I'M A TESTICULAR CANCER SURVIVOR

TEST ME

Testicular cancer survivors are at risk of developing **testosterone deficiency,** which can result in metabolic syndrome and poor cardiac health.[1-5]

The European Society for medical Oncology recommends measurement of testosterone levels during follow-up.[6]

PRESCRIBING INFORMATION TESTOGEL®(testosterone) 16.2 MG/G, GEL

For full prescribing information, including side effects, precautions and contraindications, please consult the Summary of Product Characteristics (SPC).

Presentation: Transdermal gel in a multi-dose container, one pump actuation delivers 1.25g of gel containing 20.25mg of testosterone. **Indication:** Testosterone replacement therapy for male hypogonadism when testosterone deficiency has been confirmed by clinical features and biochemical tests. **Dosage and administration:** Cutaneous use. The recommended dose is two pump actuations of gel (i.e. 40.5mg of testosterone) applied once daily. The daily dose should not exceed four pump actuations (81 mg testosterone) per day. Adjustment of dosage should be achieved by increments of one pump actuation, usually based on measurements of blood testosterone levels and/or clinical response. The gel should be administered by the patient himself, onto clean, dry, healthy skin on the right and left upper arms and shoulders. **Contraindications:** Cases of known or suspected cancer of the prostate or breast, known hypersensitivity to testosterone or to any other constituent of the gel. **Warnings and precautions for use:** Testosterone deficiency should be clearly demonstrated by clinical features and confirmed by 2 separate blood testosterone measurements. Testosterone levels should be monitored at baseline and at regular intervals during treatment. In addition, in patients receiving long-term androgen treatment the following laboratory parameters should be checked regularly: haemoglobin, haematocrit (to detect polycythaemia), liver function tests and lipid profile. Testogel may affect results of laboratory tests of thyroid function. Risk of pre-existing prostatic cancer should be excluded and the prostate gland and breast monitored during Testogel treatment. Androgens may accelerate the progression of sub-clinical prostate cancer and benign prostate hyperplasia. Testogel should be used with caution in cancer patients at risk of hypercalcaemia and associated hypercalciuria due to bone metastases; regular monitoring of blood calcium levels is recommended in these patients. Testogel may cause oedema with or without congestive cardiac failure in patients suffering from severe cardiac, hepatic or renal insufficiency or ischaemic heart disease. If this occurs, treatment must be stopped immediately. Testogel should be used with caution in patients with ischaemic heart disease. Testosterone may cause a rise in blood pressure and should be used with caution in men with hypertension. Testogel should be used with caution in patients with thrombophilia or risk factors for venous thromboembolism (VTE), as there have been post-marketing reports of thrombotic events in these patients during testosterone therapy. In thrombophilic patients, VTE cases have been reported even under anticoagulation treatment, therefore continuing testosterone therapy after first thrombotic event should be carefully evaluated. In case of treatment continuation, further measures should be taken to minimise the individual VTE risk. Spermatogenesis may be suppressed leading to adverse effects on semen parameters. Gynaecomastia occasionally develops and occasionally persists. Irritability, nervousness, weight gain, prolonged or frequent erections may indicate excessive androgen exposure requiring dosage adjustment. Testogel should be used with caution in patients with epilepsy and migraine. Do not apply to the genital areas as the high alcohol content may cause local irritation. Testogel is flammable until dry. Testogel can be transferred to other persons by close skin to skin contact. There is limited experience regarding safety and efficacy of Testogel in patients over 65 years of age. Testogel is not indicated for use in women or in children under 18 years of age. Testogel is not a treatment for male impotence or sterility. FOR THE FULL LIST OF WARNINGS AND PRECAUTIONS PLEASE CONSULT SECTION 4.4 OF THE FULL SPC. **Interactions:** May increase the activity of oral anticoagulants. Concomitant administration of testosterone and ACTH or corticosteroids may increase the risk of developing oedema. Testogel may cause changes in insulin sensitivity, glucose intolerance, glycaemic control, blood glucose and glycosylated haemoglobin levels. **Pregnancy and lactation:** Pregnant women must avoid any contact with Testogel application sites. This product may have adverse virilising effects on the foetus. **Undesirable effects:** Local skin reactions include: acne, alopecia, dry skin, skin lesions, contact dermatitis, hair colour changes, rash, sweating, hypertrichosis, application site hypersensitivity, application site pruritus. The following commonly (≥1/100; (1/10) occur with Testogel: emotional symptoms, prostate specific antigen (PSA) increased, increased haematocrit, increased haemoglobin and increased red blood cell count. The following uncommonly (≥1/1000 to (1/100) occur with Testogel: malignant hypertension, flushing, phlebitis, diarrhoea, abdominal distention, oral pain, gynaecomastia, nipple disorder, testicular pain, increased erection and pitting oedema. Other adverse reaction identified during post-approval use of Testogel : testis disorder, headache, dizziness, paraesthesia, vasodilation (hot flushes), deep vein thrombosis, dyspnoea, polycythaemia, anaemia, musculoskeletal pain, gynaecomastia, testis disorder, prostate enlargement, oligospermia, benign prostate hyperplasia, impaired urination, anxiety, depression, aggression, insomnia, nausea, asthenia, oedema, malaise and weight increase. In case of severe application site reactions, treatment should be reviewed and discontinued if necessary.

NHS Price: £31.11 per 88g pump pack. **Legal category:** POM. **Marketing Authorisation Number:** PL 28387/0007. **Marketing Authorisation Holder:** Besins Healthcare, Avenue Louise, 287, Brussels, Belgium. **Date of preparation of Prescribing Information:** February 2021 TES/2021/016

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Besins Healthcare (UK) Ltd Drug Safety on 0203 862 0920 or Email: pharmacovigilance@besins-healthcare.com

References: 1. Lunenfeld B, Mskhalaya G, Zitzmann M, et al. The Aging Male. 2015;18(1):5-15. 2. Khera M, Adaikan G, Buvat J, et al. J Sex Med. 2016;13(12):1787-1804.3. Zarotsky V, Huang M-Y, Carman W, et al. Andrology. 2014;2(6):819-834. 4. Sharma R, Oni OA, Gupta K, et al. Eur Heart J. 2015;36(40):2706-2715. 5. Zeller T, Schnabel RB, Appelbaum S, et al. Eur J Prev Cardiol. 2018;25(11):1133-1139. 6. Oldenburg J, Fossa SD, Nuver J, et al. Ann Oncol. 2013;24 Suppl 6:vi125-132.

TES/2021/067 | July 2021

BESINS HEALTHCARE
Innovating for Well-being

BJU Int 2021 doi:10.1111/bju.15496

BJUI
BJU International

Research Communication

Renal oncocytoma: landscape of diagnosis and management

Renal oncocytoma represents between 6% and 12% of T1 renal tumours in surgical series [1–2]. Contemporary imaging cannot differentiate oncocytoma from malignant renal cell carcinoma (RCC). Uptake of renal tumour biopsy in clinical practice has been variable [3] and surgery with partial or radical nephrectomy is the first line in the management of RCC [4,5]. Many patients with renal masses therefore undergo empirical surgery for presumed RCC but have a postoperative histological diagnosis of benign oncocytoma.

While nephron-sparing and minimally invasive surgical techniques have undoubtedly improved surgical outcomes and reduced morbidity, there remains substantial risk associated with surgical resection. Recent national data for the surgical management of oncocytoma showed that 20% of patients experienced inpatient complications, and there was a 60-day mortality rate of 0.4% [6].

To understand the landscape of current oncocytoma diagnosis and management, we conducted a clinician survey to establish clinical practice. Sixty-eight clinicians from six countries took part in an online questionnaire openly distributed via social media. Just over half of respondents were UK-based, one-third were from North America, and the remainder were from across Europe, Africa and Australasia. The majority of respondents were consultants (72%), and more than half (54%) were involved in over 40 radical or partial nephrectomy cases per year. The majority (54%) saw six or more patients a year with renal oncocytoma in their practice. Renal tumour biopsy of small renal masses (≤4 cm) was routine practice for only 29% of respondents, 20% offered it 'often (20–50% of the time)', 26% 'occasionally (10–20% of the time)', and 25% offered it 'rarely' or 'almost never (<10% of the time)'. Barriers to biopsy were identified as high non-diagnostic rate, concern regarding hybrid tumours, diagnostic accuracy and it not being standard practice in the department.

Each survey participant was invited to describe their usual initial management strategy for biopsy-confirmed oncocytoma in a variety of clinical scenarios. Clinical scenarios involved patients of different ages (50, 60 and 80 years), American Society of Anaesthesiologists scores (1–2 or 3–4) and tumour sizes (3 cm or 6 cm). A chi-squared test was used to assess if the proportion of clinicians who would usually adopt initial conservative management with active surveillance or watchful waiting was associated with patient or tumour characteristics. The results for patients aged 60 years are shown in Fig. 1.

An initial conservative management strategy with active surveillance or watchful waiting was associated with smaller tumours ($P < 0.001$), and older ($P < 0.001$) and more comorbid patients ($P < 0.001$), with the majority of respondents usually adopting a conservative strategy for small tumours in elderly or comorbid patients. However, there was a lack of consensus for the management of younger patients and larger tumours. For example, a 3-cm oncocytoma diagnosed in a fit 50-year-old patient would usually be managed with active surveillance or watchful waiting by 52% of respondents, and surgery or ablation by 33%, while the remaining 15% would usually adopt either strategy according to patient preference. Similarly, for a fit 60-year-old patient with a 6-cm oncocytoma, 47% would usually treat with surgery or ablation, and 44% with active surveillance, with 9% adopting either strategy according to patient preference.

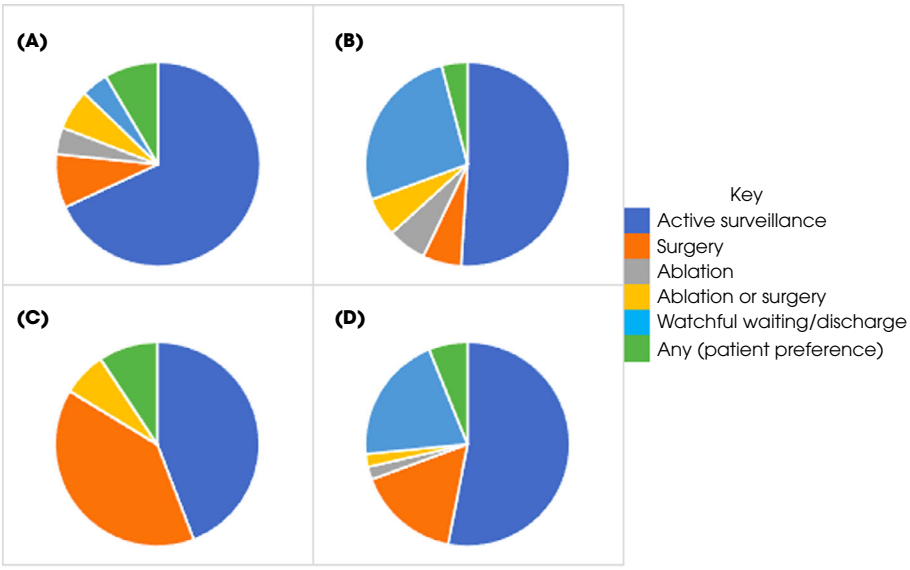
There was also variation in preferred imaging method for surveillance of biopsy-confirmed oncocytoma, with 49% favouring CT, 36% ultrasonography and 15% MRI. For frequency of surveillance imaging, two-thirds of respondents favoured imaging at 6 months and annually thereafter across each imaging method. The majority of respondents agreed that a change in imaging characteristics (87%), development of symptoms (61%) and an increase in size >25% in 1 year (61%) would warrant a change in management strategy.

The survey also demonstrated variation in follow-up regimens for patients with completely surgically excised oncocytoma. After complete surgical resection of an oncocytoma with no aggressive features on histology, 54% would discharge the patient after the first postoperative review, while 22% would continue surveillance imaging for up to 5 years. If surgical pathology demonstrated either fat or vascular invasion, however, only 14% chose to discharge after the first postoperative review, with 49% favouring surveillance imaging for up to 5 years.

Strengths of the present study include the snapshot of international practice from a large number of high-volume surgeons. Limitations include the fact that the survey was not distributed to all practising urologists, and there may be bias introduced by recruiting clinicians via social media networks. Additionally, patient factors but not surgeon factors influencing diagnostics and management strategy were evaluated.

The poor uptake of renal tumour biopsy highlights the need for improved diagnostics of benign renal tumours that are

Fig. 1 Results of the clinician survey demonstrating the usual management strategy for a 60-year-old patient with biopsy-proven oncocytoma in the following clinical scenarios: (**A**) 3-cm oncocytoma, patient American Society of Anaesthesiologists (ASA) score 1–2; (**B**) 3-cm oncocytoma, patient ASA score 3–4; (**C**) 6-cm oncocytoma, patient ASA score 1–2; and (**D**) 6-cm oncocytoma, patient ASA score 3–4.



accurate and acceptable to patients and clinicians alike. Technetium (^{99m}Tc)-sestamibi single-photon emission CT (SPECT)/CT has shown promise in small trials in the USA and Sweden in distinguishing benign oncocytoma from RCC [7–9]. ^{99m}Tc-sestamibi is a radiotracer preferentially taken up by cells with abundant mitochondria such as oncocytoma, and actively transported out of cells in RCCs. Oncocytomas therefore light up brightly on SPECT/CT, appearing 'hot', while RCCs are devoid of tracer and appear 'cold'. A prospective study of 50 patients reported sensitivity and specificity of 87.5% and 95.2%, respectively, for 99mTc-Sestamibi SPECT/CT in diagnosing oncocytomas and indolent hybrid oncocytic/chromophobe tumours [7]. In our clinician survey a majority of respondents expressed interest in recruiting patients to a trial assessing the utility of ^{99m}Tc-Sestamibi SPECT/CT in the evaluation of renal masses, with 76% responding 'yes' and 21% responding 'potentially – need more information'. A prospective single-centre trial has recently opened in the UK to assess the acceptability and feasibility in the NHS setting (ISRCTN23705289).

The survey demonstrates that the majority of participating clinicians support management of renal oncocytomas with surveillance in select clinical scenarios; however, it also demonstrated variable practice, which highlights research gaps in the field.

Key evidence gaps highlighted by this survey are underpinned by the lack of understanding of the natural history of oncocytomas and the dearth of randomized controlled trials to inform best practice. Our own group has reported the safety of oncocytoma active surveillance in just under 100 patients over a median follow-up of 2 years [10], consistent with smaller longitudinal cohort studies [11,12]. However, reporting of outcomes over the longer term is needed to increase confidence in managing these tumours conservatively in patients with long life expectancy. Research into tumour behaviour stratified by size at presentation may also help select patients for surveillance. Further, tumour recurrence rates for surgically excised oncocytoma both with and without invasive features on pathology are required to inform appropriate surveillance strategies after operative management. Finally, well-designed randomized controlled trials are required to provide high-level evidence for guideline recommendations and to standardize practice for each stage of the patient pathway (diagnosis, management and follow-up).

Acknowledgements

We would like to thank all of the clinicians who kindly participated and shared the survey with their networks.

Disclosure of Interest

None declared.

Hannah Warren[1], Joana B. Neves[2,3] and Maxine G. B. Tran[2,3]

[1]Department of Urology, King's College Hospital NHS Foundation Trust, [2]Division of Surgery and Interventional Science, University College London, and [3]Specialist Centre for Kidney Cancer, Royal Free London NHS Foundation Trust, London, UK

References

1 **Lane BR**, **Babineau D**, **Kattan MW et al**. A preoperative prognostic nomogram for solid enhancing renal tumors 7 cm or less amenable to partial nephrectomy. *J Urol* 2007; 178(2): 429–34

2 **Snyder ME**, **Bach A**, **Kattan MW**, **Raj GV**, **Reuter VE**, **Russo P**. Incidence of benign lesions for clinically localized renal masses smaller Than 7 cm in radiological diameter: Influence of sex. *J Urol* 2006; 176(6 Pt 1): 2391–6

3 **Kutikov A**, **Smaldone MC**, **Uzzo RG**, **Haifler M**, **Bratslavsky G**, **Leibovich BC**. Renal mass biopsy: always, sometimes, or never? *Eur Urol* 2016; 70: 403–6

4 **Ljungberg B**, **Albiges L**, **Abu-Ghanem Y et al**. European association of urology guidelines on renal cell carcinoma: The 2019 update. *Eur Urol* 2019; 75: 799–810

5 **Gervais DA**, **Giambarresi L**, **Lane BR et al**. Renal mass and localized renal cancer: AUA guideline. *J Urol* 2017; 198: 520–9

6 **Neves JB**, **Withington J**, **Fowler S et al**. Contemporary surgical management of renal oncocytoma: a nation's outcome. *BJU Int* 2018; 121 (6): 893–9

7 **Gorin MA**, **Rowe SP**, **Baras AS et al**. Prospective evaluation of 99mTc-sestamibi SPECT/CT for the diagnosis of renal oncocytomas and hybrid oncocytic/chromophobe tumors. *Euro Urol* 2016; 69: 413–6

8 **Tzortzakakis A**, **Gustafsson O**, **Karlsson M**, **Ekström-Ehn L**, **Ghaffarpour R**, **Axelsson R**. Visual evaluation and differentiation of renal oncocytomas from renal cell carcinomas by means of 99mTc-sestamibi SPECT/CT. *EJNMMI Res.* 2017; 7: 29

9 **Sistani G**, **Bjazevic J**, **Kassam Z**, **Romsa J**, **Pautler S**. Evaluation and risk stratification of renal masses with 99MTC-Sestamibi SPECT/CT. *J Urol* 2020; 203(4S Suppl): e913

10 **Neves JB**, **Varley R**, **Agnesi S**, **et al.** Growth and renal function dynamics of renal oncocytomas on active surveillance. *BJU International.* 2021; https://doi.org/10.1111/bju.15499

11 **Liu S**, **Lee S**, **Rashid P et al**. Active surveillance is suitable for intermediate term follow-up of renal oncocytoma diagnosed by percutaneous core biopsy. *BJU Int* 2016; 118: 30–4

12 **Neuzillet Y**, **Lechevallier E**, **Andre M**, **Daniel L**, **Nahon O**, **Coulange C**. Follow-up of renal oncocytoma diagnosed by percutaneous tumor biopsy. *Urology* 2005; 66: 1181–5

Correspondence: Maxine G. B. Tran, UCL Division of Surgery and Interventional Science, Royal Free Hospital, Pond street, 9th Floor, London NW3 2QG, UK.

e-mail: m.tran@ucl.ac.uk

Abbreviation: 99mTc, technetium; RCC, renal cell cacinoma; SPECT, single-photon emission CT.

Prescribing information and adverse event reporting information can be found at the bottom of this page

PROSTATE CANCER QUESTION HOUR

RCT to RWE: The evolution of non-metastatic castration-resistant prostate cancer treatment

Thursday 2 December 2021
18:00–19:00 GMT

REGISTER HERE FOR THIS PROMOTIONAL WEBINAR

Please join us for what promises to be a highly informative event, featuring a faculty of top international experts:

Professor Heather Payne,
Consultant Clinical Oncologist,
University College Hospital,
London, UK

Dr Thiraviyam Elumalai,
Consultant Clinical Oncologist,
Addenbrooke's Hospital,
Cambridge University Hospitals NHS Foundation Trust,
Cambridge, UK

Professor Karim Fizazi,
Medical Oncologist,
Head of the Department of Cancer Medicine,
Gustave Roussy Institute,
Villejuif, France

Mr William Cross,
Consultant Urological Surgeon,
St James's University Hospital,
Leeds Teaching Hospitals NHS Trust,
Leeds, UK

▼ NUBEQA® (Darolutamide) 300 mg film-coated tablets Prescribing Information
(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. **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. **Children & adolescents:** There is no relevant use of darolutamide in the paediatric population for the indication of treatment of nmCRPC. **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 m2) 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:** 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 darolutamide (e.g CYP3A4, P-gp inducers and CYP3A4, P-gp and BCRP inhibitors and UGT1A9 inhibitors) and the action of darolutamide on other medicinal products (BCRP, OATP1B1, OATP1B3 substrates, P-gp substrates, CYP3A4 substrates and other medicinal products that prolong the QT interval) refer to the SmPC. **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:** Very common: fatigue/asthenic conditions (incl. fatigue and asthenia, lethargy and malaise), neutrophil count decreased, bilirubin increased, AST increased. Common: ischaemic heart disease (including arteriosclerosis coronary artery, coronary artery disease, coronary artery occlusion, coronary artery stenosis, acute coronary syndrome, acute myocardial infarction, angina pectoris, angina unstable, myocardial infarction, myocardial ischaemia), heart failure (including cardiac failure, cardiac failure acute, cardiac failure chronic, cardiac failure congestive, cardiogenic shock), rash, pain in extremity, musculoskeletal pain, fractures. Prescribers should consult the SmPC in relation to other side effects. **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):** EU/1/20/1432/001 **Further information available from:** Bayer plc, 400 South Oak Way, Reading RG2 6AD, United Kingdom. Telephone: 0118 206 3000. **Date of preparation:** March 2020

NUBEQA® is a trademark of the Bayer Group

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

nmCRPC, non-metastatic castration-resistant prostate cancer; RCT, randomised controlled trial; RWE, real-world evidence.
This promotional meeting has been organised and funded by Bayer and is for healthcare professionals only.

PP-NUB-GB-0446 | October 2021