BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

ERLEADA™ (apalutamide) Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and/or Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Medical Necessity Requirements for ERLEADA (apalutamide)

Criteria for Initial Therapy:

Prescriber Qualifications
- Prescribed by an Oncologist or Urologist, or in consultation with an Oncologist or Urologist

Indication
- Diagnosis of prostate cancer and used as ONE of the following:
  - Metastatic castration-sensitive prostate cancer
  - Non-metastatic castration-resistant prostate cancer

ORIGINAL EFFECTIVE DATE: 03/15/2018 | ARCHIVE DATE: | LAST REVIEW DATE: 05/15/2025 | LAST CRITERIA REVISION DATE: 05/16/2024

- Other oncologic direct treatment use listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

Age Requirement
- 18 years or older

Baseline Clinical Evaluation
- Eastern Cooperative Oncology Group Performance Status of 0–1
- Concurrent use of a gonadotropin-releasing hormone analog or history of bilateral orchiectomy

Brand Specific Criteria
- Have failure, contraindication, or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the United States Food and Drug Administration (FDA) (see Definitions section)

Documentation Requirements
- A completed request form must be submitted, including:
  - Chart notes
  - Lab results (including ECOG status)
  - Supporting clinical documentation

Initial Therapy Criteria Approval Duration:
- 6 months OR end of plan year

Criteria for Continuation of Therapy (renewal therapy)
Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy

Prescriber Qualifications
- Continues to be seen by a physician specializing in or is in consultation with an Oncologist or Urologist

Clinical Response
- Positive clinical response defined as no evidence of disease progression or unacceptable toxicity

Adherence
- Adherence to the prescribed therapy regimen has been documented

Brand Specific Criteria
- Have failure, contraindication, or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

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Safety
- No significant drug-drug interactions or contraindications such as:
  - Seizure
  - Cerebrovascular and ischemic cardiovascular event
  - Severe cutaneous adverse reaction

Documentation Requirements
- Chart notes
- Supporting clinical documentation with evidence of improvement in given indication
- Lab values that confirm safe use from above criteria

Continuation Therapy Criteria Approval Duration:
- 12 months OR end of plan year

Criteria for Off-Label Use Requests:

Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. Off-Label Use of Non-Cancer Medications

2. Off-Label Use of Cancer Medications

Description:

Erleada (apalutamide) is an androgen receptor inhibitor indicated for the treatment of patients with non-metastatic castration-resistant prostate cancer and for patients with metastatic castration-sensitive prostate cancer. Patients should also use of a gonadotropin-releasing hormone (GnRH) analog (also known as luteinizing hormone releasing hormone (LHRH) agonist or analog) **or** should have had bilateral orchiectomy.

Patients who do not achieve adequate suppression of serum testosterone (< 50 ng/dL) with medical or surgical castration can be considered for additional hormonal manipulations.

In the setting in which patients have no or minimal symptoms, administration of secondary hormonal therapy including addition of, or switching to, a different antiandrogen, addition of adrenal/paracrine androgen synthesis inhibitors, or use of an estrogen can be considered.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

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Castration-resistant prostate cancer (CRPC):
CRPC demonstrated during continuous ADT, defined as 3 PSA rises, at least 1 week apart, with the last PSA greater than (>) 2 nanogram per milliliter (ng/mL)

Prostate Specific Antigen Doubling Time (PSADT:
PSADT is calculated by using at least three prostate-specific antigen (PSA) values obtained during continuous ADT (androgen deprivation therapy)

Staging System for Prostate Cancer, excerpts:

N0 – No positive regional nodes

N1 – Metastases in regional lymph node(s)

M0 – No distant metastasis

M1 – Distant metastasis
- M1a: Non-regional lymph node(s)
- M1b: Bone(s)
- M1c: Other site(s) with or without bone disease
- [Note: When more than one site of metastasis is present, the most advanced category is used – M1c

Gonadotropin-releasing hormone (GnRH) analogs or agonists: (Also referred to as luteinizing hormone releasing hormone (LHRH) agonists or analogs)

Zoladex (goserelin acetate) subcutaneous implant
Vantas (histrelin acetate) subcutaneous implant
Eligard (leuprolide acetate) subcutaneous injection
Lupron Depot (leuprolide acetate) intramuscular injection
Trelstar (triptorelin pamoate) intramuscular injection

Gonadotropin-releasing hormone antagonist:

Firmagon (dagarelix) subcutaneous injection
Orgovyx (relugolix)

Antiandrogens, oral: to maintain castrate serum levels of testosterone (< 50 ng/dL)

Zytiga (abiraterone acetate)
Erleada (apalutamide)
Casodex (bicalutamide)
Nubequa (darolutamide)
Xtandi (enzalutamide)
Flutamide
Nilandron (nilutamide)

ECOG Performance status:

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Eastern Co-operative Oncology Group (ECOG) Performance Status	
Grade	ECOG description
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair
5	Dead
Oken, M.M., Creech, R.H., Tormey, D.C., Horton, J., Davis, T.E., McFadden, E.T., Carbone, P.P.: Toxicity And Response Criteria Of The Eastern Cooperative Oncology Group. Am J Clin Oncol 5:649-655, 1982	

NCCN recommendation definitions:

Category 1:
Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2A:
Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2B:
Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.

Category 3:
Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate

Resources:

Erleada (apalutamide) product information, revised by Janssen Products, LP. 08-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed February 21, 2025.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Prostate Cancer Version 1.2025 – Updated December 04, 2024. Available at https://www.nccn.org. Accessed April 02, 2025.

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.