Evolent Clinical Guideline 3156 for Nubeqa™ (darolutamide)

Guideline Number:	Applicable Codes	
Evolent_CG_3156		
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Original Date:	**Last Revised Date:**	**Implementation Date:**
August 2019	March 2026	March 2026

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STATEMENT

Purpose

To define and describe the accepted indications for Nubeqa (darolutamide) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

INDICATIONS

Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided

- The member has not experienced disease progression on the requested medication AND
- The requested medication was used within the last year without a lapse of more than 30 days of having an active authorization AND
- Additional medication(s) are not being added to the continuation request.

Prostate Cancer

- Nubeqa (darolutamide) may be used in combination with Androgen Deprivation Therapy (e.g., with an LHRH analog or following orchiectomy) and with ANY of the following criteria:
    - Non-Metastatic Castration Resistant Prostate cancer, (M0) disease, a PSA doubling time of 10 months or less, AND the absence of documented metastases to any site by conventional imaging (pelvic lymph nodes below aortic bifurcation less than 2 cm are allowed), OR
    - Metastatic Castration Sensitive Prostate Cancer as a single agent, OR
    - Metastatic Castration Sensitive Prostate Cancer, in combination with Taxotere (docetaxel). The first dose of Taxotere (docetaxel) is started within 6 weeks after the start of Nubeqa (darolutamide) and may be given up to 6 cycles.
    - Members should also receive a gonadotropin-releasing hormone (GnRH) agonist or antagonist concurrently or have had bilateral orchiectomy.

CONTRAINDICATIONS/WARNINGS

- None

EXCLUSION CRITERIA

- Disease progression on or after treatment with Nubeqa (darolutamide) or another Androgen Receptor Signaling Inhibitor [e.g., Xtandi (enzalutamide) or Erleada (apalutamide)].
- Concurrent use with other Androgen Receptor Signaling Inhibitors [e.g., Xtandi (enzalutamide)] or CYP17 inhibitors [e.g., Zytiga (abiraterone)].
- Dosing exceeds single dose limit of Nubeqa (darolutamide) 600 mg.
- Treatment exceeds the maximum limit of 120 (300 mg) tablets/month.
- Investigational use of Nubeqa (darolutamide) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:
    - Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
    - Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
    - Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definition of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
    - Whether the experimental design, in light of the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
    - That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
    - That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
    - That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

CODING AND STANDARDS

Codes

- J8999 - darolutamide

Applicable Lines of Business

☐	CHIP (Children's Health Insurance Program)
☒	Commercial
☒	Exchange/Marketplace
☒	Medicaid
☐	Medicare Advantage

POLICY HISTORY

Date	Summary
March 2026	• Updated indication section • Updated references
July 2025	• Converted to new Evolent guideline template • This guideline replaces UM ONC_1363 Nubeqa (darolutamide) • Updated indication section • Updated references
September 2024	• Updated NCH verbiage to Evolent

LEGAL AND COMPLIANCE

Guideline Approval

Committee

Reviewed / Approved by Evolent Specialty Services Clinical Guideline Review Committee

Disclaimer

Evolent Clinical Guidelines do not constitute medical advice. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Evolent uses Clinical Guidelines in accordance with its contractual obligations to provide utilization management. Coverage for services varies for individual members according to the terms of their health care coverage or government program. Individual members' health care coverage may not utilize some Evolent Clinical Guidelines. Evolent clinical guidelines contain guidance that requires prior authorization and service limitations. A list of procedure

codes, services or drugs may not be all inclusive and does not imply that a service or drug is a covered or non-covered service or drug. Evolent reserves the right to review and update this Clinical Guideline in its sole discretion. Notice of any changes shall be provided as required by applicable provider agreements and laws or regulations. Members should contact their Plan customer service representative for specific coverage information.

REFERENCES

1. Saad F, et al; ARANOTE Study Investigators. Darolutamide in Combination With Androgen-Deprivation Therapy in Patients With Metastatic Hormone-Sensitive Prostate Cancer From the Phase III ARANOTE Trial. *J Clin Oncol*. 2024 Dec 20;42(36):4271-4281. doi: 10.1200/JCO-24-01798.
2. Smith MR, et al; ARASENS Trial Investigators. Darolutamide and Survival in Metastatic, Hormone-Sensitive Prostate Cancer. *N Engl J Med*. 2022 Mar 24;386(12):1132-1142. doi: 10.1056/NEJMoa2119115.
3. Fizazi K, et al; ARAMIS Investigators. Darolutamide in Nonmetastatic, Castration-Resistant Prostate Cancer. *N Engl J Med*. 2019 Mar 28;380(13):1235-1246. doi: 10.1056/NEJMoa1815671.
4. Nubeqa prescribing information. Bayer HealthCare Pharmaceuticals Inc. Whippany, NJ 2025.
5. Clinical Pharmacology Elsevier Gold Standard 2026.
6. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2026.
7. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2026.
8. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2026.
9. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. *J Clin Oncol*. 2014 Apr 20;32(12):1277-80.
10. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: **https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf**.
11. Current and Resolved Drug Shortages and Discontinuations Reported to the FDA: **http://www.accessdata.fda.gov/scripts/drugshortages/default.cfm**.