Washington State Health Care Authority

Antiandrogens (Oral) – apalutamide, darolutamide, enzalutamide

Medical policy no. 21.40.24-1 Effective Date: 10/1/2025

Related medical policies:

Policy Name	Indications
Androgen Biosynthesis Inhibitor	Prostate Cancer

Note: *New-to-market drugs included in this class based on the Apple Health Preferred Drug List are non-preferred and subject to this prior authorization (PA) criteria. Non-preferred agents in this class require an inadequate response or documented intolerance due to severe adverse reaction or contraindication to at least TWO preferred agents. If there is only one preferred agent in the class documentation of inadequate response to ONE preferred agent is needed. If a drug within this policy receives a new indication approved by the Food and Drug Administration (FDA), medical necessity for the new indication will be determined on a case-by-case basis following FDA labeling.*

To see the list of the current Apple Health Preferred Drug List (AHPDL), please visit: https://www.hca.wa.gov/assets/billers-and-providers/apple-health-preferred-drug-list.xlsx

Medical necessity

Drug	Medical Necessity
Apalutamide (Erleada) Darolutamide (Nubeqa) Enzalutamide (Xtandi)	**Antiandrogens (Oral)** may be considered medically necessary in patients who meet the criteria described in the clinical policy below. If all criteria are not met, the clinical reviewer may determine there is a medically necessary need and approve on a case-by-case basis. The clinical reviewer may choose to use the reauthorization criteria when a patient has been previously established on therapy and is new to Apple Health.

Clinical policy:

Clinical Criteria	
Non-metastatic castration-resistant prostate cancer (nmCRPC) apalutamide (Erleada) darolutamide (Nubeqa) **Non-metastatic, castration-sensitive prostate cancer with biochemical recurrence at high risk for metastasis** enzalutamide (Xtandi)	Apalutamide (Erleada), darolutamide (Nubeqa), enzalutamide (Xtandi) may be approved when all the following documented criteria are met: 1. Patient is 18 years of age or older, **AND** 2. Prescribed by or in consultation with an oncologist or urologist; **AND** 3. Patient must meet one of the following: a. Patient has either had a bilateral orchiectomy; **OR** b. Patient will use hormone suppression (e.g., GnRH therapy) concurrently; **AND** 4. Diagnosis of one of the following: a. Non-metastatic castration resistant prostate cancer; **OR**

	b. Non-metastatic castration sensitive prostate cancer; **AND** 5. Experienced prostate-specific antigen (PSA) doubling time of <6 months or PSA ≥ 20 ng/mL on androgen deprivation therapy (e.g. GnRH analogs) 6. For enzalutamide requests: the patient is in the high-risk or very high-risk group defined by the following: a. The patient is node positive; **OR** b. The patient is node negative and has at least TWO of the following risk factors: i. Gleason Score ≥ 8 ii. Tumor stage T3 or T4 iii. Prostate-specific antigen (PSA) concentration ≥40 ng/mL. If ALL criteria are met, the request will be authorized for **6 months.**
	Criteria (Reauthorization) Apalutamide (Erleada), darolutamide (Nubeqa), enzalutamide (Xtandi) may be approved when all the following criteria are met: 1. Documentation is submitted demonstrating disease stability or a positive clinical response to therapy (e.g., stabilization of disease, decrease in tumor size or tumor spread, lack of disease progression). If ALL criteria are met, the request will be authorized for **6 months.**
Castration-resistant prostate cancer Enzalutamide (Xtandi)	Enzalutamide (Xtandi) may be approved when all the following criteria are met: 1. Patient is 18 years of age or older, **AND** 2. Prescribed by, or in consultation with, an oncologist or urologist; **AND** 3. Patient must meet one of the following: a. Patient has either had a bilateral orchiectomy; **OR** b. Patient will use hormone suppression (e.g., GnRH therapy) concurrently; **AND** 4. Diagnosis of castration resistant prostate cancer; **AND** 5. Medication will be used as monotherapy; **OR** 6. If the request is for use in setting of HRR mutation, enzalutamide (Xtandi) will be used in combination with talazoparib (Talzenna); **AND** 7. Treatment with abiraterone has been ineffective unless it is contraindicated or not tolerated. If ALL criteria are met, the request will be authorized for **6 months.**
	Criteria (Reauthorization)

	Enzalutamide (Xtandi) may be approved when all the following criteria are met: 1. Documentation is submitted demonstrating disease stability or a positive clinical response to therapy (e.g., stabilization of disease, decrease in tumor size or tumor spread, lack of disease progression). If ALL criteria are met, the request will be authorized for **6 months.**
Metastatic castration-sensitive prostate cancer apalutamide (Erleada) enzalutamide (Xtandi) **Metastatic hormone-sensitive prostate cancer (mHSPC) in combination with docetaxel** darolutamide (Nubeqa)	Apalutamide (Erleada), darolutamide (Nubeqa), enzalutamide (Xtandi) may be approved when all the following criteria are met: 1. Patient is 18 years of age or older, **AND** 2. Prescribed by, or in consultation with, an oncologist or urologist; **AND** 3. Patient must meet one of the following: a. Patient has either had a bilateral orchiectomy; **OR** b. Patient will use hormone suppression (e.g., GnRH therapy) concurrently; **AND** 4. Diagnosis of one of the following: a. Metastatic castration sensitive prostate cancer; **OR** b. Metastatic hormone sensitive prostate cancer; **AND** 5. The patient has at least TWO of the following risk factors: a. Gleason Score ≥ 7 (Grade Group ≥ 2) b. Bone lesions c. Presence of measurable visceral metastases; **AND** 6. Treatment with abiraterone has been ineffective unless it is contraindicated or not tolerated; **AND** 7. If the request is for darolutamide (Nubeqa), it will be used in combination with docetaxel If ALL criteria are met, the request will be authorized for **6 months.**
	Criteria (Reauthorization) Apalutamide (Erleada), darolutamide (Nubeqa), enzalutamide (Xtandi) may be approved when all the following criteria are met: 1. Criteria #4 above continues to be met; **AND** 2. Documentation is submitted demonstrating disease stability or a positive clinical response to therapy [e.g., stabilization of disease, decrease in tumor size or tumor spread, lack of disease progression]. If ALL criteria are met, the request will be authorized for **6 months.**

Dosage and quantity limits

Drug	Indication	FDA Approved Dosing	Dosage Form and Quantity Limit
Erleada	Metastatic castration-sensitive prostate cancer Non-metastatic castration-resistant prostate cancer (nmCRPC)	240 mg once daily	• 60 mg tablets: 4 tablets per day • 240 mg tablets: 1 tablet per day
Nubeqa	Non-metastatic castration-resistant prostate cancer (nmCRPC) Metastatic hormone-sensitive prostate cancer (mHSPC) in combination with docetaxel	600 mg (two 300 mg tablets) twice daily	• 300 mg tablets: 4 tablets per day
Xtandi	Castration-resistant prostate cancer Metastatic castration-sensitive prostate cancer Non-metastatic, castration-sensitive prostate cancer with biochemical recurrence at high risk for metastasis	160 mg once daily	• 40 mg capsules: 4 capsules per day • 40 mg tablets: 4 tablets per day • 80 mg tablets: 2 tablet per day

Coding:

HCPCS Code	Description
<HCPCS Code>	N/A

Background:

Prostate cancer is amongst the most common cancers in males worldwide. In the United States, 11 percent of males are diagnosed with prostate cancer over their lifetime, with the incidence generally rising with age. There are an estimated 268,490 cases and 34,500 deaths annually. Androgen deprivation therapy (ADT) with or without an androgen receptor pathway inhibitor is a usual first-line option for males with advanced prostate cancer. Many treatment options exist, and initial and further line therapy are contingent upon patient specific characteristics. These options include, but are not limited National Comprehensive Cancer Network Prostate Cancer guideline recommended radiation therapy, prostatectomy, androgen deprivation pharmacotherapy, bilateral orchiectomy, chemotherapy, abiraterone (Zytiga, Yonsa), or androgen receptor inhibitors (e.g., enzalutamide (Xtandi), darolutamide (Nubeqa), apalutamide (Erleada)). Multi-modal therapy, such as abiraterone or enzalutamide with ADT, is commonly utilized; however, abiraterone and/or androgen receptor inhibitor combinations have not been evaluated for safety and efficacy to date outside of therapies listed in the

policy. Continuation of ADT is commonly employed and is recommended as discontinuation of GnRH agonists are likely to result in an increase in serum testosterone and disease progression. Second generation anti-androgen agents act by competitively inhibiting androgen binding to androgen receptors.

References

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History

Approved Date	Effective Date	Version	Action and Summary of Changes
4/16/2025	**10/01/2025**	21.40.24-1	Approved by DUR Board New policy created