Nubeqa (darolutamide)

NEW PRODUCT SLIDESHOW

MPR

Introduction

- **Brand name:** Nubeqa
- **Generic name:** Darolutamide
- **Pharmacological class:** Androgen receptor inhibitor
- **Strength and Formulation:** 300mg; tablets
- **Manufacturer:** Bayer Healthcare
- **How supplied:** Bottles—120
- **Legal Classification:** Rx

Nubeqa


NDC 50419-395-01
Rx Only
NUBEQA®
(darolutamide) tablets
300 mg
— 120 film-coated tablets
— Oral use
300
50419-395-01
Rx Only
NUBEQA®
(darolutamide) tablets
300 mg
120 film-coated tablets
Bayer

Indication

- Treatment of non-metastatic, castration-resistant prostate cancer

Dosage & Administration

- Swallow whole
- Take with food
- 600mg twice daily
- Give concurrent GnRH analog or patient should have had bilateral orchiectomy
- Severe renal impairment (eGFR 15–29mL/min/1.73m^2) not on hemodialysis: 300mg twice daily
- Moderate hepatic impairment (Child-Pugh Class B): 300mg twice daily
- Dose modification: see full labeling

Considerations for Special Populations

- **Pregnancy:** may cause embryo-fetal harm
- **Geriatric:** of the 954 patients who received Nubeqa in ARAMIS, 88% of patients were ≥65 years, and 49% were ≥75 years
  - No overall differences in safety or efficacy were observed between these patients and younger patients
- **Renal impairment:** severe (eGFR 15–29 mL/min/1.73 m^2) and not receiving hemodialysis: reduce dose; ESRD: effects unknown
- **Hepatic impairment:** moderate (Child-Pugh B): reduce dose; severe (Child-Pugh C): effects unknown

Warnings/Precautions

- Embryo-fetal toxicity
- Advise males (w. female partners of reproductive potential) to use effective contraception during and for 1 week after last dose

Interactions

- Antagonized by combined P-gp and strong or moderate CYP3A4 inducers; avoid
- Potentiated by combined P-gp and strong CYP3A4 inhibitors; monitor and adjust dose
- Avoid concomitant use with BCRP substrates; if unavoidable, monitor and consider dose reduction of the substrate drug

Adverse Reactions

- **Most common** (≥2%): fatigue, pain in extremity, rash
- **Others**: ischemic heart disease, heart failure, lab abnormalities (increased AST and bilirubin, decreased neutrophil count)

Mechanism of Action

- Darolutamide is an androgen receptor (AR) inhibitor
- It competitively inhibits androgen binding, AR nuclear translocation, and AR-mediated transcription
- Darolutamide functioned as a progesterone receptor antagonist *in vitro* (approximately 1% activity compared to AR)
- Darolutamide decreased prostate cancer cell proliferation *in vitro* and tumor volume in mouse xenograft models of prostate cancer

Clinical Trials

- The safety and efficacy of Nubeqa was evaluated in the ARAMIS trial in 1509 patients with non-metastatic castration resistant prostate cancer with a prostate-specific antigen doubling time (PSADT) of ≤10 months
- Patients were randomized 2:1 to receive either darolutamide 600mg twice daily (n=955) or placebo(n=554)
- Treatment continued until radiographic disease progression, unacceptable toxicity or withdrawal
- All patients received a gonadotropin-releasing hormone (GnRH) analog concurrently or had a bilateral orchiectomy

Clinical Trials

- The major efficacy end point was **metastasis free survival** (MFS), defined as the time from randomization to the time of first evidence of BICR-confirmed distant metastasis or death from any cause within 33 weeks after the last evaluable scan, whichever occurred first
- **Distant metastasis** was defined as new bone or soft tissue lesions or enlarged lymph nodes above the aortic bifurcation
- **Overall survival** (OS) and **time to pain progression** were additional efficacy end points

Clinical Trials

- Results demonstrated that patients treated with Nubeqa plus androgen deprivation therapy (ADT) had a **statistically significant improvement in MFS** with a median MFS of 40.4 months compared with 18.4 months for placebo plus ADT (hazard ratio [HR] 0.41, 95% CI (0.34, 0.50); *P* <.0001)
- MFS findings were also consistent across patient subgroups for PSADT or prior use of bone-targeting agents

Clinical Trials

- A **delay in time to pain progression** (defined as at least a 2-point worsening from baseline of the pain score on Brief Pain Inventory-Short Form or initiation of opioids) was noted in patients treated with Nubeqa compared with placebo
- OS data were not mature at the time of final MFS analysis

New Product Monograph

- For more information view the product monograph available at:

  https://www.empr.com/drug/nubeqa/