Report NUBEQA® - Darolutamide

Product & Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
Substance: Darolutamide **Brand Name:** Nubeqa **Originator/licensee:** Bayer AG **Classification:** NI **ATC code:** L02BB **Orphan Status:** **Eu:** No **Us:** / **Mechanism of action:** The active substance is darolutamide, an androgen receptor inhibitor. This means that it binds to the receptor of androgens, such as testosterone, and blocks them from stimulating prostate cancer cells from growing [1].	**Authorized Indication:** **EMA**: Darolutamide is indicated for the treatment of adult men with mHSPC in combination with ADT [1]. **FDA:** In November 2024, the FDA has accepted a supplemental new drug application seeking expanded indication for darolutamide for use in combination with ADT for the treatment of pts. with mHSPC [2]. **Route of administration:** OS **Licensing status** **EU CHMP P.O. date:** 19/06/2025 **FDA M.A. date:** / **EU Speed Approval Pathway:** No **FDA Speed Approval Pathway:** / --- **ABBREVIATIONS:** **ADT:** Androgen deprivation therapy **AE**: Adverse Event **CHMP**: Committee for Medicinal Products for Human Use **CI**: Confidential Interval **ECOG**: Eastern Cooperative Oncology Group **HR**: Hazard Ratio **M.A.:** Marketing Authorization **MM**: Multiple myeloma **mHSPC**: Metastatic hormone-sensitive prostate cancer **PCWG3**: Prostate Cancer Working Group 3 **P.O.**: Positive Opinion **PSA**: Prostate-specific antigen **PS**: Performance Status **Pts**: Patients **RECIST**: Response Evaluation Criteria in Solid Tumours **rPFS**: Radiological Progression-Free Survival **SAE**: Serious adverse events **SC**: Subcutaneously **TRAE**: Treatment related AEs **WHO**: World Health Organization	**Summary of clinical EFFICACY:** **ARANOTE (NCT NA)** was a global, randomized, double-blind, placebo-controlled, phase III trial to assess the efficacy and safety of darolutamide plus ADT in pts. with mHSPC. Pts. ≥18 years of age with histologically or cytologically confirmed adenocarcinoma of the prostate and metastatic disease and ECOG PS of 0-2 were eligible. All pts. started ADT of the investigator's choice (luteinizing hormone-releasing hormone agonist or antagonist or orchiectomy) within 12 weeks before initiating study treatment. Pts. (n= 669) were randomly assigned in a 2:1 ratio to receive darolutamide 600 mg (n=446) twice daily or matched placebo (n=223). Randomization was stratified based on the presence of visceral metastases and use of prior local therapy. The primary end point was rPFS based on central review of conventional imaging and using RECIST v1.1 for soft tissue metastases and PCWG3 criteria for bone metastases. At the primary cut-off date (June 7, 2024), darolutamide plus ADT reduced the risk of radiological progression or death by 46% versus placebo plus ADT (HR 0.54 [95% CI, 0.41 to 0.71]; P < .0001). The benefit was consistent across all subgroups analysed, regardless of disease volume, performance status, or baseline PSA [3]. **Summary of clinical SAFETY:** The safety analysis set included all randomly assigned pts., who received at least one dose of study drug and are analysed according to the treatment they received. Grade 3 or 4 AE occurred in 30.8% and 30.3% of pts receiving darolutamide and placebo, respectively. The most common grade 3-4 AEs in darolutamide group were hypertension, anaemia and increased aspartate aminotransferase. SAEs were reported in 23.6% of pts. in the darolutamide group and 23.5% of pts. in the placebo group. The frequency of death due to adverse events was similar in the two groups (21 of 445 pts in the darolutamide group [4.7%] and 12 of 221 pts in the placebo group [5.4%]) [3]. **Ongoing studies:** ● ***For the same indication:*** Yes ● ***For other indications:*** No **Discontinued studies (for the same indication):** No --- **References:** [1] https://www.ema.europa.eu/en/medicines/human/EPAR/nubeqa [2] https://www.targetedonc.com/view/fda-accepts-snda-for-darolutamide-plus-adt-in-mhspc [3] https://ascopubs.org/doi/pdf/10.1200/JCO-24-01798 [4] https://gallery.farmadati.it/Home.aspx [5] https://uroweb.org/guidelines/prostate-cancer/chapter/epidemiology-and-aetiology [6] https://www.aiom.it/wp-content/uploads/2024/02/2023_AIOM_NDC-web_def.pdf [7] https://www.aiom.it/wp-content/uploads/2020/12/2020_LG_AIOM_Carcinoma_Prostata.pdf [8] https://www.esmoopen.com/article/S2059-7029(23)00416-7/fulltext	**Cost of therapy:** In Italy, 300 tablets of NUBQA® 300 mg cost € 3,242.75 (ex-factory price) [4]. **Epidemiology:** Prostate cancer is the second most diagnosed cancer in men, with an estimated 1.4 million diagnoses and 375,000 deaths worldwide in 2020 [5]. In Italy, prostate cancer is currently the most common malignancy among males, with 41,100 new diagnoses estimated, accounting for over 20% of all cancers diagnosed from the age of 50 onwards [6,7]. --- **POSSIBLE PLACE IN THERAPY**: For pts. with mHSPC ADT represent the standard treatment. This therapy is often combined with others in doublet regimens. The two main doublet therapy options are ADT plus six cycles of docetaxel (DOCE), or ADT plus an androgen receptor signalling inhibitor (ARSI), such as abiraterone acetate (with prednisone), enzalutamide, or apalutamide. Recently, triplet therapies have also been introduced, involving a triple combination treatment initiated from the early stages of the disease [8]. The addition of Darolutamide to these regimens could represent a further opportunity for these pts. **OTHER INDICATIONS IN DEVELOPMENT: -** **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT**: - **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION:** capivasertib+abiraterone (NCT04493853); enzalutamide (NCT04076059, NCT02677896); Pembrolizumab (NCT04934722; NCT04191096); Niraparib (NCT04497844); *Service reorganization: No *Possible off label use: Yes

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