

**Positive Quality Intervention: Elacestrant (Orserdu™)**

Description: The purpose of this PQI is to provide awareness of an oral estrogen receptor antagonist option for patients undergoing treatment for breast cancer and to discuss counseling, monitoring parameters, and patient management strategies to optimize adherence and improve patient outcomes.

Background: Elacestrant is a first-of-its-kind, once daily, orally administered single-agent treatment that works by binding to estrogen receptor alpha (ER α) and acting as an antagonist, thus inducing breakdown of important proteins needed for the proliferation of malignant tumor cells.¹ This mechanism of action can generally be classified as Selective Estrogen Receptor Degraders (SERD). Elacestrant gained FDA approval for ER-positive, HER2-negative, ESR1-mutated advanced or metastatic breast cancer with disease progression following at least one line of endocrine therapy based on results from the EMERALD trial, a randomized, open-label, active-controlled, multicenter trial that enrolled 478 postmenopausal women and men with ER+/HER2- advanced or metastatic breast cancer. Of the enrolled patients, 228 patients had ESR1 mutations. Inclusion criteria included subjects who experienced disease progression on one/two lines of endocrine therapy, with at least one line including a CDK4/6 inhibitor. Subjects were randomized to receive either elacestrant 345 mg orally once daily or investigator's choice of endocrine therapy, including aromatase inhibitor or fulvestrant. The primary outcome was progression free survival (PFS) which a blinded imaging review committee assessed. The EMERALD trial observed a statistically significant difference in PFS in the intention to treat (ITT) population as well as in the ESR1-mutation subgroup in favor of the elacestrant arm. Among the 228 patients with ESR1 mutations, the median PFS was 3.8 months (95% CI, 2.2-7.3) in the elacestrant arm and 1.9 months (95% CI, 1.9-2.1) in the standard of care (SoC) arm (hazard ratio [HR], 0.55 [95% CI, 0.39-0.77]; 2-sided P =.0005). In a post-hoc analysis of PFS based on duration of prior CDK4/6i treatment, patients with an ESR1m who had at least 12 months of CDK4/6i had mPFS of 8.6 months with elacestrant vs 1.9 mo with SOC.² The most common adverse events shared between the elacestrant and other endocrine therapy cohorts were musculoskeletal pain (41% vs. 39%), nausea (35% vs. 19%), fatigue (26% vs. 27%), and hot flush (11% vs. 8%). Elacestrant was also found to cause some laboratory abnormalities, including increase in cholesterol (30% vs. 17%), triglycerides (27% vs. 15%), and serum creatinine (16% vs. 6%), as well as decreased hemoglobin (26% vs. 20%).³ Dosage modifications have been found to be beneficial in patients experiencing Grade 3 or greater adverse events (AE) following an interruption in treatment back to Grade \leq 1 or baseline in AE severity. Dose should be decreased to 258 mg (three 86 mg tablets) for the first reduction and 172 mg (two 86 mg tablets) for the second reduction. If Grade 4 AEs are recurrent or intolerable, permanent discontinuation of elacestrant is recommended.¹ Treatment-emergent AEs leading to the discontinuation of elacestrant and SoC were infrequent in both arms (6.3% vs 4.4%). Dose reductions were 3.0% in the elacestrant arm and 0% in the SoC arm.

PQI Process:¹ Upon receipt of an order of elacestrant (Orserdu™)

- Ensure the patient is a postmenopausal woman or adult man with ER-positive, HER2-negative, ESR1-mutated advanced or metastatic breast cancer
 - These patients should have disease progression following at least one line of endocrine therapy
 - ESR1 mutation status can be identified using the FDA approved companion diagnostic Guardant360 CDx assay
 - There may be other tests available by different manufacturers which claim ESR1 coverage; prior to utilizing such tests, it is recommended to verify with the manufacturer that their test detects the same set of ESR1 mutations covered by the Guardant360 CDx assay at a minimum
- Elacestrant is dosed 345 mg once daily until disease progression or unacceptable toxicity occurs

IMPORTANT NOTICE: NCODA has developed this Positive Quality Intervention platform. This platform is intended as an educational aid, does not provide individual medical advice, and does not substitute for the advice of a qualified healthcare professional. This platform does not cover all existing information related to the possible uses, directions, doses, precautions, warning, interactions, adverse effects, or risks associated with the medication. The materials contained in this platform do not constitute or imply endorsement, recommendation, or favoring of this medication by NCODA. NCODA does not ensure the accuracy of the information presented and assumes no liability relating to its accuracy. All decisions related to taking this medication should be made with the guidance and under the direction of a qualified healthcare professional. It is the individual's sole responsibility to seek guidance from a qualified healthcare professional. *Updated 11.29.23*

- Avoid concomitant use of elacestrant with strong or moderate CYP3A4 inducers and inhibitors
 - Pharmacists should review all concomitant prescription medications, vitamins and supplements, and over-the-counter medications
- Elacestrant is a P-gp inhibitor and BCRP inhibitor
 - Dose reduction required of P-gp and BCRP substrates per their prescribing information when minimal concentration changes may lead to serious or life-threatening adverse reactions
- Dose modification is necessary in patients with moderate hepatic impairment (Child-Pugh B) (see supplemental information)
 - Avoid use of elacestrant in patients with severe hepatic impairment (Child-Pugh C)
- Discuss incidence of hypercholesterolemia and hypertriglyceridemia
 - Monitor patient’s lipid profile prior to initiation and periodically during treatment
- Advise females of reproductive potential and males with female partners of reproductive potential to use contraception during treatment with elacestrant and for one week after the last dose

Patient-Centered Activities:

- Provide Oral Chemotherapy Education (OCE) sheet
- Counsel to administer once daily
 - Take with food at approximately same time each day
 - Do not take two doses at once; missed doses can be taken if within 6 hours of scheduled time
 - If you miss a dose, document the missed dose and report it to your healthcare provider
 - Avoid consuming grapefruit & grapefruit juice while taking elacestrant
- Ensure proper monitoring for adverse effects
- Evaluate medication adherence at follow-up assessment and provide counseling to improve compliance if needed
- Provide strategies to reduce the incidence of and manage adverse events
 - Maintain a diary to document cases of muscle pain, especially when it interferes with activities of daily living (ADL)
 - Stay as active as you can, but understand that it is okay to rest if needed
 - Eat small, more frequent meals to reduce the incidence of nausea. Eat and drink slowly
- Patient Assistance: NCODA Financial Assistance Tool

Supplemental Information:

Table 1: Elacestrant Dose Reduction Levels for Adverse Reactions¹

Dose Reduction	Dosage	Number and Strength of Tablets
First-dose reduction	258 mg once daily	Three 86 mg tablets
Second-dose reduction	172 mg once daily ¹	Two 86 mg tablets

¹If further dose reduction below 172 mg once daily is required, permanently discontinue elacestrant

Table 2: Elacestrant Dose Modification Guidelines for Adverse Reactions¹

Severity	Dosage Modification
Grade 1	Continue elacestrant at current dose level
Grade 2	Consider interruption of elacestrant until recovery to Grade ≤ 1 or baseline. Then resume elacestrant at the same dose level.
Grade 3	Interrupt elacestrant until recovery to Grade ≤ 1 or baseline. Then resume elacestrant at the next lower dose level. If the Grade 3 toxicity recurs, interrupt elacestrant until recovery to Grade ≤ 1 or baseline. Then resume elacestrant reduced by another dose level.

Grade 4	Interrupt elacestrant until recovery to Grade \leq 1 or baseline. Then resume elacestrant reduced by one dose level. If a Grade 4 or intolerable adverse reaction recurs, permanently discontinue elacestrant.
---------	--

References:

1. Orserdu™ (elacestrant) [package insert]
2. Kaklamani, Virginia, et al. “Oral Elacestrant vs Standard-of-Care in Estrogen Receptor-Positive, HER2-Negative (ER+/HER2-) Advanced or Metastatic Breast Cancer (MBC) without Detectable ESR1 Mutation (EMERALD): Subgroup Analysis by Prior Duration of CDK4/6i plus Endocrine Therapy (ET).” *Journal of Clinical Oncology*, vol. 41, no. 16_suppl, 1 June 2023, pp. 1070–1070, https://doi.org/10.1200/jco.2023.41.16_suppl.1070. Accessed 24 Aug. 2023.
3. Bidard F-C, Kaklamani VG, Neven P, et al.. Elacestrant (oral selective estrogen receptor degrader) versus standard endocrine therapy for estrogen receptor–positive, human epidermal growth factor receptor 2–negative advanced breast cancer: results from the randomized phase III EMERALD trial. *J Clin Oncol* 2022; 40: 3246–3256