Pharmacy Policy Bulletin: J-0201 Androgen Receptor Inhibitors – Commercial and Healthcare Reform	
Number: J-0201	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial (1.):** **1.** Miscellaneous Specialty Drugs Oral = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0201-012	**Original Date:** 11/06/2019
Effective Date: 10/08/2025	**Review Date:** 09/17/2025

Drugs Product(s):	• Erleada (apalutamide) • Nubeqa (darolutamide) • Xtandi (enzalutamide)

FDA-Approved Indication(s):	• Erleada
	  ○ Treatment of patients with metastatic castration-sensitive prostate cancer (CSPC)
	  ○ Treatment of patients with non-metastatic castration-resistant prostate cancer (CRPC)
	• Nubeqa
	  ○ Treatment of adult patients with non-metastatic CRPC
	  ○ Treatment of adult patients with metastatic CSPC
	  ○ Treatment of adult patients with metastatic CSPC in combination with docetaxel
	• Xtandi
	  ○ Treatment of patients with CRPC
	  ○ Treatment of patients with metastatic CSPC
	  ○ Treatment of patients with non-metastatic CSPC with biochemical recurrence at high risk for metastasis

Background:	• Erleada, Nubeqa, and Xtandi are androgen receptor (AR) inhibitors which bind to the AR in order to inhibit AR nuclear translocation and DNA binding to impede AR-mediated transcription. This decreases tumor cell proliferation and growth. • Androgen-deprivation therapy, either bilateral orchiectomy or treatment with a gonadotropin-releasing hormone analogue agonist or antagonist, is the mainstay of treatment for metastatic prostate cancer. • Castrate-resistant prostate cancer is defined by disease progression despite androgen depletion therapy. • Patients should receive a gonadotropin-releasing hormone (GnRH) analog (e.g., Zoladex [goserelin acetate], Lupron [leuprolide acetate], Vantas [histrelin], etc.) concurrently with Erleada, Nubeqa, or Xtandi (for CRPC and metastatic CSPC), or should have had bilateral orchiectomy. Patients may be treated with or without

	a GnRH analog when using Xtandi for non-metastatic CSPC with biochemical recurrence at high risk for metastasis. • The clinical trial assessing efficacy of Xtandi in non-metastatic CSPC with high-risk biochemical recurrence (BCR) included patients that had high-risk BCR (defined by a prostate-specific antigen [PSA] doubling time ≤ 9 months) and PSA values ≥ 1 ng/mL if they had prior radical prostatectomy (with or without radiotherapy) as the primary treatment for prostate cancer or PSA values ≥ 2 ng/mL above the nadir if they had prior radiotherapy only. • The ICD-10 codes D07.5 “Carcinoma in situ of prostate” and C61 “Malignant neoplasm of prostate” may apply to the drug(s) addressed in this policy; however, the prescriber must confirm that the member is castration-sensitive or castration-resistant. • Prescribing Considerations: o Erleada, Nubeqa, and Xtandi should be prescribed under the supervision of a hematologist/oncologist. o Safety and effectiveness of Erleada, Nubeqa, and Xtandi has not been established in pediatric patients. o Male patients with female partners of reproductive potential should be advised to use effective contraception during treatment and for 3 months after the last dose of Xtandi and Erleada, and 1 week after the last dose of Nubeqa. o Patients should be evaluated for fracture and fall risk when taking Erleada or Xtandi. o Patients should be advised of the risk of developing a seizure while receiving Xtandi or Erleada. o Dosage reduction below 300 mg twice daily is not recommended for Nubeqa. o Patients receiving Erleada, Nubeqa, and Xtandi should be advised of the risk of cerebrovascular and ischemic cardiovascular events and should be monitored for signs and symptoms of ischemic heart disease and cerebrovascular disorders.

Approval Criteria

I. Initial Authorization

A. Erleada

When a benefit, coverage of Erleada may be approved when all of the following criteria are met **(1., 2., and 3.)**:

1. The member is 18 years of age or older.

2. The member meets one (1) of the following criteria **(a. or b.)**:

a. The member has a diagnosis of metastatic castration-sensitive prostate cancer (ICD-10: C61, Z19.1).

b. The member has a diagnosis of non-metastatic castration-resistant prostate cancer (ICD-10: C61, Z19.2).

3. The member meets one (1) of the following criteria **(a. or b.)**:

a. Erleada is being used in combination with a GnRH analog.

b. The member has had a bilateral orchiectomy.

B. Nubeqa

1. Castration-resistant Prostate Cancer

When a benefit, coverage of Nubeqa may be approved when all of the following criteria are met **(a., b., and c.)**:

a. The member is 18 years of age or older.

b. The member has a diagnosis of non-metastatic castration-resistant prostate cancer (ICD-10: C61, Z19.2).

c. The member meets one (1) of the following criteria **(i. or ii.)**:
- **i.** Nubeqa is being used in combination with a GnRH analog.
- **ii.** The member has had a bilateral orchiectomy.

2. Castration-sensitive Prostate Cancer
When a benefit, coverage of Nubeqa may be approved when all of the following criteria are met **(a., b., and c.)**:
- **a.** The member is 18 years of age or older.
- **b.** The member has a diagnosis of metastatic castration-sensitive prostate cancer (ICD-10: C61, Z19.1).
- **c.** The member meets one (1) of the following criteria **(i. or ii.)**:
  - **i.** Nubeqa is being used in combination with a GnRH analog.
  - **ii.** The member has had a bilateral orchiectomy.

C. Xtandi

1. Castration-Resistant Prostate Cancer
When a benefit, coverage of Xtandi may be approved when all of the following criteria are met **(a., b., and c.)**:
- **a.** The member is 18 years of age or older.
- **b.** The member has a diagnosis of castration-resistant prostate cancer (ICD-10: C61, Z19.2).
- **c.** The member meets one (1) of the following criteria **(i. or ii.)**:
  - **i.** Xtandi is being used in combination with a GnRH analog.
  - **ii.** The member has had a bilateral orchiectomy.

2. Metastatic Castration-Sensitive Prostate Cancer
When a benefit, coverage of Xtandi may be approved when all of the following criteria are met **(a., b., and c.)**:
- **a.** The member is 18 years of age or older.
- **b.** The member has a diagnosis of metastatic castration-sensitive prostate cancer (ICD-10: C61, Z19.1).
- **c.** The member meets one (1) of the following criteria **(i. or ii.)**:
  - **i.** Xtandi is being used in combination with a GnRH analog.
  - **ii.** The member has had a bilateral orchiectomy.

3. Non-Metastatic Castration-Sensitive Prostate Cancer
When a benefit, coverage of Xtandi may be approved when all of the following criteria are met **(a., b., and c.)**:
- **a.** The member is 18 years of age or older.
- **b.** The member has a diagnosis of non-metastatic castration-sensitive prostate cancer (ICD-10: C61, D07.5)
- **c.** The member has biochemical recurrence at high risk for metastasis.

II. Reauthorization
When a benefit, reauthorization of an androgen receptor inhibitor may be approved when the following criterion is met **(A.)**:
- **A.** The prescriber attests that the member is tolerating therapy and has experienced a therapeutic response defined as one (1) of the following **(1. or 2.)**:
  - **1.** Disease improvement
  - **2.** Delayed disease progression

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

IV. Coverage of oncology drug(s) listed in this policy may be approved on a case-by-case basis per indications supported in the most current NCCN guidelines.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.
II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 2 year authorization may be granted.

Automatic Approval Criteria

None

References:

1. Erleada [package insert]. Horsham, PA: Janssen Products, LP; August 2024.
2. Nubeqa [package insert]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc.; June 2025.
3. Xtandi [package insert]. Northbrook, IL: Astellas Pharma US, Inc.; November 2023.
4. Smith M, Saad F, Chowdhury S, et al. Apalutamide Treatment and Metastasis-free Survival in Prostate Cancer. *New England Journal of Medicine*. 2018;378:1408-18.
5. Saad F, Hotte SJ. Guidelines for the management of castrate-resistant prostate cancer. *Can Urol Assoc J*. 2010.
6. NCCN Guidelines. Prostate Cancer Version 2.2025. National Comprehensive Cancer Network. Available at: https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed August 14, 2025.