BlueCross BlueShield Arizona

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PHARMACY COVERAGE GUIDELINES	
SECTION: DRUGS	
ORIGINAL EFFECTIVE DATE:	**1/01/2016**
LAST REVIEW DATE:	**8/20/2020**
LAST CRITERIA REVISION DATE:	**8/20/2020**
ARCHIVE DATE:	

NUBEQA™ (darolutamide) oral
XTANDI® (enzalutamide) oral

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

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Criteria:

- **Criteria for initial therapy:** Xtandi (enzalutamide) or Nubeqa (darolutamide) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Oncologist or Urologist

  2. Individual is male and 18 years of age or older

  3. A confirmed diagnosis of **ONE** of the following:

     a. **For Nubeqa (darolutamide) only:**
        i. Non-metastatic (M0) castration-resistant prostate cancer (nmCRPC) with a PSA doubling time (PSADT) ≤ 10 months

     b. **For Xtandi (enzalutamide) only:**
        i. Prostate cancer 1s **ONE** of the following:
           1. Metastatic castration resistant prostate cancer (mCRPC) in either patient who received chemotherapy or in chemotherapy-naïve patients

           2. Non-metastatic (M0) castration-resistant prostate cancer (nmCRPC) with a PSA doubling time (PSADT) ≤ 10 months and PSA ≥ 2 ng/mL

           3. Metastatic castration sensitive prostate (mCSPC)

     c. Other request for a specific oncologic direct treatment use that is found and listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

  4. Used in combination with a gonadotropin-releasing hormone (GnRH) agonist or antagonist to maintain castrate serum testosterone levels (< 50 ng/dL) unless has had bilateral orchiectomy

  5. Patient has an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1

  Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Xtandi (enzalutamide) or Nubeqa (darolutamide) is considered ***medically necessary*** and will be approved with documentation of **ALL** of the following:

  1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Oncologist or Urologist

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2. Individual's condition responded while on therapy
    a. Response is defined as:
        i. No evidence of disease progression
        ii. Documented evidence of efficacy, disease stability and/or improvement

3. Individual has been adherent with the medication

4. Individual has not developed any significant level 4 adverse drug effects that may exclude continued use, such as:
    a. Posterior reversible encephalopathy syndrome (PRES) with Xtandi
    b. Seizure while on Xtandi
    c. Edema of face, tongue, or lip or any symptoms of hypersensitivity
    d. Severe ischemic heart disease

5. There are no significant interacting drugs

Renewal duration: 12 months

Description:

Xtandi (enzalutamide) is an androgen receptor inhibitor indicated for **the treatment of castration-resistant prostate cancer (CRPC) and metastatic castration-sensitive prostate cancer (mCSPC)**. Nubeqa (darolutamide) is an androgen receptor inhibitor indicated for **the treatment of patients with non-metastatic castration-resistant prostate cancer (nmCRPC).** Patients receiving either Xtandi (enzalutamide) or Nubeqa (darolutamide) should also receive a gonadotropin-releasing hormone (GnRH) analog concurrently or should have had a bilateral orchiectomy.

Enzalutamide and darolutamide act on different steps in the androgen receptor signaling pathway. They have been shown to competitively inhibit androgen binding to androgen receptors and inhibit androgen receptor nuclear translocation and interaction with deoxyribonucleic acid (DNA). Enzalutamide and darolutamide decrease proliferation and induce cell death of prostate cancer cells *in vitro*, and decrease tumor volume in a mouse prostate cancer xenograft model.

Definitions:

Antiandrogens, oral:
Zytiga (abiraterone acetate)
Erleada (apalutamide)
Bicalutamide
Nubeqa (darolutamide)
Xtandi (enzalutamide)
Flutamide

NUBEQA™ (darolutamide) oral
XTANDI® (enzalutamide) oral

Nilutamide

Gonadotropin-releasing hormone (GnRH) agonists: also referred to as luteinizing hormone releasing hormone (LHRH) agonists or analogues:
- Zoladex (goserelin acetate) subcutaneous implant
- Vantas (histrelin acetate) subcutaneous implant
- Eligard (leuroplide acetate) subcutaneous injection
- Lupron Depot (leuprolide acetate) intramuscular injection
- Trelstar (triptorelin pamoate) intramuscular injection

Gonadotropin-releasing hormone antagonist:
- Firmagon (dagarelix) subcutaneous injection

Resources:

Nubeqa (darolutamide) Package Insert, revised by manufacturer 07-2019, accessed 06-25-20 at DailyMed

Xtandi (enzalutamide) Package Insert, revised by manufacturer 12-2019, accessed 06-25-20 at DailyMed

UpToDate: Prostate cancer: Risk stratification and choice of initial treatment. Current through Aug 2017

UpToDate: Overview of the treatment of castration-resistant prostate cancer (CRPC). Current through Aug 2017

NCCN Clinical Practice Guidelines in Oncology: Prostate cancer. Version 4.2018, Aug 15. 2018

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.