide capsules and tablets - Astellas/Pfizer)**

is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indications

1. **Prostate Cancer – Castration-Resistant (Metastatic or Non-Metastatic).** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) Patient is ≥ 18 years of age; AND
   B) Patient meets ONE of the following (i or ii):
      i. The medication is used concurrently with a gonadotropin-releasing hormone (GnRH) analog; OR
      Note: Examples are leuprolide acetate, Lupron Depot (leuprolide acetate intramuscular injection), Trelstar (triptorelin pamoate intramuscular injection), Zoladex (goserelin acetate subcutaneous implant), Vantas (histrelin acetate subcutaneous implant), Firmagon (degarelix subcutaneous injection), Orgovyx (relugolix tablets).
      ii. Patient has had a bilateral orchiectomy.

2. **Prostate Cancer – Metastatic, Castration-Sensitive.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) Patient is ≥ 18 years of age; AND
   B) Patient meets ONE of the following (i or ii):
      i. The medication is used concurrently with a gonadotropin-releasing hormone (GnRH) analog; OR
      Note: Examples are leuprolide acetate, Lupron Depot (leuprolide acetate intramuscular injection), Trelstar (triptorelin pamoate intramuscular injection), Zoladex (goserelin acetate subcutaneous implant), Vantas (histrelin acetate subcutaneous implant), Firmagon (degarelix subcutaneous injection), Orgovyx (relugolix tablets).
      ii. Patient has had a bilateral orchiectomy.

3. **Prostate Cancer – Non-Metastatic, Castration-Sensitive.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has biochemical recurrence and is at high risk for metastasis.
   Note: High-risk biochemical recurrence is defined as prostate-specific antigen (PSA) doubling time ≤ 9 months.

CONDITIONS NOT COVERED

- **Xtandi® (enzalutamide capsules and tablets - Astellas/Pfizer)**

is(are) considered experimental, investigational or unproven for ANY other use(s) including the following; criteria will be updated as new published data are available

REFERENCES

1. Xtandi® capsules and tablets [prescribing information]. Northbrook, IL: Astellas/Pfizer; January 2025.

2. The NCCN Prostate Cancer Clinical Practice Guidelines in Oncology (version 1.2025 – December 4, 2024). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed March 24, 2025.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes	04/05/2023
Selected Revision	**Prostate Cancer – Non-Metastatic, Castration-Sensitive.** Added new condition and criteria based on new indication approval.	11/29/2023
Annual Revision	**Prostate Cancer – Castration-Resistant (Metastatic or Non-Metastatic).** The criterion requiring the trial of gonadotropin-releasing hormone "agonist" was changed to "analog", which allows use of both agonists and antagonists. Firmagon and Orgovyx were added as examples in the Note. The separate criterion previously asking for concurrent use of medication with Firmagon was deleted since it is no longer needed. **Prostate Cancer – Metastatic, Castration-Sensitive:** The criterion requiring the trial of gonadotropin-releasing hormone "agonist" was changed to "analog", which allows use of both agonists and antagonists. Firmagon and Orgovyx were added as examples in the Note. The separate criterion previously asking for concurrent use of medication with Firmagon was deleted since it is no longer needed.	04/10/2024
Annual Revision	No criteria changes	03/26/2025