



Positive Quality Intervention: Darolutamide (Nubeqa®) In the Treatment of Non-Metastatic Castration Resistant Prostate Cancer

Description: The purpose of this PQI is a summary of process for initiating and monitoring darolutamide therapy in the treatment of patients with non-metastatic castration-resistant prostate cancer (nmCRPC).

Background: Darolutamide is a next-generation androgen receptor antagonist approved in 2019 for the treatment of nmCRPC in combination with androgen deprivation therapy.¹ It was given a Category 1 recommendation by NCCN for patients with nmCRPC and a prostate specific antigen doubling time of ≤ 10 months based on the results of the phase 3 ARAMIS trial.² This trial demonstrated that darolutamide 600 mg twice daily improved median metastasis-free survival vs placebo in this patient population (40.4 months vs 18.4 months; HR for metastasis or death 0.41; 95% confidence interval 0.34 to 0.50; $P < 0.001$).³ In addition, patients receiving darolutamide experienced clinical benefits compared to placebo including improved overall survival, reduced time to requirement for cytotoxic chemotherapy and skeletal related events, and increased time to pain progression. Darolutamide is also well tolerated with overall low rates of serious adverse events. The most common adverse events include fatigue, decreased neutrophil count, elevated liver function tests, pain in extremities, and rash.⁴ Darolutamide is also indicated in metastatic hormone sensitive prostate cancer in combination with docetaxel (see [Darolutamide \(Nubeqa\) in combination with Docetaxel \(Taxotere\) for Metastatic Hormone Sensitive Prostate Cancer](#) PQI).

PQI Process: Upon receipt of an order for darolutamide

- Verify diagnosis of nmCRPC
- Ensure appropriate dose: darolutamide 600 mg (two tablets) twice daily⁴
- Reduce to 300 mg twice daily if eGFR 15-29 mL/min and not receiving hemodialysis or moderate hepatic impairment (Child-Pugh B)
- Ensure patient is on androgen deprivation therapy; GnRH agonist or GnRH antagonist
- Obtain labs: complete blood count with differential and comprehensive metabolic panel, PSA, and testosterone at baseline, monthly, and as needed
- Check for clinically relevant drug interactions
 - Darolutamide concentrations may decrease with PGP and moderate/strong CYP3A4 inducers; avoid concomitant use
 - Darolutamide concentrations may increase with PGP and strong CYP3A4 inhibitors; monitor for increase adverse effects
 - Darolutamide may increase the plasma concentrations of OATP1B1 or OATP1B3 substrates. If used together, monitor patients more frequently for adverse reactions and consider dose reduction of these drugs.
- Darolutamide may increase concentrations of breast cancer resistance protein substrates
- Dose modifications for toxicities—for Grade ≥ 3 toxicity or other intolerable adverse events, withhold or reduce to 300 mg twice daily until symptom resolution
 - May resume 600 mg twice daily upon resolution
 - Doses < 300 mg twice daily not recommended

Patient-Centered Activities:

- Provide [Oral Chemotherapy Education \(OCE\)](#) sheet
- Ensure patient receiving concomitant gonadotropin releasing hormone antagonist
- Take twice daily
- Swallow tablets whole and take with food

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- Missed dose: Take as soon as a dose is remembered prior to the next scheduled dose; do not take two doses together to make up for a missed dose
- Review potential side effects including fatigue, decreased neutrophil count, pain in extremities, and rash
- Males with female partners of reproductive potential should use highly effective contraception during treatment and for one week after last dose due to risk of embryo-fetal toxicity
- Patient Assistance: [NCODA Financial Assistance Tool](#)

References:

1. Bastos DA, et al. Darolutamide for castration-resistant prostate cancer. *Onco Targets Ther.* 2019; 12: 8769 – 8777.
2. National Comprehensive Cancer Network. Prostate cancer.
3. Fizazi K, et al. Darolutamide in nonmetastatic, castration-resistant prostate cancer. *New Eng J Med.* 2019; 380: 1235 – 1246.
4. [Nubeqa® \(darolutamide\) \[prescribing information\]](#).