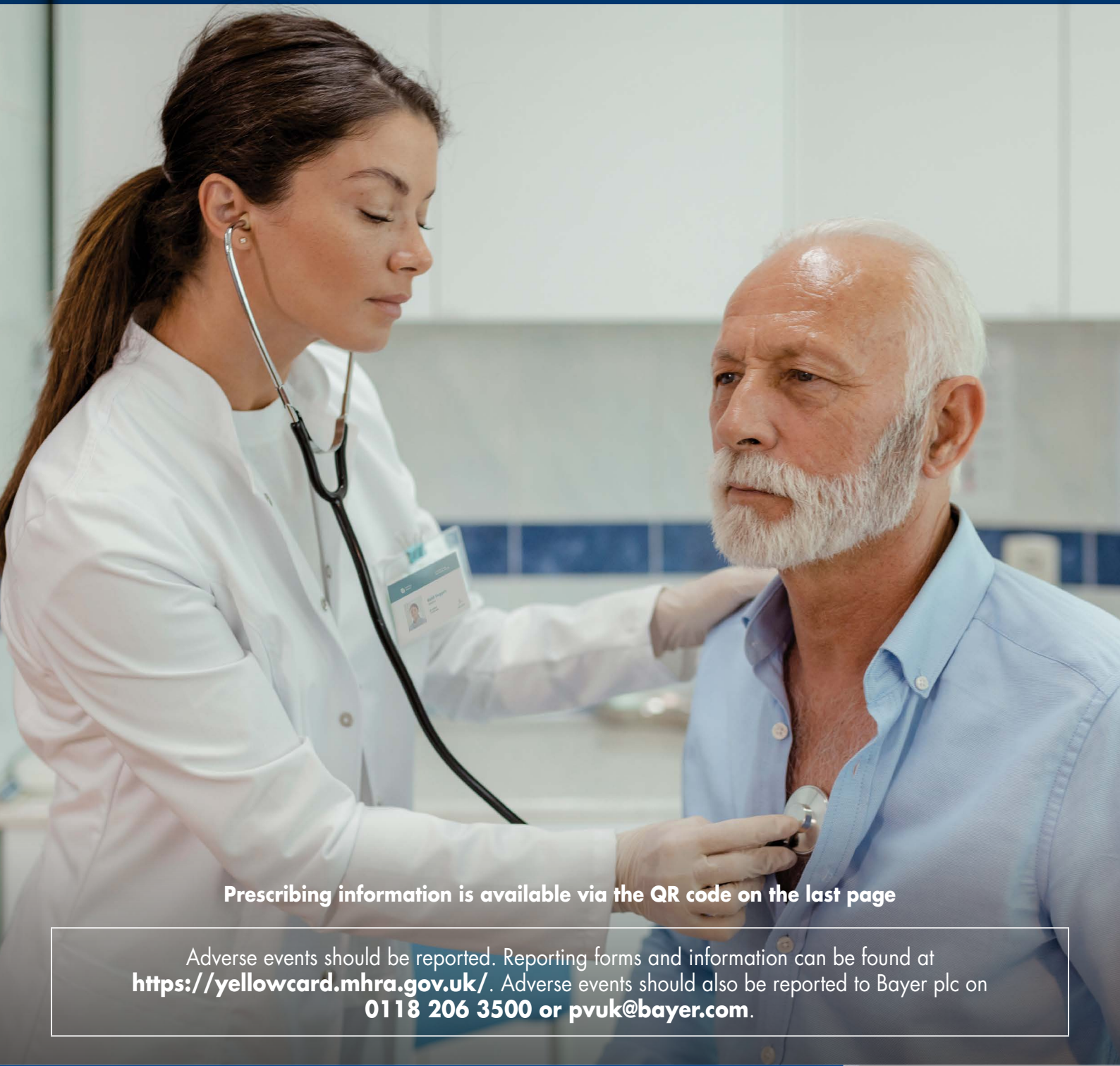
DO YOU CONSIDER YOUR PATIENTS' CARDIAC HEALTH WHEN DETERMINING THEIR PROSTATE CANCER TREATMENT?



Prescribing information is available via the QR code on the last page

Adverse events should be reported. Reporting forms and information can be found at **https://yellowcard.mhra.gov.uk/**. Adverse events should also be reported to Bayer plc on **0118 206 3500 or pvuk@bayer.com**.

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NUBEQA(darolutamide) 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.[1]

Intended for UK healthcare professionals only.

PP-NUB-GB-1907 | March 2025

NUBEQA® (darolutamide) 300 mg tablets

PATIENTS WITH ADVANCED PROSTATE CANCER ARE TYPICALLY OLDER AND OFTEN HAVE CO-EXISTING CV DISEASES[2,3]

In people ≥65 years old[4-6*]

~8 in 10

take anticoagulant medication

~9 in 10

take antihypertensive medication

Antihypertensive medications typically include calcium channel blockers.

*~8 in 10 patients 65–74 years old take anticoagulant medication, and ~9 in 10 patients ≥65 years old take antihypertensive medication.

Adding treatments for patients with CV disease can result in DDIs that lead to:[8]

INCREASED ADVERSE EVENTS

TREATMENT DISCONTINUATION

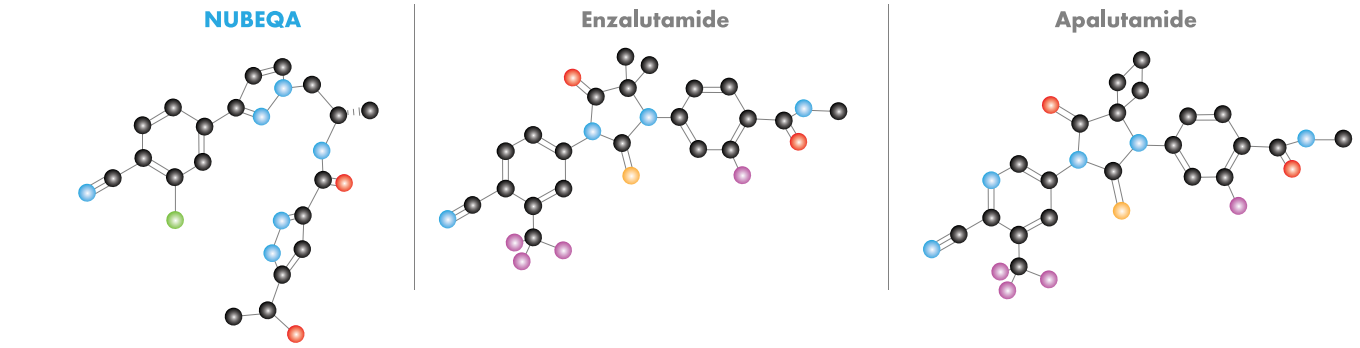
REDUCED EFFECTIVENESS OF SUITABLE TREATMENTS

DDIs between ARIs and CV treatments may require **complex coordination** between members of the MDT, your patient and their caregivers.[9]

DO YOU CONSIDER INTERACTIONS WITH CV MEDICATIONS WHEN CHOOSING A THERAPY FOR ADVANCED PROSTATE CANCER?

Efficacy that doesn't compromise your patient's QoL. Choose NUBEQA in mHSPC and nmCRPC[1,10-13**]

NUBEQA offers a distinct molecular structure and interacts with fewer drugs versus other 2nd generation ARIs, offering confidence when treating patients receiving concomitant medications[1,14-17‡§||]



Second generation ARI DDIs adapted from UK SmPCs: antithrombotics, calcium channel blockers and statins.[1,12,13†]
Please refer to the NUBEQA SmPC before dosing.

Class	Example	Type of interactions	Indications		
			NUBEQA[1,||]	Enzalutamide[12]	Apalutamide[13]
Antithrombotics	warfarin	CYP2C9-substrate		🔴	🔴
	clopidogrel	Inhibitor of CYP2C8, CYP2B6 and OATP1B1		🟠	🟠
	dabigatran	P-gp-substrate		🟠	🟠
	rivaroxaban	CYP3A4-substrate		🟠	🟠
Calcium channel blockers	felodipine	CYP3A4-substrate		🟠	🟠
	verapamil	Inhibitor of CYP3A4 (moderate) and P-gp; P-gp-substrate		🟠	🟠
	diltiazem	CYP3A4-inhibitor		🟠	🟠
	amlodipine	CYP3A4-substrate		🟠	🟠
Statins	atorvastatin	Substrate of BCRP, OATP1B1, OATP1B3 and CYP3A4	🟠	🟠	🟠
	fluvastatin	Substrate of BCRP, OATP1B1, and OATP1B3	🟠		🟠
	rosuvastatin	Substrate of BCRP, OATP1B1, and OATP1B3	🔴		🟠
	simvastatin	Substrate of BCRP, OATP1B1, OATP1B3 and CYP3A4	🟠	🟠	🟠

Key: 🟠 SmPC lists interaction as cause for adjustment or monitoring 🔴 SmPC lists as a cause for avoiding co-administration

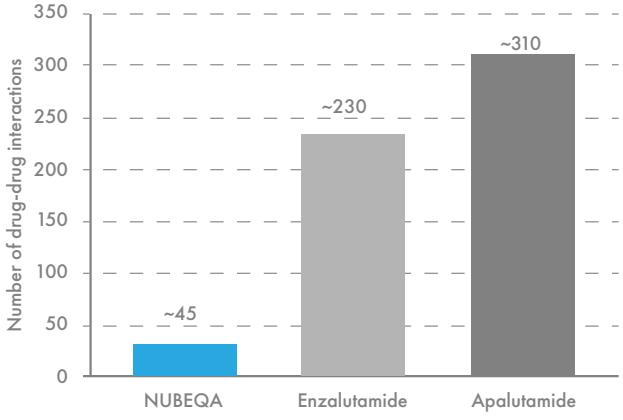
†For full DDIs, please refer to the relevant SmPC.

- Antithrombotics include both the anticoagulant and antiplatelet classes[18]

Choosing an ARI with reduced potential for drug-drug interactions can help your patients remain on their existing treatments for other comorbitities[1,12,13]

Learn more about NUBEQA's mechanism of action
This QR code will take you to a promotional Bayer website.

Number of medicines listed as an interaction in the BNF (as of February 2025)[1,12,13]



**The eligibility criteria for treatment with darolutamide for patients with high-risk nmCRPC is: No metastases detected in recent imaging, pelvic lymph nodes <2 cm permissible; Castration-resistant prostate carcinoma (testosterone <1.7 nmol/L PSA increase while on ADT, PSA ≥2 ng/ml); PSA doubling time of ≤10 months (This list is not exhaustive).[1,10,19]
‡Based on preclinical, pharmacokinetic studies. §NUBEQA is a CYP3A4, UGT1A9, and BCRP, OATP1B1/1B3 inhibitor.[1] ||Pertains to the DDI profile of NUBEQA only.
Please refer to docetaxel SmPC for full DDIs.[1]

Efficacy that doesn't compromise your patient's QoL. Choose NUBEQA in mHSPC and nmCRPC[1,10-13**]

Extends

Extended overall survival by

>30%

across **mHSPC** (vs ADT and docetaxel alone) and **nmCRPC** (vs placebo + ADT)[11,20]

Delays

Delayed tumour progression by

22 months

vs placebo + ADT in **nmCRPC**[10‡‡]

Maintains QoL

<1%

increase in AE incidence when added to ADT and docetaxel in **mHSPC**[11,21]

The only ARI

The only ARI with

<1%

increase in treatment discontinuation when added to ADT in a Phase 3 clinical trial in **nmCRPC**[10]

NUBEQA is the only NICE-recommended and SMC-accepted therapy in combination with ADT and docetaxel in mHSPC[1,22,23]

The first NICE-recommended and SMC-accepted ARI in high-risk nmCRPC[1,24,25]

EXTEND SURVIVAL.

MAINTAIN YOUR PATIENT'S QoL.[1,10-13] CHOOSE NUBEQA.

LEARN MORE ABOUT NUBEQA

This QR code will take you to a promotional Bayer website.

Prescribing information and adverse event reporting information for NUBEQA (darolutamide) is available via the QR code on the right.

Either click here or scan the QR code for prescribing information and adverse event reporting information.

For direct access to this prescribing information, please ensure your device's browser settings have automatic PDF download enabled.

ARASENS trial. Men with mHSPC. NUBEQA + ADT + docetaxel (n=651) vs. placebo + ADT + docetaxel (n=654). Primary endpoint was OS. 32.5% reduction in risk of death vs. placebo + ADT + docetaxel (HR: 0.68; 95% CI: 0.57-0.80; p<0.001). Median OS: NE months vs. 48.9 months with placebo + ADT + docetaxel. Number of patients with events 229/561 (35.2%) vs. 304/654 (46.5%) with placebo + ADT + docetaxel. Docetaxel 75 mg/m2 q3w x 6 cycles.[11]

ARAMIS trial. Men with high-risk nmCRPC. NUBEQA + ADT (n=955) vs. placebo + ADT (n=554). Primary endpoint was median MFS. Median MFS for NUBEQA + ADT was 40.4 months (n=955) vs. 18.4 months for placebo + ADT (n=554) (HR: 0.41; 95% CI: 0.34–0.50; p<0.001). Secondary endpoint was OS. 31% reduction in risk of death vs ADT alone. OS for NUBEQA + ADT was NR (95% CI: 56.1-NR) vs NR (95% CI: 46.9-NR) for placebo + ADT (HR: 0.69 (95% CI: 0.53-0.88), p=0.003). Number of patients with OS events 148/955 (15.5%) vs. 106/554 (19.1%) with placebo + ADT. Final analysis for OS was conducted after 254 deaths.[10,20]

The most common AEs in **mHSPC** patients receiving NUBEQA in combination with docetaxel were rash (17.3%), ALT increased (15.8%), AST increased (14.0%) and hypertension (13.8%).[1] The most common AE in **nmCRPC** patients receiving NUBEQA was fatigue/asthenic conditions (15.8%).[1] **Please refer to the NUBEQA SmPC for the full safety information.**

‡‡The eligibility criteria for treatment with darolutamide for patients with high-risk nmCRPC is: no metastases detected in recent imaging, pelvic lymph nodes <2 cm permissible; castration-resistant prostate carcinoma (testosterone <1.7 nmol/L, PSA increase while on ADT, PSA ≥2 ng/mL); PSA doubling time of ≤10 months (this list is not exhaustive).[10,19]

ADT, androgen deprivation therapy; AE, adverse event; ALT, alanine aminotransferase; ARI, androgen receptor inhibitor; AST, aspartate transferase; BCRP, breast cancer resistance protein; CI, confidence interval; CV, cardiovascular; CYP2B6, cytochrome P450 2B6; CYP2C8, cytochrome P4502C8; CYP2C9, cytochrome P450 2C9; CYP3A4, cytochrome P450 3A4; DDI, drug-drug interaction; HR, hazard ratio; MDT, multi-disciplinary team; MFS, metasasis-free survival; mHSPC, metastatic hormone-sensitive prostate cancer; NE, not estimable; nmCRPC, non-metastatic castration-resistant prostate cancer; NICE, National Institute of Health and Care Excellence; NR, not reached; OATP, organic-anion-transporting polypeptide; OS, overall survival; p, probability; P-gp, P-glycoprotein; PSA, prostate-specific antigen; QoL, quality of life; q3w, once every 3 weeks; SMC, Scottish Medicines Consortium; SmPC; summary of product characteristics; UGT1A9, UDP-glucuronosyltransferase 1-9.

1. NUBEQA (darolutamide) Summary of Product Characteristics. 2024. **2.** Aïdoud A, et al. J Am Heart Assoc. 2023;12(2): e026850. **3.** Tan EH, et al. JAMA Netw Open. 2024;7(9):e2434622. **4.** Lund J, et al. Open Heart. 2021;8(2):e001737. **5.** Sekkarie A, et al. MMWR Morb Mortal Wkly Rep. 2024;73(9):191-198. **6.** Khalil H, Zeltser R. StatPearls [Internet]. 2023. **7.** Leong DP, et al. JACC CardioOncol. 2024;6(6):835-846. **8.** Conde-Estévez D, et al. Expert Opin Drug Metab Toxicol. 2022;18 (9):601- 613. **9.** Shore N, et al. Future Oncol. 2023;19(5):385-395. **10.** Fizazi K, et al. N Engl J Med. 2019;380(13):1235-1246. **11.** Smith MR, et al. N Engl J Med. 2022;386(12):1132-1142. **12.** XTANDI (enzalutamide) Summary of Product Characteristics. 2024. **13.** ERLEADA (apalutamide) Summary of Product Characteristics. **14.** Heidegger I, et al. Urol Oncol. 2020;38(4):129–36. **15.** Zurth C, et al. J Clin Oncol. 2019;37(Suppl. 7):156. **16.** Williams SCR, et al. Target Oncol. 2023;18(3):403–13. **17.** Cintrón-García J and Guddati AK. Am J Cancer Res. 2020;10(8):2617–20. **18.** National Institute of Diabetes and Digestive and Kidney Diseases. LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. 2012. 19. Crawford ED, et al. Cancer Manag Res. 2020;12:5667- 5676. **20.** Fizazi K, et al. N Engl J Med. 2020;383:1040–1049. **21.** Bayer. Data on file. REF-M_DAR-GB-0641 **22.** NICE. TA903. 2023. 23. SMC. SMC2604 **24.** NICE. TA660. 2020. **25.** SMC. SMC2297.

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