Written By: Michelle Phillips, PharmD, BCOP
Wilmot Cancer Center
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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.[1] It was given a category 1 recommendation by NCCN for patients with nmCRPC and a prostate specific antigen doubling time (PSADT) 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 (see supplemental information).[4]

PQI Process:
Upon receipt of an order for darolutamide:

- Verify diagnosis of nmCRPC
- Ensure appropriate dose—darolutamide 600 mg (two tablets) twice daily[4]
- Reduce to 300 mg twice daily for eGFR 15 – 29 mL/min in patients not receiving hemodialysis or for patients with moderate hepatic impairment (Child-Pugh B)
- Obtain labs—complete blood count (CBC) with differential and comprehensive metabolic panel (CMP), PSA, and testosterone at baseline, monthly, and as needed
- Check for clinically relevant drug interactions
- Darolutamide concentrations may be decreased by combined P-glycoprotein and moderate to strong CYP3A4 inducers
- Darolutamide concentrations may be increased by combined P-glycoprotein and strong CYP3A4 inhibitors
- Darolutamide may increase concentrations of breast cancer resistance protein (BCRP) 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
- Complete Access Services by Bayer form with patient and provider
- Provides patient with 1-month free trial while obtaining insurance approval and assess for tolerability
- Must be done *prior* to patient starting treatment to qualify for free trial
    - Reminder: This process may assist in benefits investigation
    - Obtain provider signatures on pages 1 and 4, and obtain patient signatures on pages 2 and 5
    - Be sure to check the box “in office dispensing” on step 3 of page 1, if applicable

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Patient Centered Activities:

- Provide Oral Chemotherapy Education (OCE) sheet
- Ensure patient receiving concomitant gonadotropin releasing hormone (GnRH) antagonist
- Take twice daily with food
- Swallow tablets whole
- Store at room temperature in original container
- Review potential side effects including fatigue, decreased neutrophil count, pain in extremities, increased LFTs, and rash (see *Supplemental Information*). Dose adjust if needed (see *Supplemental Information*)
- 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

Copay Assistance:

- For patients with private insurance, visit https://www.nubeqacopayprogram.com/

Supplemental Information:

Adverse reactions from ARAMIS trial:

	Darolutamide		Placebo	
	All grades (%)	Grade ≥ 3	All grades (%)	Grade ≥ 3
AST increased	23	0.5	14	0.2
Decreased neutrophil count	20	4	9	0.6
Bilirubin increased	16	0.1	7	0
Fatigue	16	0.6	11	1.1
Pain in extremities	6	0	3	0.2
Rash	3	0.1	1	0

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. *NCCN Clinical Practice Guidelines in Oncology*. Version 1.2020 – March 16, 2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf
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]. Whippany, NJ; Bayer HealthCare Pharmaceuticals Inc: 2019.