NUBEQA® (darolutamide) 300 mg film-coated tablets
Prescribing Information – United Kingdom
(Refer to full Summary of Product Characteristics (SmPC) before prescribing)

Presentation: Each film-coated tablet contains 300 mg of darolutamide. **Indication(s):** NUBEQA is indicated for the treatment of adult men with non-metastatic castration resistant prostate cancer (nmCRPC) who are at high risk of developing metastatic disease or with metastatic hormone-sensitive prostate cancer (mHSPC) in combination with docetaxel. **Posology & method of administration:** Treatment should be initiated and supervised by a specialist physician experienced in treatment of prostate cancer. Medical castration with a luteinising hormone-releasing hormone (LHRH) analogue should be continued during treatment of patients not surgically castrated. For oral use. The tablets should be taken whole with food. ***Adults:*** 600 mg darolutamide (two tablets of 300 mg) taken twice daily, equivalent to a total daily dose of 1200 mg. mHSPC patients should start darolutamide in combination with docetaxel. The first of 6 cycles of docetaxel should be administered within 6 weeks after the start of darolutamide treatment. Treatment with darolutamide should be continued until disease progression or unacceptable toxicity even if a cycle of docetaxel is delayed, interrupted, or discontinued. If a patient experiences a ≥ Grade 3 toxicity or an intolerable adverse reaction related to darolutamide, dosing should be withheld or reduced to 300 mg twice daily until symptoms improve. Treatment may then be resumed at a dose of 600 mg twice daily. ***Children & adolescents:*** There is no relevant use of darolutamide in the paediatric population. ***Elderly:*** No dose adjustment is necessary. ***Renal Impairment:*** No dose adjustment is necessary for patients with mild or moderate renal impairment. For patients with severe renal impairment (eGFR 15-29 mL/min/1.73 m_2) not receiving haemodialysis, the recommended starting dose is 300 mg twice daily. ***Hepatic Impairment:*** No dose adjustment is necessary for patients with mild hepatic impairment. The available data on darolutamide pharmacokinetics in moderate hepatic impairment is limited. Darolutamide has not been studied in patients with severe hepatic impairment. For patients with moderate and severe hepatic impairment (Child-Pugh Classes B and C), the recommended starting dose is 300 mg twice daily. **Contra-indications:** Hypersensitivity to the active substance or to any of the excipients. Women who are or may become pregnant. **Warnings & precautions:** Monitor for signs and symptoms of ischaemic heart disease. Optimise management of cardiovascular risk factors. Discontinue darolutamide for Grade 3-4 ischaemic heart disease. Seizure occurred in patients receiving darolutamide. Advise patients of the risk of developing a seizure while receiving darolutamide. Consider discontinuation of darolutamide in patients who develop a seizure during treatment. Cases of idiosyncratic drug-induced liver injury (DILI) with increases in alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) to ≥5 and ≥20 x upper limit of normal (ULN) have been reported. Idiosyncratic DILI has been reported in clinical trials and the post-marketing setting. Liver function test abnormalities were reversible upon darolutamide discontinuation. In case of liver function test abnormalities suggestive of idiosyncratic drug-induced liver injury, permanently discontinue darolutamide. The available data in patients with severe renal impairment are limited. As exposure might be increased those patients should be closely monitored for adverse reactions. The available data in patients with moderate hepatic impairment are limited, and darolutamide has not been studied in patients with severe hepatic impairment. As exposure might be increased those patients should be closely monitored for adverse reactions. Patients with clinically significant cardiovascular disease in the past 6 months including stroke, myocardial infarction, severe/unstable angina pectoris, coronary/peripheral artery bypass graft, and symptomatic congestive heart failure were excluded from the clinical studies. Therefore, the safety of darolutamide in these patients has not been established. Use of strong CYP3A4 and P-gp inducers during treatment with darolutamide may decrease the plasma concentration of darolutamide and is not recommended, unless there is no therapeutic alternative. Selection of an alternate concomitant medicinal product with less potential to induce CYP3A4 or P-gp should be considered. Patients should be monitored for adverse reactions of BCRP, OATP1B1 and OATP1B3 substrates as co-administration with darolutamide may increase the plasma concentrations of these substrates. Co-administration with rosuvastatin should be avoided unless there is no therapeutic alternative. In patients with a history of risk factors for QT prolongation and in patients receiving concomitant medicinal products that might prolong the QT interval, physicians should assess the benefit-risk ratio including the potential for Torsade de pointes prior to initiating NUBEQA. NUBEQA 300mg film-coated tablets contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose galactose malabsorption should not take this medicinal product. **Interactions:** For the effect of other medicinal products on the action of darolutamide (e.g CYP3A4, P-gp inducers and CYP3A4, P-gp and BCRP inhibitors, UGT1A9 inhibitors and docetaxel) and the action of darolutamide on other medicinal products (BCRP, OATP1B1, OATP1B3 substrates, P-gp substrates, docetaxel, CYP3A4 substrates and other medicinal products that prolong the QT interval) refer to the relevant SmPCs. **Pregnancy & lactation:** Darolutamide is not indicated in women of childbearing potential, and it is not to be used in women who are, or may be, pregnant or breast-feeding. Unknown whether darolutamide or its metabolites are present in semen. If the patient is engaged in sexual activity with a woman of childbearing potential, a highly effective contraceptive method (<1% failure rate per year) should be used during and for 1 week after completion of treatment. Unknown whether darolutamide or its metabolites are excreted in human milk. No studies in animals have been conducted to evaluate the excretion of darolutamide or its metabolites into milk. A risk to the breast-fed child cannot be excluded. There are no human data on the effect of darolutamide on fertility. Based on animal studies, darolutamide may impair fertility in males of reproductive potential. **Effects on ability to drive and use machines:** Darolutamide has no or negligible influence on the ability to drive and use machines. **Undesirable effects:** *Adverse reactions observed in patients with nmCRPC Very common:* fatigue/asthenic conditions, neutrophil count decreased, bilirubin increased, AST increased. *Common:* ischaemic heart disease, heart failure, rash, pain in extremity, musculoskeletal pain, fractures. *Serious adverse reactions:* urinary retention, pneumonia, haematuria, seizure. *Adverse reactions observed in patients with mHSPC treated with darolutamide in combination with docetaxel. Very common:* hypertension, rash, blood bilirubin increased, ALT increased, AST increased. *Serious adverse reactions:* fractures, ischaemic heart disease, seizure, febrile neutropenia, neutrophil count decreased, pneumonia. Prescribers should consult the SmPC in relation to other side effects (see section 4.8 of SmPC). **Overdose:** In the event of intake of a higher than recommended dose, treatment with darolutamide can be continued with the next dose as scheduled. There is no specific antidote for darolutamide and symptoms of overdose are not established. **Legal Category:** POM**. Package Quantities & Basic NHS Costs:** Pack of 112 film-coated tablets, £4,040. **MA Number(s):** PLGB 00010/0677. **Further information available from:** Bayer plc, 400 South Oak Way, Reading RG2 6AD, United Kingdom. Telephone: 0118 206 3000. **Date of preparation:** January 2025

Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk or search for MHRA Yellow Card in Google Play or Apple App Store.
Adverse events should also be reported to Bayer plc.
Tel: 0118 206 3500, Fax: 0118 206 3703, Email: pvuk@bayer.com