Indication	For the treatment of oestrogen receptor positive, HER2-negative, locally advanced or metastatic breast cancer with an ESR1 mutation in patients previously treated with at least one prior line of endocrine therapy in combination with a CDK4/6 inhibitor and has received at least 12 calendar months of CDK4/6 inhibitor-based treatment. Patient's menopausal status must be considered and if appropriate the patient should have undergone ovarian ablation or suppression with LHRH agonist treatment. NB only 1 prior line of cytotoxic chemotherapy for advanced/ metastatic disease is permitted.
Treatment Intent	Palliative
Frequency and number of cycles	Repeat every 28 days Continue until disease progression, unacceptable toxicity or patient choice whichever occurs first.
Monitoring Parameters pre-treatment	• **Virology screening:** All new patients referred for systemic anti-cancer treatment should be screened for hepatitis B and C and the result reviewed prior to the start of treatment. Patients not previously tested who are starting a new line of treatment, should also be screened for hepatitis B and C. Further virology screening will be performed following individual risk assessment and clinician discretion. • FBC, U+Es and LFTs at baseline, day 15 of cycle 1 and at every cycle thereafter. • If platelets <100 and neuts <1 consider interrupting treatment. • Serum cholesterol and triglycerides should be checked prior to treatment and if clinically indicated throughout treatment. Where appropriate initiate or increase the dose of lipid lowering treatment. • **Hepatic impairment:** No dose adjustment is recommended in mild hepatic impairment (Child-Pugh A). In moderate hepatic impairment (Child-Pugh B), elacestrant dose should be reduced to 258 mg. Elacestrant has not been studied in severe hepatic impairment (Child-Pugh C), therefore no dose recommendation can be made for patients with severe hepatic impairment. • **Renal impairment:** No dose adjustment necessary in renal impairment (no data in severe renal impairment). • **Dose Modification for adverse reactions:** Dose interruption or reduction may be required for adverse reactions, see table 1. The recommended dose reduction for adverse reactions is 258mg OD (3 x 86mg tablets), no further dose reductions are permitted. If a patient cannot tolerate 258mg, treatment should be discontinued. NB: See below for guidance on dose reductions with a concomitant CYP3A4 inhibitor. • **Thromboembolic events:** Elacestrant should be used with caution in patients who are at risk of, or who have a history of thromboembolic events. • **Common drug interactions (for comprehensive list refer to BNF/SPC):** • Concomitant use of strong or moderate CYP3A4 inhibitors should be avoided. If a strong CYP3A4 inhibitor (e.g. clarithromycin, indinavir, itraconazole, ketoconazole, grapefruit or grapefruit juice) must be used, the elacestrant dose should be reduced to 86mg OD with close monitoring of tolerability. If a moderate CYP3A4 inhibitor (e.g. aprepitant, ciprofloxacin, ciclosporin, diltiazem, erythromycin, fluconazole) must be used, the elacestrant dose should be reduced to 172mg OD with close monitoring of tolerability. Subsequent dose reduction to 86mg OD may be considered with moderate CYP3A4 inhibitors based on tolerability. If the CYP3A4 inhibitor is discontinued, the elacestrant dose should be increased to the dose used prior to the initiation of the CYP3A4 inhibitor (after 5 half-lives of the CYP3A4 inhibitor). • Concomitant use of strong (e.g. phenytoin, rifampicin, carbamazepine and St John's Wort) or moderate (e.g. dabrafenib, lorlatinib, phenobarbital, primidone, and sotorasib) CYP3A4 inducers should be avoided. If a strong or moderate CYP3A4 inducer must be used for a short duration of time (i.e. </=3 days) or intermittently (i.e. treatment periods </= 3 days separated by at least 2

	weeks or 1 week + 5 half-lives of the CYP3A4 inducer, whichever is longer), continue elacestrant without increasing the dose. • Concomitant use with P-gp substrates (e.g. digoxin) and BRCP substrates (e.g. rosuvastatin) may increase their concentrations, which may increase the adverse reactions associated with the P-gp / BRCP substrates. The dose of co-administered P-gp/ BRCP substrates should be reduced accordingly. • **Missed dose:** If a dose is missed it can be taken if within 6 hours of the usual administration time, if more than 6 hours the dose should not be taken and the patient should resume with the next scheduled daily dose. If a patient vomits after taking the dose no extra dose should be taken, resume with the next scheduled daily dose. • **Driving and machinery:** Fatigue, asthenia, and insomnia have been reported in some patients taking elacestrant, caution should be observed by patients who experience those adverse reactions when driving or operating machinery. • For oral self-administration: refer to local Trust policy on oral anti-cancer medicines and supply Patient Information Leaflet.
References	SPC accessed online 24.12.2024 CDF list V1.340 accessed online 24.12.2024 BT form accessed online 24.12.24.

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

Table 1: Dose modification guidelines for adverse reactions

Severity	Dose modification
Grade 2	Consider interruption until recovery to </= Grade 1 or baseline. Then resume at the same dose level.
Grade 3	Treatment should be interrupted until recovery to </= Grade 1 or baseline. The dose should be reduced to 258 mg once daily when resuming therapy. If the Grade 3 toxicity recurs, treatment should be interrupted until recovery to </= Grade 1 or baseline. The reduced dose of 258 mg may be resumed if at the discretion of the treating physician the patient is benefiting from treatment. If a Grade 3 or intolerable adverse reaction recurs, treatment should be permanently discontinued.
Grade 4	Interrupt until recovery to </= Grade 1 or baseline. The dose should be reduced to 258 mg once daily when resuming therapy. If a Grade 4 or intolerable adverse reaction recurs, permanently discontinue.

Repeat every 28 days continuously

TTO	Drug	Dose	Route	Directions
Day 1	**ELACESTRANT**	**345mg***	PO	OD at approximately the same time every day. Take with a light meal. Grapefruit or grapefruit juice should be avoided. Swallow whole, do not crush, split or chew the tablets. Available as 86mg and 345mg tablets
	Metoclopramide	10mg	PO	Up to TDS PRN. Do not take for more than 5 days continuously. Dispense on cycle 1 then only if required.
	Loperamide	2-4mg	PO	Take 4mg (2 capsules) initially, then 2mg (1 capsule) after each loose stool when required. Maximum 16mg (8 capsules) a day. Dispense 30 capsules on cycle 1 then only if required.
	*see monitoring parameters for dose modification requirements when used with CYP3A4 inhibitors			