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| **Indication** | Metastatic hormone-relapsed prostate cancer:<br>• In adults whose disease has progressed during or after docetaxel-containing chemotherapy.<br>• In people who have no or mild symptoms after ADT has failed and before chemotherapy is indicated.<br>**NB** In metastatic hormone-relapsed prostate cancer, patients should have not previously received treatment with enzalutamide or darolutamide or apalutamide or abiraterone, unless abiraterone has had to be stopped within 3 months of its start solely as a consequence of dose-limiting toxicity and in the clear absence of disease progression.<br><br>**and**<br>Newly diagnosed metastatic hormone-sensitive prostate cancer in combination with androgen deprivation therapy (ADT).<br><br>**NB** In newly diagnosed metastatic hormone-sensitive prostate cancer, patients should have not previously received any androgen receptor targeted therapy unless they received apalutamide for newly diagnosed metastatic hormone-sensitive prostate cancer which had to be stopped due to dose-limiting toxicity in the clear absence of disease progression or the patient has progressive disease following treatment with 2 years of ADT plus abiraterone with or without enzalutamide for high risk non-metastatic disease as part of the STAMPEDE trial and did not progress whilst on such treatment. |
| **Treatment Intent** | Palliative |
| **Frequency and number of cycles** | Repeat every 28 days, continuously.<br>Continue until disease progression, unacceptable toxicity or patient's choice to stop treatment. |
| **Monitoring Parameters pre-treatment** | • Monitor FBC, U&Es and LFTs and BP with each cycle for 6 months and then every 3 months thereafter if clinically indicated.<br>• **<u>Hepatic Impairment</u>**<br>• Use with caution in severe hepatic impairment (Child-Pugh Class C).<br>• **<u>Renal Impairment</u>**<br>• No dose adjustment is necessary in mild to moderate renal impairment. Use with caution in severe renal impairment or end-stage renal disease no data available.<br>• **<u>Dose reductions:</u>**<br>• If a patient experiences a >/= Grade 3 toxicity or an intolerable adverse reaction, dosing should be withheld for one week or until symptoms improve to </= Grade 2, then resumed at the same or a reduced dose (120 mg or 80 mg) if warranted.<br>• **<u>Drug interactions (for comprehensive list refer to BNF/SPC):</u>**<br>• The concomitant use of strong CYP2C8 inhibitors (e.g. gemfibrozil) should be avoided if possible, or used with caution. If patients must be co-administered a strong CYP2C8 inhibitor, the dose of enzalutamide should be reduced to 80 mg once daily. If co-administration of the strong CYP2C8 inhibitor is discontinued, the enzalutamide dose should be returned to the dose used prior to initiation of the strong CYP2C8 inhibitor.<br>• Enzalutamide is a potent enzyme inducer and increases the synthesis of many enzymes and transporters; therefore, interaction with many common medicinal products that are substrates of enzymes or transporters is expected. In consideration of the long half-life of enzalutamide, effects on enzymes may persist for one month or longer after stopping enzalutamide. (See SPC). For example, medicinal products with a narrow therapeutic range that are substrates |

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| | for P-gp (e.g. colchicine, dabigatran etexilate, digoxin) should be used with caution when administered concomitantly with enzalutamide.<br>• Co-administration with warfarin and coumarin-like anticoagulants should be avoided; if treatment is clinically unavoidable increased INR monitoring should be conducted.<br>• **Adverse reactions:**<br>• Posterior Reversible Encephalopathy Syndrome (PRES) has been rarely reported with enzalutamide. In patients developing PRES, treatment of specific symptoms including control of hypertension is recommended along with discontinuation of enzalutamide.<br>• Severe cutaneous adverse reactions (SCARs) have been reported with enzalutamide. Patients should be advised of the signs and symptoms and monitored closely for skin reactions.<br>• **Delayed or missed doses:**<br>• If a patient misses a dose at the usual time, the prescribed dose should be taken as close as possible to the usual time. If a patient misses a dose for a whole day, treatment should be resumed the following day with the usual daily dose.<br>• Patient should be advised of the possible risks of driving or operating machinery whilst taking enzalutamide. |
| **References** | KMCC proforma URO-022 v5 SPC accessed online 21.04.2022 blueteq form accessed online 21.04.2022 |

NB For funding information, refer to CDF and NICE Drugs Funding List

**Repeat every 28 days.**

| TTO | Drug | Dose | Route | Directions |
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| Day 1 | **ENZALUTAMIDE** | **160mg** | PO | Each day as a single dose continuously for 28 days. Swallow this medicine whole.<br>Do not chew or crush.<br>Can be taken with or without food.<br>(available as 40mg tablets) |
| | NB: For newly diagnosed metastatic hormone-sensitive prostate cancer ADT must be prescribed. | | | |