Clinical Policy: Apalutamide (Erleada)

Reference Number: CP.PHAR.376
Effective Date: 06.01.18
Last Review Date: 05.24
Line of Business: Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Apalutamide (Erleada®) is an androgen receptor inhibitor.

FDA Approved Indication(s)

Erleada is indicated for the treatment of patients with:

- Non-metastatic castration-resistant prostate cancer (CRPC)
- Metastatic castration-sensitive prostate cancer (CSPC)

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Erleada is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Prostate Cancer (must meet all)**:**

1. Diagnosis of prostate cancer that is characterized as one of the following (a or b):
   a. Non-metastatic and both of the following (i and ii):
      i. Castration-resistant, as evidenced by disease progression despite bilateral orchiectomy or other androgen deprivation therapy (*see Appendix D*);
      ii. Prostate-specific antigen doubling time (PSADT) ≤ 10 months;
   b. Metastatic and castration-sensitive;
2. Prescribed by or in consultation with an oncologist or urologist;
3. Age ≥ 18 years;
4. Member will use a gonadotropin-releasing hormone (GnRH) analog concurrently or has had a bilateral orchiectomy;
5. For members with metastatic disease, failure of generic abiraterone, unless one of the following (a or b):
   a. Contraindicated or clinically significant adverse effects are experienced;
   b. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix E*);
6. For brand Erleada requests, member must use generic apalutamide, if available, unless contraindicated or clinically significant adverse effects are experienced;
7. Request meets one of the following (a or b):*
   a. Dose does not exceed 240 mg per day (1 tablet per day);

b. Dose is supported by practice guideline or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Prostate Cancer (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Erleada for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If CRPC, there is no evidence of metastases;
4. Member continues to use a gonadotropin-releasing hormone (GnRH) analog concurrently or has had a bilateral orchiectomy;
5. For brand Erleada requests, member must use generic apalutamide, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed 240 mg per day (1 tablet per day);
   b. New dose is supported by practice guideline or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
CRPC: castration-resistant prostate cancer
CSPC: castration-sensitive prostate cancer
GnRH: gonadotropin-releasing hormone
LHRH: luteinizing-hormone releasing-hormone
PSADT: prostate-specific antigen doubling time

Appendix B: Therapeutic Alternatives

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
abiraterone (Zytiga®)	1,000 mg (four 250 mg tablets) PO QD in combination with prednisone 5 mg PO BID (CRPC) or prednisone 5 mg PO QD (CSPC)	1,000 mg QD; 1,000 mg BID if taking a strong CYP3A4 inducer

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: General Information

- CRPC is prostate cancer that progresses clinically, radiographically, or biochemically despite castrate levels of serum testosterone (< 50 ng/dL). Per the NCCN, androgen deprivation therapy should be continued in the setting of CRPC while additional therapies are applied.
- Examples of androgen deprivation therapy include:
  - Bilateral orchiectomy (surgical castration)
  - Luteinizing-hormone releasing-hormone (LHRH) agonist given with or without an anti-androgen:
    - LHRH agonists: Zoladex® (goserelin), leuprolide (Lupron Depot® or Eligard®), Trelstar® (triptorelin)
    - Anti-androgens: bicalutamide (Casodex®), flutamide (Eulexin®), nilutamide (Nilandron®), Xtandi® (enzalutamide), Erleada® (apalutamide), Nubeqa® (darolutamide)

- LHRH antagonists: Firmagon® (degarelix), Orgovyx™ (relugolix)

Appendix E: States with Regulations against Redirections in Cancer

State	Step Therapy Prohibited?	Notes
FL	Yes	For stage 4 metastatic cancer and associated conditions
GA	Yes	For stage 4 metastatic cancer. Redirection does not refer to review of medical necessity or clinical appropriateness
IA	Yes	For standard of care stage 4 cancer drug use, supported by peer-reviewed, evidence-based literature, and approved by FDA
LA	Yes	For stage 4 advanced, metastatic cancer or associated conditions. Exception if "clinically equivalent therapy, contains identical active ingredient(s), and proven to have same efficacy
NV	Yes	Stage 3 and stage 4 cancer patients for a prescription drug to treat the cancer or any symptom thereof of the covered person
OH	Yes	**Applies to Commercial and HIM requests only** For stage 4 metastatic cancer and associated conditions
OK	Yes	**Applies to HIM requests only** For advanced metastatic cancer and associated conditions
PA	Yes	For stage 4 advanced, metastatic cancer
TN	Yes	For advanced metastatic cancer and associated conditions
TX	Yes	For stage 4 advanced, metastatic cancer and associated conditions

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Non-metastatic CRPC, metastatic CSPC	240 mg PO QD	240 mg/day

VI. Product Availability

Tablets: 60 mg, 240 mg

VII. References

1. Erleada Prescribing Information. Horsham, PA: Janssen Pharmaceutical Companies; December 2023. Available at: www.erleada.com. Accessed January 9, 2024.
2. Apalutamide. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed January 9, 2024.
3. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology: Prostate Cancer. Version 4.2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed January 9, 2024.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2020 annual review; no significant changes; added HIM line of business; references reviewed and updated.	02.03.20	05.20

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2021 annual review: added that PSADT ≤ 10 months for non-metastatic CRPC; added that member continues to use a gonadotropin-releasing hormone (GnRH) analog concurrently or has had a bilateral orchiectomy; added generic redirection language to "must use" since oral oncology product; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated.	02.20.21	05.21
Per November SDC and prior clinical guidance, removed Commercial and HIM line of business (separated to new policy CP.PCH.45); added redirection to generic abiraterone for members with metastatic disease.	11.30.21	02.22
2Q 2022 annual review: no significant changes; references reviewed and updated.	01.25.22	05.22
Template changes applied to other diagnoses/indications.	09.22.22	
2Q 2023 annual review: no significant changes; updated *Appendix D* examples of androgen deprivation therapy per NCCN; references reviewed and updated. RT4: added new 240 mg tablet strength to Section VI.	03.15.23	05.23
2Q 2024 annual review: for generic abiraterone redirection added additional bypass if request is for a State with regulations against step therapy in certain oncology settings, along with Appendix E; added clarification for daily quantity of 1 tablet per day; references reviewed and updated.	01.09.24	05.24

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy,

contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.