LifeWise
Health Plan of Washington

PHARMACY / MEDICAL POLICY – 5.01.544

Prostate Cancer Targeted Therapies

Effective Date:	Sep. 1, 2026
Last Revised:	Aug. 11, 2026
Replaces:	N/A

RELATED MEDICAL POLICIES:

5.01.517	Use of Vascular Endothelial Growth Factor Receptor (VEGF) Inhibitors and Other Angiogenesis Inhibitors in Oncology Treatment
5.01.518	BCR-ABL Kinase Inhibitors
5.01.534	Multiple Receptor Tyrosine Kinase Inhibitors
5.01.540	Miscellaneous Oncology Drugs
5.01.603	Epidermal Growth Factor Receptor (EGFR) Inhibitors
6.01.525	Therapeutic Radiopharmaceuticals in Oncology

Select a hyperlink below to be directed to that section.

POLICY CRITERIA | CODING | RELATED INFORMATION
EVIDENCE REVIEW | APPENDIX | REFERENCES | HISTORY

∞ Clicking this icon returns you to the hyperlinks menu above.

Introduction

The prostate gland is found only in men and produces some of the fluid that makes up semen. The gland is below the bladder. An enlarged prostate and prostate cancer are two separate conditions. An enlarged prostate is a prostate that simply gets bigger as a man ages. Prostate cancer arises from prostate cells that grow uncontrollably. There are several ways of treating prostate cancer. This policy describes when certain drugs may be covered to treat prostate cancer that doesn't respond to medication or hormone therapy, or has spread to other parts of the body.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria

Drug	Medical Necessity
Oral Drugs	

• **Abirtega (abiraterone)**
• **Generic abiraterone**
	Abirtega (abiraterone) and generic abiraterone may be considered medically necessary for the treatment of individuals when all of the following criteria are met:
	• The individual has been diagnosed with 1 of the following:
	  ○ Metastatic castration-resistant prostate cancer (CRPC)
	OR
	  ○ Deleterious or suspected deleterious BRCA-mutated (BRCAm) metastatic castration-resistant prostate cancer (mCRPC) when used in combination with Lynparza (olaparib)
	OR
	  ○ Metastatic high-risk castration-sensitive prostate cancer (CSPC)
	OR
	  ○ Metastatic androgen pathway modulation-naïve or sensitive (mAPMN/S) prostate cancer that is PTEN-deficient when used in combination with capivasertib
	AND
	• Medication is used in combination with androgen deprivation therapy (ADT) as documented by:
	  ○ Concurrently receiving a gonadotropin-releasing hormone (GnRH) analog
	OR
	  ○ Having had bilateral orchiectomy
	AND
	• Medication will be used in combination with prednisone

Akeega (niraparib and abiraterone acetate)	**Akeega (niraparib and abiraterone acetate) may be considered medically necessary for the treatment of adult individuals when all of the following criteria are met:** • The individual has been diagnosed with 1 of the following: ○ Deleterious or suspected deleterious BRCA-mutated (BRCAm) metastatic castration-resistant prostate cancer (mCRPC) **OR**

Drug	Medical Necessity
Oral Drugs	
	○ Deleterious or suspected deleterious BRCA2-mutated (BRCA2m) metastatic castration-sensitive prostate cancer (mCSPC) **AND** • Akeega (niraparib and abiraterone acetate) is used in combination with androgen deprivation therapy (ADT) as documented by: ○ Concurrently receiving a gonadotropin-releasing hormone (GnRH) analog **OR** ○ Having had bilateral orchiectomy **AND** • Akeega (niraparib and abiraterone acetate) will be used in combination with prednisone
Erleada (apalutamide)	**Erleada (apalutamide) may be considered medically necessary for the treatment of individuals when all of the following criteria are met:** • The individual has been diagnosed with 1 of the following: ○ Metastatic castration-sensitive prostate cancer **OR** ○ Non-metastatic castration-resistant prostate cancer **AND** • Erleada (apalutamide) is used in combination with androgen deprivation therapy (ADT) as documented by: ○ Concurrently receiving a gonadotropin-releasing hormone (GnRH) analog **OR** ○ Having had bilateral orchiectomy
Nubeqa (darolutamide)	**Nubeqa (darolutamide) may be considered medically necessary for the treatment of individuals when all of the following criteria are met:** • The individual has been diagnosed with 1 of the following: ○ Non-metastatic castration-resistant prostate cancer (nmCRPC) **OR** ○ Metastatic castration-sensitive prostate cancer (mCSPC)

Drug	Medical Necessity
Oral Drugs	
	OR ○ Metastatic castration-sensitive prostate cancer (mCSPC) in combination with docetaxel **AND** • Nubeqa (darolutamide) is used in combination with androgen deprivation therapy (ADT) as documented by: ○ Concurrently receiving a gonadotropin-releasing hormone (GnRH) analog **OR** ○ Having had bilateral orchiectomy
Xtandi (enzalutamide)	**Xtandi (enzalutamide) may be considered medically necessary for the treatment of individuals when all of the following criteria are met:** • The individual has been diagnosed with 1 of the following: ○ Castration-resistant prostate cancer (CRPC) **OR** ○ Metastatic castration-sensitive prostate cancer (mCSPC) **OR** ○ In combination with Talzenna (talazoparib), for the treatment of adult individuals with HRR gene-mutated metastatic castration- resistant prostate cancer (mCRPC) (see **Appendix**) **OR** ○ Non-metastatic castration-sensitive prostate cancer with biochemical recurrence at high risk for metastasis **AND** • Xtandi (enzalutamide) is used in combination with androgen deprivation therapy (ADT) as documented by: ○ Concurrently receiving a gonadotropin-releasing hormone (GnRH) analog **OR** ○ Having had bilateral orchiectomy
Yonsa (abiraterone)	**Yonsa (abiraterone) may be considered medically necessary for the treatment of individuals with metastatic castration-**

Drug	Medical Necessity
Oral Drugs	

	resistant prostate cancer (CRPC) when all of the following criteria are met:
	• Yonsa (abiraterone) is used in combination with androgen deprivation therapy (ADT) as documented by:
	  ○ Concurrently receiving a gonadotropin-releasing hormone (GnRH) analog
	OR
	  ○ Having had bilateral orchiectomy
	AND
	• Yonsa (abiraterone) will be used in combination with methylprednisolone or another corticosteroid
	AND
	• The individual has tried and had an inadequate response or intolerance to Abirtega (abiraterone) or generic abiraterone

Zytiga (abiraterone)	**Zytiga (abiraterone) may be considered medically necessary for the treatment of individuals when all of the following criteria are met:**
	• The individual has been diagnosed with 1 of the following:
	  ○ Metastatic castration-resistant prostate cancer (CRPC)
	OR
	  ○ Deleterious or suspected deleterious BRCA-mutated (BRCAm) metastatic castration-resistant prostate cancer (mCRPC) when used in combination with Lynparza (olaparib)
	OR
	  ○ Metastatic high-risk castration-sensitive prostate cancer (CSPC)
	OR
	  ○ Metastatic androgen pathway modulation-naïve or sensitive (mAPMN/S) prostate cancer that is PTEN-deficient when used in combination with capivasertib
	AND
	• The individual has tried and had an inadequate response or intolerance to Abirtega (abiraterone) or generic abiraterone
	AND

Drug	Medical Necessity
Oral Drugs	

	• Zytiga (abiraterone) is used in combination with androgen deprivation therapy (ADT) as documented by:
	  ○ Concurrently receiving a gonadotropin-releasing hormone (GnRH) analog
	  OR
	  ○ Having had bilateral orchiectomy
	AND
	• Zytiga (abiraterone) will be used in combination with prednisone

Drug	Medical Necessity
Intravenous Drugs	
Jevtana (cabazitaxel) IV	**Jevtana (cabazitaxel) may be considered medically necessary for the treatment of metastatic castration-resistant prostate cancer when ALL the following are met:** • Jevtana (cabazitaxel) will be used in combination with prednisone **AND** • The individual has been previously treated with a docetaxel-containing treatment regimen

Drug	Investigational
As listed	**All other uses of the medications listed in this policy are considered investigational.** **The medications listed in this policy are subject to the product's US Food and Drug Administration (FDA) dosage and administration prescribing information.**

Length of Approval	
Approval	**Criteria**
Initial authorization	**All drugs listed in this policy may be approved up to 6 months.**

Length of Approval	
Approval	**Criteria**
Re-authorization criteria	**All drugs listed in this policy may be approved up to 12 months as long as the drug-specific coverage criteria are met and chart notes demonstrate that the individual continues to show a positive clinical response to therapy.**

Documentation Requirements

The individual's medical records submitted for review for all conditions should document that medical necessity criteria are met. The record should include the following:

- Office visit notes that contain the diagnosis, relevant history, physical evaluation and medication history

Coding

Code	Description
HCPCS	
J9043	Injection, cabazitaxel (Jevtana), 1 mg

Related Information

Benefit Application

Pharmacy Benefit

Abirtega (abiraterone), Akeega (niraparib and abiraterone acetate), Erleada (apalutamide), Nubeqa (darolutamide), Xtandi (enzalutamide), Yonsa (abiraterone), and Zytiga (abiraterone) are managed through the pharmacy benefit.

Medical Benefit

Jevtana (cabazitaxel) is managed through the medical benefit.

Evidence Review

Description

Prostate cancer is a neoplastic disease of the prostate gland. Prostate cancer arises from mutations in cells of the prostate that cause overexpression of enzymes that support androgen biosynthesis, loss of regulation of cell death within the tumor cells, and up regulation of androgen receptors. Androgen receptor binding by androgens plays a crucial role in prostate cancer progression. Most prostate cancers respond to androgen deprivation.

Approximately 60% of all cases of prostate cancer are diagnosed in men 65 years of age or older and 97% occur in men 50 and older. CRPC is a term used to describe prostate cancer which has progressed despite local therapy and first-line hormonal therapy assuring castrate levels of testosterone. Prostate cancers typically progress slowly and there is a high rate of survival for disease detected in early stages, but not for advanced disease stages. In the US, the 5-year survival rate is effectively 100% when the disease is local or regional, but this drops to 31% for disease with distant metastases.

Disease Burden

Prostate cancer is the second most common cause of cancer death in American men. In 2022, an estimated 268,490 men are expected to be diagnosed with prostate cancer, and approximately 34,500 are expected to have died from the disease. While it is prevalent, only 15% of all prostate cancer individuals develop mCRPC prior to chemotherapy, and just 9% of all prostate cancer individuals progress to mCRPC on first-line docetaxel chemotherapy.

The condition is associated with a substantial economic burden, due to high incidence rates and high costs associated with management of advanced cancer stages. The high management cost burden arises from the requirement for hospitalizations, chemotherapy, palliative surgical procedures, and computed tomography (CT) or magnetic resonance imaging (MRI) scans to monitor potential bone metastases. In 2007, per-individual per-month CRPC costs for men over

the age of 40 were approximately $1,800, with ambulatory visits ($1,152) and inpatient stays ($559) comprising the majority of these costs. Total all-cause healthcare costs for these same individuals totaled $3,500 per-individual per-month.

Rationale

Treatment Alternatives

Several approved pharmacotherapeutic alternatives for mCRPC have demonstrated some benefit in estimated survival compared with acceptable controls.

Zytiga (abiraterone) + prednisone

Zytiga (abiraterone) acetate is an oral drug that is converted in vivo to abiraterone a CYP17 complex (17α-hydroxylase/C17,20-lyase) inhibitor that interrupts androgen biosynthesis throughout the body (testes, adrenal gland, and prostate tumor). Prostate cancer is very often an androgen-driven disease. CYP17 inhibition may also lead to increased mineralocorticoid production by the adrenal gland secondary to increased adrenocorticotropin hormone (ACTH) production from a feedback mechanism induced by low cortisol levels. Up regulated ACTH leads to increased deoxycorticosterone which exhibits mineralocorticoid activity. Results from clinical trials have shown that coadministration of a corticosteroid (e.g., prednisone) with abiraterone reduces the incidence and severity of mineralocorticoid excess associated adverse reactions. An RCT showed that abiraterone and prednisone improved radiographic progression-free survival, time to initiation of chemotherapy, time to onset or worsening of pain, and time to deterioration in improvement status.

Xtandi (enzalutamide)

Xtandi (enzalutamide) is indicated for the treatment of CRPC or mCSPC or HRR gene-mutated (HRRm) mCRPC. The efficacy was demonstrated in five randomized, multicenter clinical trials. All individuals received concomitant GnRH therapy or had prior bilateral orchiectomy. One well-designed RCT has shown enzalutamide prolongs overall survival (OS) by 4.8 months, time to prostate-specific antigen (PSA) progression (TTPP), radiographic progression-free survival (rPFS), and time to first skeletal-related event (SRE) compared with placebo. There is currently no direct evidence with which to assess real world comparative effectiveness. Indirect evidence suggests a

similar modest (2-5 month) increase in overall survival and hazard for risk of death with enzalutamide, abiraterone, or cabazitaxel in individuals with mCRPC previously treated with a docetaxel-based regimen. However, it is important to note that the abiraterone and cabazitaxel studies had control arms which included agents with anti-tumor activity (prednisone and mitoxantrone + prednisone, respectively) compared to placebo control for enzalutamide. The most common adverse reactions (≥ 10%) that occurred more frequently (≥ 2% over placebo) in the Xtandi-treated individuals are asthenia/fatigue, back pain, hot flush, constipation, arthralgia, decreased appetite, diarrhea, and hypertension. The most significant warning reported is for seizure, although this occurs rarely (incidence about 0.5%).

Indirect evidence suggests favorable safety and tolerability compared to other second-line treatments with survival benefit for mCRPC. Enzalutamide lacks the detrimental effects of mineralocorticoid excess induced by Xtandi (enzalutamide), and thus does not require co-administration with corticosteroids, which may complicate CRPC treatment. Unlike Jevtana (cabazitaxel), Xtandi (enzalutamide) is not reported to commonly cause neuropathy or severe myelosuppression, two significant toxicities which can lead to morbidity and limit additional therapy in this patient population.

The efficacy of Xtandi in combination with Talzenana was evaluated in TALAPRO-2 trial, which was randomized, double-blind, placebo-controlled, multi-cohort trial. In this trial 399 individuals with HRR gene-mutated (HRRm) mCRPC were randomized 1:1 to receive either enzalutamide 160 mg daily plus either Talzenna 0.5 mg or placebo daily until individual experiences unacceptable toxicity or progression. All the individuals received a GnRH analog or had prior bilateral orchiectomy and they were progressed on prior androgen deprivation therapy. Mutation in HRR gene was determined using either circulating tumor DNA based next generation sequencing assays or solid tumor tissue. The primary efficacy outcome was to evaluate radiographic progression-free survival (rPFS) and another efficacy outcome measure was overall survival. The number of rPFS events were in 33% individual in the treatment group versus 52% in the placebo group with p-value < 0.0001.

Akeega (niraparib and abiraterone acetate)

Akeega is a combination of both niraparib and abiraterone acetate. Niraparib is a poly (ADP-ribose) polymerase (PARP) inhibitor, including PARP-1 and PARP-2, which play role in DNA repair. Abiraterone acetate is an androgen biosynthesis inhibitor, which inhibits 17 α-hydroxylase/C17,20-lyase (CYP17). CYP17 enzyme can be found in testicular, adrenal, and prostatic tumor tissues. Abiraterone has decreased serum testosterone and other androgen in individuals in the clinical trial.

Akeega should be given concurrently with a gonadotropin-releasing hormone (GnRH) analog or should have had bilateral orchiectomy. Androgen deprivation therapies can decrease the androgen production in testes but do not affect androgen production by the adrenals or in the tumor.

The efficacy and safety of Akeega was studied in Cohort 1 of Magnitude, a randomized, double-blind, placebo-controlled, multi-cohort study, where 423 individuals with homologous recombination repair (HRR) gene mutated mCRPC were randomized 1:1 to receive either niraparib 200 mg and abiraterone 1,000 mg (n = 212), or placebo and abiraterone (n = 211) until individual had unacceptable toxicity or progression. All the individuals also received prednisone 10 mg once daily and GnRH analog or had prior bilateral orchiectomy. Out of 423 individuals, about 53% (n = 225) individuals had BRCA gene mutations determined by FDA-approved test. Out of all individuals, 7% individuals had BRCA1 mutation, 78% had BRCA2 mutations, and 15% had BRCA mutations in combination with mutations in other HRR genes.

The primary efficacy endpoint was radiographic progression free survival. The additional efficacy outcome was overall survival (OS). In the BRCAm subgroup of the study, 40% (n = 45) individuals in Akeega group had event of disease progression or death, while 57% (n = 64) individuals in the placebo group had event of disease progression or death. The results in the non BRCAm subgroup were different. In the non-BRCAm subgroup, rPFS hazard ratio was 0.99 and the OS hazard ratio was 1.13. These results indicate that the overall improvement was primarily attributed to the subgroup of individuals with BRCAm. For the efficacy related to OS, there were 60 deaths in the treatment group and 70 deaths in the placebo group.

The efficacy of AKEEGA was investigated in AMPLITUDE (NCT04497844), a randomized double-blind, placebo-controlled, multi-cohort, multi-center study in which 696 patients with homologous recombination repair (HRR) gene-mutated (HRRm) mCSPC were randomized (1:1) to receive niraparib 200 mg and abiraterone acetate 1,000 mg (N=348) or placebo and abiraterone acetate (N=348). All patients received prednisone 5 mg daily and were required to have androgen deprivation therapy (ADT) (medical or surgical) more than 14 days prior to randomization. The only allowable prior systemic therapy in the mCSPC setting, was up to 45 days of abiraterone acetate, up to 6 cycles of docetaxel, and up to 6 months of ADT. Randomization was stratified by HRR gene alteration (BRCA2 versus CDK12 versus all other pathogenic alterations), prior docetaxel use (yes versus no), and volume of disease at screening (high versus low). Of the 696 patients enrolled, 323 were randomized as having BRCA2 gene mutation (BRCA2m). Mutation status was determined prospectively using the Foundation One CDx tissue assay or other clinical trial assays.

The major efficacy outcome measure was radiographic progression free survival (rPFS) determined by investigator-assessed radiographic progression by bone scan (according to

PCWG3 criteria) or soft tissue lesions by CT or MRI (according to RECIST 1.1 criteria) or death, whichever occurred first. Overall Survival (OS) and Time to Symptomatic Progression (TSP) were additional efficacy outcome measures. A statistically significant improvement in rPFS for niraparib and abiraterone acetate compared to placebo and abiraterone acetate was observed in the overall population of patients with HRRm. In an exploratory analysis in the subgroup of 373 patients with non-BRCA2 mutations, the investigator-assessed rPFS hazard ratio was 0.88 (95% CI: 0.63, 1.24), indicating that the improvement in the overall population was primarily attributed to the results seen in the subgroup of patients with BRCA2 mutation.

Guideline Recommendations

The latest prostate cancer guidelines from the National Comprehensive Cancer Network (NCCN) recommend the following systemic therapies for advanced disease (primarily category 2a unless otherwise labeled):

Metastatic Castration-Recurrent prostate cancer

- Asymptomatic visceral disease: Sipuleucel-T or secondary hormone therapy (including abiraterone or enzalutamide) or docetaxel or clinical trial
- Bone metastases: Denosumab (1) or zoledronic acid (1)
- Disease recurrence post-abiraterone or enzalutamide or intolerance: Docetaxel (1) or abiraterone or enzalutamide or olaparib for HRRm (1) or Radium-223 for symptomatic bone metastases (1) or Sipuleucel-T* or other secondary hormone therapy or clinical trial
- Disease recurrence post-docetaxel or intolerance: Abiraterone (1) or enzalutamide (1) or cabazitaxel (1) or Radium-223 for symptomatic bone metastases (1) or mitoxantrone or other secondary hormone therapy or Provenge (sipuleucel-T) * or clinical trial

  ***Note:** Provenge (sipuleucel-T) is recommended only for asymptomatic or minimally symptomatic individuals with an ECOG performance status of 0-1. It is not indicated for individuals with hepatic metastases or life expectancy <6 months.

- General: Maintain castrate serum testosterone levels
- Symptomatic visceral disease: Docetaxel or mitoxantrone (for individuals not candidates for docetaxel) or abiraterone or enzalutamide or palliative care for symptomatic bone metastases or clinical trial

Non-Metastatic Castration-Resistant Prostate Cancer

NCCN guidelines recommend apalutamide, darolutamide, or enzalutamide, especially if PSA doubling time is $\leq$ 10 months. Additionally, bone support should be used in individuals receiving this medication (fracture 11% vs 6.5% placebo).

National Comprehensive Cancer Network (NCCN) Compendium

The National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium is based directly on the NCCN Clinical Practice Guidelines in Oncology. The compendium lists specific panel recommendations for off-label uses of drugs, and each recommendation is supported by a level of evidence category.

The NCCN Categories of Evidence and Consensus used in the recommendations are:

- Category 1: The recommendation is based on high level evidence (e.g., randomized controlled trials) and there is uniform NCCN consensus.
- Category 2A: The recommendation is based on lower level evidence and there is uniform NCCN consensus.
- Category 2B: The recommendation is based on lower level evidence and there is nonuniform NCCN consensus (but no major disagreement).
- Category 3: The recommendation is based on any level of evidence but reflects major disagreement.

2014 Update

A search of the literature from 7/1/13 to 10/31/14 did not identify new evidence requiring changes to this policy.

2015 Update

Updated new indications and NCCN recommendations for Xtandi (enzalutamide). A search of the literature from 7/1/14 to 8/31/15 did not identify new evidence requiring changes to this policy.

2016 Update

Updated policy based on new NCCN recommendations. Zytiga (abiraterone acetate) step removed for Xtandi (enzalutamide).

2018 Update

Updated new product labeling and NCCN recommendations which now include Erleada. A search of the literature from 4/11/2017 to 3/13/2018 did not identify new evidence requiring changes to this policy. Yonsa (abiraterone) criteria was added.

2019 Update

Reviewed prescribing information for all drugs and updated Erleada (apalutamide) coverage criteria adding coverage for the treatment of individuals with metastatic castration-sensitive prostate cancer. No new evidence was identified that would require changes to other drugs listed in this policy. Added coverage criteria for a new drug Nubeqa (darolutamide).

2020 Update

Reviewed prescribing information for all drugs in policy. Updated NCCN Guideline recommendations. No new information was identified that would require changes to the policy statements.

2021 Update

Reviewed prescribing information for all drugs in policy. Updated NCCN Guideline recommendations. Added criteria for generic abiraterone, Zytiga (abiraterone), Yonsa (abiraterone), Nubeqa (darolutamide), and Erleada (apalutamide) to include necessity to be used in combination with androgen deprivation therapy. No additional new information was identified that would require changes to the policy statements.

2022 Update

Reviewed prescribing information for all drugs in policy and identified a new indication for Nubeqa (darolutamide). Added coverage to Nubeqa for the treatment of metastatic hormone-sensitive prostate cancer (mHSPC) in combination with docetaxel.

2023 Update

Reviewed prescribing information for all drugs in policy and identified a new indication for Zytiga (abiraterone acetate) and generic abiraterone. Added coverage to Zytiga and generic abiraterone for the treatment of deleterious or suspected deleterious BRCA-mutated (BRCAm) metastatic castration-resistant prostate cancer (mCRPC) when used in combination with prednisone and olaparib. based on the updated Lynparza FDA label. Added coverage to Xtandi criteria for the treatment of adult individuals with HRR gen-mutated metastatic castration-resistant prostate cancer (mCRPC) when used in combination with Talzenna based on the updated Talzenna FDA label. Added coverage criteria for Akeega for the treatment of adult individuals with deleterious or suspected deleterious BRCA-mutated (BRCAm) metastatic castration-resistant prostate cancer (mCRPC).

2024 Update

Reviewed prescribing information for all drugs in policy. Updated Xtandi (enzalutamide) to include coverage criteria for certain individuals with non-metastatic castration-sensitive prostate cancer. Added criteria to Yonsa to include trial and failure of generic abiraterone.

2025 Update

Reviewed prescribing information for all drugs in policy. Clarified that the medications listed in this policy are subject to the product's FDA dosage and administration prescribing information. Clarified that non-formulary exception review authorizations for all drugs listed in this policy may be approved up to 12 months.

2026 Update

Reviewed prescribing information for all drugs in policy. Updated Akeega (niraparib and abiraterone acetate) adding a new indication for the treatment of deleterious or suspected deleterious BRCA2-mutated (BRCA2m) metastatic castration-sensitive prostate cancer (mCSPC) when used in combination with prednisone.

Appendix

Homologous recombination repair (HRR) Gene mutation

HRR gene mutations can be found in 23% of metastatic castration-resistant prostate cancer. The most frequent gene mutations are found on breast cancer susceptibility gene (BRCA)2, ataxia-telangiectasia mutated (ATM), checkpoint kinase 2 (CHECK2), and BRCA1 genes.

Select individuals for the treatment of HRR gene-mutated mCRPC with Talzenna based on the following HRR gene mutations: ATM, ATR, BRCA1, BRCA2, CDK12, CHEK2, FANCA, MLH1, MRE11A, NBN, PALB2, or RAD51C.

The FDA approved test to detect HRR gene mutation for use with Talzenna is not available currently.

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14. Jevtana (cabazitaxel). Prescribing Information. Sanofi-Aventis U.S. LLC. Bridgewater, NJ. Revised June 2023.
15. Nubeqa (darolutamide). Prescribing Information. Bayer HealthCare Pharmaceuticals Inc; Whippany, NJ. Revised June 2025.
16. Lynparza (olaparib). Prescribing Information. AstraZeneca Pharmaceuticals LP; Wilmington, DE. Revised July 2025.
17. Talzenna (talazoparib). Prescribing Information. Pfizer Labs; New York, NY 10001. Revised June 2025.
18. Akeega (niraparib and abiraterone acetate). Prescribing Information. Janssen Biotech, Inc; Horsham, PA 19044. Revised December 2025.
19. Xtandi (enzalutamide). Prescribing Information. Astellas Pharma US, Inc; Northbrook, IL. Revised December 2025.
20. Yonsa (abiraterone acetate). Prescribing Information. Sun Pharmaceutical Industries, Inc. Cranbury, NJ. Revised March 2022.
21. Zytiga (abiraterone acetate). Prescribing Information. Patheon Inc. Mississauga, Canada. Revised August 2021.

History

Date	Comments
04/09/13	New policy effective May 1, 2013. Add to Prescription Drug Section. Enzalutamide (Xtandi) is approved for the treatment of prostate cancer when conditions are met.
07/08/13	Minor Update – Clarification was added to the policy that it is managed through the member's pharmacy benefit; this is now listed in the header and within the coding section.
12/04/13	Replace policy. Policy section updated with the addition of abiraterone (Zytiga), considered medically necessary for treating castration-resistant prostate cancer in combination with prednisone. (This was previously addressed in policy 5.01.540.) Rationale section updated in support of this addition.
12/08/14	Annual review. Policy updated with literature review; no change in policy statements
10/13/15	Annual Review. Updated enzalutamide (Xtandi) for new indications.
12/08/15	Interim Update. Medical necessity coverage criteria for enzalutamide (Xtandi) expanded.
10/25/16	Minor formatting update. Added second level bullet, Policy section under Enzalutamide (Xtandi) criteria.
01/01/17	Annual Review, changes approved December 13, 2016. Updated enzalutamide and abiraterone acetate for new indications. Medical necessity coverage criteria updated (Zytiga step removed).
05/01/17	Annual Review, changes approved April 11, 2017. A statement outlining the length of therapy for initial and subsequent approval has been added to the policy.
11/01/17	Interim Review, approved October 19, 2017. Updated criteria for Zytiga and Xtandi.
03/01/18	Interim Review, approved February 27, 2018. Added FDA approved Erleada to policy. Zytiga criteria was revised to include new FDA label update.
07/01/18	Annual Review, approved June 22, 2018. Literature review 04/11/2017 to 3/13/2018. NCCN guidelines updated. Yonsa (abiraterone) criteria was added to policy.
11/01/18	Interim Review, approved October 26, 2018. Updated Yonsa indication to allow any corticosteroid. Updated Xtandi indication per label.
12/01/19	Annual Review, approved November 12, 2019. Added criteria for Nubeqa (darolutamide). Updated criteria for Erleada (apalutamide).
03/01/20	Interim Review, approved February 20, 2020. Added to Xtandi (enzalutamide) coverage criteria for the treatment of metastatic castration-sensitive prostate cancer.
07/01/20	Interim Review, approved June 9, 2020, effective for dates of service on or after October 2, 2020, following 90-day provider notification. Added coverage criteria for Jevtana (cabazitaxel) and Xofigo (radium Ra 223 dichloride). HCPCS codes A9606 and J9043 added.
12/01/20	Annual Review, approved November 3, 2020. No changes to policy statements.

Date	Comments
03/01/21	Interim Review, approved February 18, 2021. Added generic abiraterone to policy for the same covered indications as Zytiga (abiraterone). Updated Zytiga coverage criteria to require the individual has first tried generic abiraterone.
10/01/21	Annual Review, approved September 23, 2021. Added criteria to generic abiraterone, Zytiga (abiraterone), Yonsa (abiraterone), Nubeqa (darolutamide), and Erleada (apalutamide) to include necessity to be used in combination with androgen deprivation therapy.
08/01/22	Interim Review, approved July 12, 2022. Removed Radium (Ra) 223 as it has moved to 6.01.525 Therapeutic Radiopharmaceuticals in Oncology. Removed HCPCS code A9606.
11/01/22	Annual Review, approved October 11, 2022. Added a new indication to Nubeqa (darolutamide) for the treatment of metastatic hormone-sensitive prostate cancer (mHSPC). Changed the wording from "patient" to "individual" throughout the policy for standardization.
08/01/23	Annual Review, approved July 11, 2023. Added coverage to Zytiga and generic abiraterone for the treatment of deleterious or suspected deleterious BRCA-mutated (BRCAm) metastatic castration-resistant prostate cancer (mCRPC) when used in combination with prednisone and olaparib based on the updated Lynparza FDA label.
09/01/23	Interim Review, approved August 8, 2023. Added coverage to Xtandi criteria for the treatment of adult individuals with HRR gene-mutated metastatic castration- resistant prostate cancer (mCRPC) when used in combination with Talzenna based on the updated Talzenna FDA label.
10/01/23	Interim Review, approved September 12, 2023. Added coverage criteria for Akeega for the treatment of adult individuals with deleterious or suspected deleterious BRCA-mutated (BRCAm) metastatic castration-resistant prostate cancer (mCRPC).
04/01/24	Annual Review, approved March 12, 2024. Updated Xtandi (enzalutamide) to include coverage criteria for certain individuals with non-metastatic castration-sensitive prostate cancer.
12/01/24	Interim Review, approved November 12, 2024. Added criteria to Yonsa (abiraterone) to include trial and failure of generic abiraterone.
05/01/25	Annual Review, approved April 21, 2025. Clarified that the medications listed in this policy are subject to the product's FDA dosage and administration prescribing information. Clarified that non-formulary exception review authorizations for all drugs listed in this policy may be approved up to 12 months.
07/01/25	Interim Review, approved June 10, 2025. Added coverage for Abirtega (abiraterone) with the same coverage criteria as generic abiraterone.

Date	Comments
08/01/25	Interim Review, approved July 8, 2025. Added a new indication to Nubeqa (darolutamide) for the treatment of metastatic castration-sensitive prostate cancer (use can now be either with or without docetaxel).
02/01/26	Annual Review, approved January 13, 2026. Updated Akeega (niraparib and abiraterone acetate) adding a new indication for the treatment of deleterious or suspected deleterious BRCA2-mutated (BRCA2m) metastatic castration-sensitive prostate cancer (mCSPC) when used in combination with prednisone.
05/01/26	Interim Review, approved April 13, 2026. Updated initial authorization for all other reviews for all oral drugs listed in the policy from 3 months to 6 months.
09/01/26	Interim Review, approved August 11, 2026. Updated Abirtega (abiraterone), generic abiraterone, and Zytiga (abiraterone) adding criteria for the treatment of metastatic androgen pathway modulation-naïve or sensitive (mAPMN/S) prostate cancer that is PTEN-deficient when used in combination with capivasertib. Removed reference to non-formulary exception reviews.

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. The Company adopts policies after careful review of published peer-reviewed scientific literature, national guidelines and local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). ©2026 Premera All Rights Reserved.

Scope: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.