Healthcare Improvement Scotland | SMC Advice on new medicines

SMC2933

elacestrant film-coated tablets (Korserdu®)

Menarini Stemline UK Ltd

07 August 2026

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and, following review by the SMC executive, advises NHS Boards and Area Drug and Therapeutics Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following a resubmission

elacestrant (Korserdu®) is accepted for restricted use within NHSScotland.

Indication under review: as monotherapy for the treatment of postmenopausal women, and men, with estrogen receptor (ER)-positive, HER2-negative, locally advanced or metastatic breast cancer with an activating ESR1 mutation who have disease progression following at least one line of endocrine therapy including a CDK 4/6 inhibitor.

SMC restriction: patients who have disease progression after receiving ≥12 months prior treatment with endocrine therapy plus a cyclin-dependent kinase (CDK) 4/6 inhibitor

In an open-label phase III study, elacestrant significantly improved progression-free survival (PFS) compared with investigator's choice of endocrine monotherapy, which may be relevant in a small proportion of patients in Scotland. Indirect data suggested elacestrant may improve PFS versus everolimus-exemestane, which may also be used in a small subset of patients. Indirect evidence did not suggest a difference between elacestrant and capecitabine, the comparator considered most relevant to Scottish practice.

This advice applies only in the context of approved NHSScotland Patient Access Scheme (PAS) arrangements delivering the cost-effectiveness results upon which the decision was based, or PAS/ list prices that are equivalent or lower.

Chair
Scottish Medicines Consortium

1. Clinical Context

1.1. Medicine background

Elacestrant is a selective oestrogen receptor (ER)-alpha antagonist and degrader that binds to and inhibits the growth of ER alpha-positive breast cancer cells, including those with oestrogen receptor 1 (ESR1) gene mutations. The recommended dose is 345 mg taken orally once daily with a light meal. Treatment should continue as long as clinical benefit is observed or until unacceptable toxicity occurs.[1]

1.2. Disease background

Locally advanced or metastatic breast cancer is an incurable disease, comprising a variety of subtypes defined by molecular markers; the 5-year survival rate is approximately 38%. Around 70% of breast cancers are hormone receptor (HR)-positive and human epidermal growth factor receptor 2 (HER2)-negative. ESR1 mutations are associated with resistance to endocrine therapy, particularly aromatase inhibitors, and develop following progression on an endocrine treatment. The mutation is more common in metastatic disease and has been associated with poorer survival outcomes.[2-4]

1.3. Company proposed position

The submitting company has requested that elacestrant is restricted for use in patients who have disease progression after receiving ≥12 months prior treatment with endocrine therapy plus a cyclin-dependent kinase (CDK) 4/6 inhibitor.

1.4. Treatment pathway and relevant comparators

Standard first-line therapy for HR-positive, HER2-negative metastatic breast cancer is a CDK 4/6 inhibitor (abemaciclib, palbociclib or ribociclib) plus endocrine therapy. The latter can include an aromatase inhibitor (steroidal: exemestane; non-steroidal: letrozole or anastrozole) for patients who have not relapsed on or within 12 months of stopping adjuvant aromatase inhibitor therapy, or fulvestrant (a selective oestrogen receptor degrader [SERD]) for those who have.

Choice of second-line treatment (including chemotherapy or further endocrine-based therapy) is based on disease aggressiveness, organ function and toxicity profiles. Patients who have rapid progression on first-line therapy should be considered for chemotherapy with or without maintenance endocrine monotherapy. For those with an initial good response, the optimal sequence of subsequent therapy is uncertain and is individualised. Some patients may receive single agent chemotherapy (such as capecitabine or paclitaxel) while others may continue with second-line endocrine-based therapy. The mammalian target of rapamycin (mTOR) inhibitor, everolimus, has been accepted by SMC (872/13) for use in combination with exemestane in postmenopausal women who have disease recurrence or progression following a non-steroidal aromatase inhibitor. Fulvestrant monotherapy is another treatment option following disease relapse or disease progression on anti-oestrogen therapy (SMC114/04). Alpelisib, an α-specific class I (PI3Kα) inhibitor, is licensed for second-line use after endocrine-based therapy, in combination with fulvestrant for the subgroup of patients with HR-positive, HER2-negative locally advanced or metastatic breast cancer with PIK3CA mutations. However, SMC published advice

(SMC2481) in December 2022 that it is not accepted for use within NHS Scotland for this indication.

Cancer Medicines Outcome Programme Public Health Scotland (CMOP-PHS) data (which excluded patients on endocrine monotherapy) indicate that most patients (with ER-positive, HER2-negative, metastatic breast cancer prescribed systemic anticancer therapy sequentially after a CDK4/6 inhibitor) received capecitabine (59%) or paclitaxel monotherapy (19%); a small proportion received everolimus with or without exemestane (6.2%).[5-7]

The submitting company considered everolimus plus exemestane to be the only relevant comparator for this submission. However, SMC clinical experts indicated that single agent chemotherapy, particularly capecitabine, and endocrine monotherapy with fulvestrant are also relevant comparators.

1.5. Category for decision-making process

Eligibility for a PACE meeting

Elacestrant meets SMC end of life and orphan equivalent criteria for this indication.

2. Summary of Clinical Evidence

2.1. Evidence for the licensed indication under review

Evidence to support the efficacy and safety of elacestrant for the indication under review comes from the EMERALD study as detailed in Table 2.1.

Table 2.1. Overview of relevant study

Criteria	EMERALD[2, 8]
Study design	A multicentre, open-label, phase III study.
Eligible patients	• Female (postmenopausal) or male patients aged ≥18 years with oestrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast adenocarcinoma that was locally advanced and not amenable to resection or radiation therapy with curative intent, or metastatic disease not amenable to curative therapy. • Appropriate candidate to receive endocrine monotherapy. • Disease progression during or within 28 days after treatment with one or two lines of endocrine therapy for advanced or metastatic disease. Progression on previous cyclin-dependent kinase (CDK) 4/6 inhibitor treatment in combination with either fulvestrant or an aromatase inhibitor (AI) was required. • One chemotherapy regimen in the advanced or metastatic setting was permitted. • Eastern Cooperative Oncology Group (ECOG) performance status 0 or 1 and measurable disease per Response Evaluation Criteria in Solid Tumours (RECIST) version 1.1 or evaluable bone-only disease with at least one lytic or mixed lytic-blastic bone lesion (blastic-only metastases were not allowed). • Patients with symptomatic metastatic visceral disease were excluded from the study.
Treatments	Elacestrant 400 mg (equivalent to 345 mg elacestrant free base) orally once daily or investigator's choice of endocrine monotherapy: • Fulvestrant 500 mg intramuscularly on days 1 and 15 of cycle one, day 1 of cycle two and then on day 1 of each subsequent 28-day cycle (dose reductions to 250 mg were permitted) • Anastrozole 1 mg orally once daily • Letrozole 2.5 mg orally once daily • Exemestane monotherapy 25 mg orally once daily

	Choice of endocrine monotherapy was based on general guidance: fulvestrant was used in patients without prior exposure (unless contraindicated), an AI was used after progression on fulvestrant, and the AI was selected according to prior AI therapy and contraindications. Treatment continued until investigator-assessed disease progression, clinically significant adverse events, significant study non-compliance, unable to receive study treatment for >14 consecutive days, treatment discontinuation in the best interest of the patient, or patient refuses treatment.
Randomisation	Patients were randomised equally and stratified according to oestrogen receptor 1 (ESR1) mutation status (detected, or not detected), prior treatment with fulvestrant (yes or no) and presence of visceral metastases (yes or no).
Primary outcomes	Progression-free survival (PFS), tested in the ESR1-mutation positive subpopulation and in the overall population. It was defined as the time between date of randomisation to the date of first progression assessed by blinded independent central review (BICR) per RECIST v1.1 or death due to any cause, whichever occurred first.
Selected secondary outcome	Overall survival (OS), defined as the time from randomisation until the date of death from any cause.
Statistical analysis	PFS and OS were tested in the ESR1-mutation positive subpopulation and in the overall population. PFS and OS outcomes were controlled for multiplicity in both populations.

The ESR1-mutation positive subpopulation of the EMERALD study represents the UK marketing authorisation; the overall study population is broader and therefore results in the full intention-to-treat population have not been presented here. The primary analysis PFS was conducted at the 06 September 2021 data cut-off (DCO; at which time median overall survival [OS] follow-up was 14 months). The final OS analysis was conducted at the 02 September 2022 DCO, when 53% of deaths had occurred. Results are detailed in Table 2.2.[2, 8-10]

Table 2.2: Primary and selected secondary outcomes from the EMERALD study for ESR1-mutation positive patients[2, 8, 11]

	Elacestrant (n=115)	**Endocrine monotherapy (n=113)**
PFS assessed by BICR per RECIST v1.1 (06 September 2021 data cut-off)		
PFS events	62	78
Median PFS	3.8 months	1.9 months
HR (95% CI)	0.55 (0.39 to 0.77), p<0.001	
KM estimated 6-month PFS	41%	19%
Overall survival (02 September 2022 data cut-off)		
Median follow-up	26.8 months	
Deaths	61	60
Median OS	24.2 months	23.5 months
HR (95% CI)	0.90 (0.63 to 1.30), p=0.58	
KM estimated 12-month OS	83%	74%
KM estimated 24-month OS	51%	49%

Abbreviations: BICR = blinded independent central review; CI = confidence interval; CR = complete response; ESR1 = oestrogen receptor 1; HR = hazard ratio; KM = Kaplan-Meier; OS = overall survival; PFS = progression-free survival; PR = partial response; RECIST v1.1 = Response Evaluation Criteria in Solid Tumours version 1.1.

PFS was also assessed by the local investigator. Results from the September 2021 DCO in ESR1-mutation positive patients indicated differences between blinded independent central review (BICR) and investigator-assessed PFS. The investigator-assessed median PFS was 3.6 months and 2.1 months in the elacestrant and endocrine monotherapy groups respectively, with a hazard ratio of 0.65 (95% confidence interval [CI] 0.48 to 0.88).[2]

Most patients in the endocrine monotherapy group received fulvestrant (83/113 [73%]). Post hoc analyses comparing elacestrant with fulvestrant suggested that the PFS results were similar to the primary analysis: median PFS was 3.8 months versus 1.9 months, with a hazard ratio of 0.50 (95% CI 0.34 to 0.74).[2]

2.2. Evidence to support the positioning proposed by the submitting company

The submitting company provided results from exploratory post hoc analyses in a subgroup of ESR1-mutation positive patients who received ≥12 months of prior treatment with a CDK 4/6 inhibitor plus endocrine therapy to support the proposed positioning. The results from the September 2022 DCO are detailed in Table 2.3.[12, 13]

Table 2.3: Post hoc analyses of outcomes from the EMERALD study for ESR1-mutation positive patients who received ≥12 months of prior CDK 4/6 inhibitor plus endocrine therapy (data cut-off 02 September 2022)[12, 13]

	Elacestrant (n=78)	Endocrine monotherapy (n=81)
PFS assessed by BICR per RECIST v1.1		
PFS events	39	53
Median PFS	8.6 months	1.9 months
HR (95% CI)	0.41 (0.26 to 0.63)	
KM estimated 12-month PFS	36%	8.4%

Abbreviations: BICR = blinded independent central review; CDK 4/6 = cyclin-dependent kinase 4/6; CI = confidence interval; ESR1 = oestrogen receptor 1; HR = hazard ratio; KM = Kaplan-Meier; OS = overall survival; PFS = progression-free survival; RECIST v1.1 = Response Evaluation Criteria in Solid Tumours version 1.1

Overall survival results for patients who received ≥12 months of prior CDK 4/6 inhibitor plus endocrine therapy were considered confidential by the company.*

*Other data were also assessed but remain confidential.**

2.3. Health-related quality of life outcomes

Health-related quality of life (HRQoL) was assessed using the EQ-5D-5L, the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ-C30) and the Patient-Reported Outcome-Common Terminology Criteria for Adverse Events (PRO-CTCAE) questionnaire. The completion rates for some of the instruments were low and results are descriptive only. Overall, baseline scores in the ESR1-mutation positive subpopulation were similar between treatment groups with no meaningful differences over time in either group. Results in the ≥12 months of prior CDK 4/6 inhibitor plus endocrine therapy subgroup were broadly consistent.[2, 14]

2.4. Supportive studies

The submitting company presented two new real-world studies from the US as confirmatory evidence to support the efficacy of elacestrant.

A retrospective observational study used the Komodo Research Dataset (US healthcare claims) linked with Foundation Medicine Inc. clinico-genomic data. The study included 306 patients with ER-positive, HER2-negative, ESR1-mutant metastatic breast cancer who initiated elacestrant between January 2023 and February 2025. All had received prior endocrine therapy (100%; including with CDK4/6 inhibitors in 90% of patients), with half having received chemotherapy and 72% prior fulvestrant; 56% had received 3 or more prior lines of endocrine therapy. Median follow-up was 8.4 months. The primary outcome was time to next treatment (TTNT). The study reported a median TTNT of 7.9 months overall. In patients with 1 or 2 prior lines of endocrine therapy with or without CDK4/6i for 12 months or longer (N=116), median TTNT was 8.4 months.[15]

A retrospective observational study used the GuardantINFORM database, a large real-world clinical–genomic dataset linking sequencing data (Guardant360) with US healthcare claims. The study included 756 patients with ER-positive, HER2-negative, ESR1-mutant metastatic breast cancer who initiated elacestrant between January 2023 to March 2024. Most patients (76%) had received prior CDK4/6 inhibitors, 52% prior fulvestrant, and 38% prior chemotherapy; 53% had received 3 or more prior lines of metastatic therapy, 38% had received 1 or 2 prior lines, and 9% had received no prior line. Clinical outcomes measured were TTNT, time to treatment discontinuation (TTD), and OS. In the 742 patients eligible for outcomes analysis on elacestrant, median TTNT was 6.4 months, and the median TTD was 4.6 months. Median OS was not reached, with 118 events observed.[16]

2.5. Indirect evidence to support clinical and cost-effectiveness comparisons

In the absence of direct evidence versus everolimus plus exemestane, the submitting company presented an unanchored matching adjusted indirect comparison (MAIC). For this resubmission, a new propensity score matching indirect comparison of elacestrant versus chemotherapy (capecitabine monotherapy, paclitaxel monotherapy or pooled chemotherapy comprising a mix of capecitabine and paclitaxel monotherapies) has been provided following SMC's identification of chemotherapy as a relevant comparator. See Table 2.4 for details. All indirect treatment comparisons (ITCs), except paclitaxel monotherapy, were incorporated into the economic base case.

In addition, a supportive MAIC against everolimus plus endocrine therapy was provided to validate the findings from the MAIC against everolimus plus exemestane; this has not been used in the economic case.

Table 2.4: Summary of indirect treatment comparisons

Criteria	Overview
Design	Unanchored MAIC. Propensity score matching.
Population	Postmenopausal women with ER-positive, HER2-negative locally advanced or metastatic breast cancer with an activating ESR1 mutation and ≥12 months prior treatment with CDK 4/6 inhibitor plus endocrine therapy.
Comparators	MAIC: everolimus plus exemestane (supportive validation MAIC: everolimus plus endocrine therapy) Propensity score matching: capecitabine only, paclitaxel only, and pooled chemotherapy (comprising capecitabine and paclitaxel).
Studies included	EMERALD[8, 12] (for elacestrant, N=78), and Flatiron real-world database [17] (for everolimus plus exemestane, N=32; capecitabine, N=98; paclitaxel, N=12 and pooled chemotherapy [comprising capecitabine and paclitaxel, N=110]), and evERA[18] (for everolimus plus endocrine therapy, N=190 [ITT population; N=105 in ESR1-mut population])
Outcomes	OS and PFS
Results	• **MAIC - elacestrant versus everolimus plus exemestane:** The results suggest that elacestrant had superior efficacy to everolimus plus exemestane for PFS, however there was no evidence of a difference in OS.[19] PFS: HR 0.59 (95% CI 0.36 to 0.96) OS: HR 0.64 (95% CI 0.35 to 1.16) The results from the supportive MAIC suggest a possible superior efficacy (in PFS and OS) compared to everolimus + endocrine therapy (SoC arm). • **Propensity score matching:** 1. **Elacestrant versus capecitabine:** There was no evidence to suggest superiority over capecitabine (the 95% CI of the PFS and OS HR include 1) PFS: HR 0.68 (95% CI 0.45 to 1.03) OS: HR 0.66 (95% CI 0.40 to 1.08) 2. **Elacestrant versus paclitaxel:** The results of the comparison of elacestrant versus paclitaxel, which should be interpreted with caution due to the small sample size, suggest a potential superior OS but there was no evidence of a difference in PFS. PFS: HR 0.40 (95% CI 0.11 to 1.47) OS: HR 0.05 (95% CI 0.01 to 0.39) 3. **Elacestrant versus pooled chemotherapy:** The results of the comparison versus pooled chemotherapy suggest that elacestrant had superior efficacy with greater OS and PFS. PFS: HR 0.64 (95% CI 0.41 to 0.99) OS: HR 0.51 (95% CI 0.31 to 0.83)

Abbreviations: CDK = cyclin-dependent kinase; CI = confidence interval; ER = oestrogen receptor; ESR1 = oestrogen receptor 1; HER2 = human epidermal growth factor receptor 2; HR = hazard ratio; MAIC = matching adjusted indirect comparison; OS = overall survival; PFS = progression-free survival; SoC = standard of care.

3. Summary of Safety Evidence

Evidence from the EMERALD study supports the relative safety of elacestrant compared with endocrine monotherapy for the treatment of patients with advanced or metastatic breast cancer. Fulvestrant, the most common investigator's choice of endocrine monotherapy, may be a relevant comparator for some patients.

Any treatment-emergent adverse event (AE) was reported by 91% (105/115) of patients in the elacestrant group and 87% (92/106) in the endocrine monotherapy group, and these were considered treatment-related in 62% and 46%, respectively. In the elacestrant and endocrine monotherapy groups respectively, patients reporting a grade 3 or higher AE were 28% versus 22%, patients with a reported serious AE were 12% versus 11%, patients with a dose reduction due to treatment-emergent AEs were 5.2% versus 0, the proportion of AEs that led to dose interruptions were 22% versus 6.6% and patients discontinuing therapy due to an AE was 5.2% versus 3.8%. Results at the July 2022 DCO were consistent.[2, 8, 10]

In patients with an ESR1 mutation, the most frequently reported grade 3 or 4 treatment-emergent AEs with an incidence ≥2% in the elacestrant group versus the endocrine monotherapy group were: nausea (4.3% versus 0.9%), back pain (4.3% versus 0), bone pain (2.6% versus 0.9%), asthenia (2.6% versus 0.9%) and neutropenia (0 versus 2.8%). Elacestrant was associated with an increase in treatment-emergent gastrointestinal AEs compared with endocrine monotherapy, including nausea (35% versus 18%), vomiting (18% versus 9.4%), decreased appetite (16% versus 7.5%), dyspepsia (11% versus 2.8%) and constipation (10% versus 7.5%). The European regulator noted that most of these were grade 1 or 2 in severity and occurred during the first treatment cycle.[2, 8, 10]

Safety data for the proposed positioning subpopulation (ESR1-mutant patients with ≥12 months of prior CDK4/6 inhibitor plus endocrine therapy) were consistent with those observed in the licensed population. [12]

*Other data were also assessed but remain confidential.**

4. Summary of Clinical Effectiveness Considerations

4.1. Key strengths

- Elacestrant is the first targeted treatment licensed for patients with advanced breast cancer with an activating ESR1 mutation.
- In the phase III EMERALD study, at the September 2021 DCO, treatment with elacestrant was associated with a 1.9-month improvement in median PFS compared with endocrine monotherapy in the subpopulation of patients with an activating ESR1 mutation; the difference between groups was statistically significant. The European regulator described the increase in median PFS as small but clinically relevant in the context of a clinically manageable safety profile. Results from a subsequent DCO in September 2022 were consistent.[2, 8]
- In the post hoc subgroup analysis of patients who received ≥12 months of prior treatment with a CDK 4/6 inhibitor plus endocrine therapy (the subpopulation that is representative of the

proposed positioning), there was an improvement in median PFS of 6.7 months with elacestrant compared with endocrine monotherapy.[12]

4.2. Key uncertainties

- The EMERALD study showed no significant OS benefit versus investigator's choice of endocrine therapy, which may be relevant in Scottish practice, although likely only for a small proportion of patients based on feedback from SMC-consulted clinical experts. Regulator noted that Kaplan-Meier curves in the ESR1-mutation positive subpopulation did not show signals of a detriment.[2, 8]
- There is no direct evidence against single agent chemotherapy (capecitabine in particular), which is considered the most relevant comparator based on CMOP-PHS data and clinical experts consulted by SMC. It should be noted that the CMOP-PHS data excluded patients receiving endocrine monotherapy, and the population is broader than the indication and positioning under review.[6] Although the company provided indirect data against chemotherapy in response to SMC's request, the results are highly uncertain, and the comparisons are considered to be flawed. Limitations include the use of an inappropriate matching approach resulting in substantial post-matching imbalances in baseline characteristics, reliance on the US real-world database Flatiron and small sample sizes.
- The MAIC comparing elacestrant with everolimus plus exemestane was associated with several limitations, including differences in study design and sample sizes; reliance on a small US real-world cohort, limited matching of baseline characteristics, residual imbalances after matching, and wide credible intervals around the point estimates. Due to these limitations, the results are considered highly uncertain. To validate these results the submitting company provided a new MAIC against everolimus plus endocrine therapy. However, it is also associated with substantial limitations, including an uncertain matching process, and a lack of sufficient pre- and post-matching data to assess comparability, leaving high uncertainty around its validity. In addition, CMOP-PHS data and feedback from SMC clinical experts suggest that everolimus plus exemestane is a less relevant comparator in Scottish practice.
- Evidence to support the proposed positioning is from an exploratory post hoc subgroup analysis with a limited number of patients in each group and are considered descriptive only.
- EMERALD was an open-label study, which could introduce bias for subjective efficacy, safety and HRQoL outcomes. This risk was mitigated for the primary outcome which was assessed by BICR.[2, 8]
- The supportive real-word evidence is associated with several limitations, including its retrospective, non-comparative design, reliance on surrogate outcomes (such as TTNT [which the submitting company suggests may be a surrogate for PFS]/TTD that may be influenced by factors unrelated to disease progression), and use of insurance claims data with limited clinical detail and completeness.

4.3. Clinical expert input

Clinical experts consulted by SMC considered that the introduction of elacestrant for advanced or metastatic breast cancer would be a therapeutic advancement and fills an unmet need as it is a targeted treatment option for patients with an ESR1 mutation. They suggested it would provide an additional treatment option for patients who had disease progression after at least 12 months of treatment with endocrine therapy and a CDK 4/6 inhibitor.

4.4. Service implications

Diagnostic test required to identify patients eligible for treatment: contact local laboratory for information.

5. Summary of Patient and Carer Involvement

The following information reflects the views of the specified Patient Groups.

- We received patient group submissions from Breast Cancer Now, Make 2nds Count and METUP UK. All three organisations are registered charities.

- Breast Cancer Now has received 0.52% pharmaceutical company funding in the past two years, including from the submitting company. Make 2nds Count has received 17% pharmaceutical company funding in the past two years, including from the submitting company. METUP UK has not received any pharmaceutical company funding in the past two years.

- Secondary breast cancer is incurable with treatment aimed at slowing progression and maintaining quality of life. The emotional burden is universal – patients often live scan to scan with constant fear, anxiety and uncertainty. People with ER-positive, HER2 negative metastatic breast cancer who have experienced progression after endocrine treatments face limited options for further treatment. This can have a devastating impact on the patient and their family and friends.

- ESR1 mutations are a common source of resistance to endocrine therapy in breast cancer. There are currently no targeted treatments for HR+/HER2- secondary breast cancer patients with an ESR1 mutation.

- People with a diagnosis of secondary breast cancer are keen for more and better treatment options. Elacestrant would provide a targeted treatment option for those with ESR1 mutations and is an oral medicine that can be taken at home reducing the need for hospital visits and giving the patient more independence. It may also delay the need for chemotherapy. Extra lines of treatment give patients and families more time together and help them see important life milestones.

- Patients can experience side effects including nausea, fatigue, vomiting, decreased appetite and arthralgia. These would need to be appropriately managed and discussed

with the patient, so they are able to make their own choice balancing them against the potential benefit of the treatment.

6. Summary of Comparative Health Economic Evidence

6.1. Economic case

Details of the economic case are summarised in Table 6.1.

Table 6.1 Description of economic analysis

Criteria	Overview
Analysis type	Cost-utility analysis
Time horizon	34 years based on an assumed starting age of 66 years
Population	Postmenopausal women, and men, with ER+/HER2-, locally advanced/mBC with an activating *ESR1-mut* who have disease progression following ≥12 months prior treatment with ET + CDK4/6i.
Comparators	Capecitabine, pooled chemotherapy (capecitabine or paclitaxel) and everolimus plus exemestane (EVE+EXE) were the comparators in the analysis.
Model description	The analysis used a partitioned survival analysis model, comprised of three health states: progression-free, progressed disease and death. A 1-week cycle length was assumed to be short enough to adequately capture meaningful changes in health status for patients with advanced/mBC, being treated with elacestrant or a comparator. Thus, no half-cycle correction was applied.
Clinical data	The main source of clinical evidence was the EMERALD study[8, 12], a randomised, phase III, controlled study in patients with ER+/HER2-, advanced or mBC, whose disease had progressed on 1 to 2 prior lines of ET, including a CDK4/6i. This data informed survival outcomes (OS and PFS) for patients receiving elacestrant. To inform the survival outcomes of patients receiving comparator treatments, ITCs were performed (see Table 2.4 for details).
Extrapolation	Long-term OS and PFS were extrapolated using independent parametric survival modelling for all treatments. Curve selection was based on goodness of fit statistics, visual fit and clinical expert opinion. For patients receiving elacestrant, compared to capecitabine or pooled chemotherapy, log-normal and log-logistic curves were fitted to data observed in the EMERALD study for PFS and OS respectively. To model PFS for patients receiving capecitabine, a gamma curve was applied to propensity matched PFS data from the Flatiron database. A Weibull curve was applied to OS data. The same approach was used for the pooled chemotherapy comparator, with gamma and Weibull curves was used for PFS and OS respectively. For elacestrant patients, in the comparison with EVE+EXE, a log-normal curve and a log-logistic curve were fitted to MAIC reweighted data for PFS and OS respectively. To model the EVE+EXE arm, a log-normal and gamma curve were fitted to pseudo patient-level data created from digitising Kaplan-Meier survival curves.

Quality of life	Quality of life data were collected from participants in EMERALD via the EQ-5D-5L. The EQ-5D-5L was cross-walked to EQ-5D-3L. The estimated utility values were considered academic in confidence by the submitting company and so cannot de presented here. Disutilities were not included in the base case as these were assumed to be captured in the collected EQ-5D-5L data.
Costs and resource use	Costs included in the model were drug acquisition costs, healthcare resource use costs, cost of adverse reactions, and the costs of subsequent treatments. Other costs include end of life care costs, and ESR1-mut testing costs.
PAS/contract price	A Patient Access Scheme (PAS) was submitted by the company and assessed by the Patient Access Scheme Assessment Group (PASAG) as acceptable for implementation in NHSScotland. Under the PAS, a discount was offered on the list price. PAS discounts are in place for everolimus and trastuzumab deruxtecan and contract prices are in place for paclitaxel and docetaxel. These were included in the results used for decision-making.

6.2. Results

SMC would wish to present the with-PAS cost-effectiveness results that were used for decision-making. However, SMC is unable to publish these results due to commercial in confidence concerns regarding the PAS.

*Other data were also assessed but remain confidential.**

6.3. Sensitivity analyses

A range of sensitivity and scenario analyses were considered and descriptions of these key scenarios are provided in Table 6.2.

Table 6.2 Scenario Analysis Results

	Parameter	Base case	Scenario
1a	Time horizon	34 years	10 years
1b			20 years
2	MAIC approach	Independent PSM extrapolation	HR
3	RDI	Include	Exclude
4	ESR1-mut testing costs	Include	Exclude
5	Subsequent treatment costs	Include	Exclude
6	elacestrant subsequent treatment distribution	100% capecitabine	80% capecitabine, 20% trastuzumab deruxtecan
7	Progressed utility source	EMERALD EQ-5D analysis	Lloyd et al. (2006)[20], absolute approach (0.601)
8	Age-adjusted utilities	Enabled	Disabled
9a	ITC-adjusted curves	ITC hazard ratios OS	1
9b		ITC hazard ratios PFS	1
C1	9a + 9b	ITC hazard ratios	1 (cost minimisation analysis)

C2	C1 + 6	ITC hazard ratios + elacestrant subsequent treatment distribution	OS and PFS HR: 1 Elacestrant subsequent treatment distribution: 80% capecitabine, 20% trastuzumab deruxtecan

Abbreviations: C= combined; HR = hazard ratio; Incr. = incremental; ICER =incremental cost-effectiveness ratio; ITC = indirect treatment comparison; OS= overall survival; PFS = progression-free survival; PSM = parametric survival model; QALY = quality-adjusted life year; RDI =relative dose intensity; TTD = time to treatment discontinuation.

6.4. Key strengths

- The model uses a partitioned survival structure which appeared reasonable and is common to many oncology indications.
- The EMERALD study generated mature survival data for patients receiving elacestrant as well as directly observed quality of life data.

6.5. Key uncertainties

- The lack of direct evidence against any of the comparators used in the economics necessitated the use of several ITCs. The ITCs were associated with a number of limitations and increased uncertainty within the economic case. Changing the assumptions regarding the relative efficacy of elacestrant versus the comparators would lead to changes in the estimated cost-effectiveness.
- Alternative survival projections led to differing economic results, and so were a source of uncertainty. However, the impact on the decision-making ICERs was minimal. The largest changes in economic results were generated from scenarios where: subsequent treatment proportions were changed (see Scenario 6, Table 6.2) or when alternative distributions were selected for the extrapolation of OS for patients receiving elacestrant in comparison to everolimus plus exemestane.

7. Conclusion

After considering all the available evidence, the Committee accepted elacestrant for restricted use in NHSScotland.

8. Guidelines and Protocols

The European Society for Medical Oncology (ESMO) published a clinical practice guideline for the diagnosis, staging and treatment of patients with metastatic breast cancer in December 2021. The ESMO living guideline: metastatic breast cancer was published in April 2025.[4, 21]

The National Institute for Health and Care Excellence (NICE) clinical guideline number 81: Advanced breast cancer: diagnosis and treatment was published in February 2009 and updated in February 2025.[22] NICE also published in 2018 guideline NG101: Early and locally advanced breast cancer: diagnosis and management. This guideline was last updated in April 2025. [23]

9. Additional Information

9.1. Product availability date

January 2024

Table 9.1 List price of medicine under review

Medicine	Dose regimen	Cost per 28-days (£)
elacestrant	**345 mg orally once daily**	**7,340**

Costs from BNF online on 05/06/26. Costs do not take any patient access schemes into consideration.

10. Company Estimate of Eligible Population and Estimated Budget Impact

The submitting company estimated there would be 173 patients eligible for treatment with elacestrant in year 1, rising to 383 in year 3.

SMC is unable to publish the with-PAS budget impact due to commercial in confidence issues. A budget impact template is provided in confidence to NHS health boards to enable them to estimate the predicted budget with the PAS. This template does not incorporate any PAS discounts associated with comparator medicines or PAS associated with medicines used in a combination regimen.

*Other data were also assessed but remain confidential.**

References

1. Menarini Stemline UK Ltd. Elacestrant film-coated tablets (Korserdu®) Summary of product characteristics. Electronic Medicines Compendium www.medicines.org.uk Last updated: 11 February 2025.
2. European Medicines Agency (EMA). European Public Assessment Report. Orserdu. 20/07/2023, EMEA/H/C/005898/0000. www.ema.europa.eu
3. Surveillance, Epidemiology, and End Results (SEER) Program. SEER Cancer Stat Facts: Female Breast Cancer Subtypes. National Cancer Institute. Available at: www.seer.cancer.gov
4. Gennari A, André F, Barrios CH, Cortés J, Azambuja dE, DeMichele A*, et al.* ESMO Clinical Practice Guideline for the diagnosis, staging and treatment of patients with metastatic breast cancer. Annals of Oncology. 2021;32(12):1475-95.
5. Healthcare Improvement Scotland. Right Decision Service: Hormone Positive Metastatic Breast Cancer, 27 March 2024. https://rightdecisions.scot.nhs.uk/scottish-cancer-network-clinical-management-pathways/breast-cancer/systemic-anti-cancer-therapy-sact/metastatic-breast-cancer-mbc-sact/hormone-positive-metastatic-breast-cancer/.
6. Public Health Scotland. Cancer Medicines Outcome Programme Public Health Scotland (CMOP-PHS) report for the Scottish Medicines Consortium (SMC). Systemic anti-cancer therapy (SACT) after CDK4/6 inhibitors for the treatment of metastatic / locally advanced breast cancer: SMC2807. Publication date: 29 July 2025. Available at: https://publichealthscotland.scot/publications/cancer-medicines-outcomes-programme-public-health-scotland-cmop-phs-report-for-the-scottish-medicines-consortium-smc/systemic-anti-cancer-therapy-sact-after-cdk-46-inhibitors-for-the-treatment-of-metastatic-locally-advanced-breast-cancer-smc2807.
7. Right Decision Service. NHS Scotland Cancer Collaborative: Clinical Management Pathways. Public Services Delivery Scotland. Hormone Positive Metastatic Breast Cancer. Last reviewed: 13/08/2025. Available at: https://www.rightdecisions.scot.nhs.uk/.
8. Bidard F-C, Kaklamani VG, Neven P, Streich G, Montero AJ, Forget F*, 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(28):3246-56.
9. Menarini Stemline. Overall Survival Addendum to Clinical Study Report v.2 RAD1901-308 | Elacestrant monotherapy vs. standard of care for the treatment of patients with ER+/HER2- advanced breast cancer following CDK4/6 inhibitor therapy: a Phase 3 randomized, open-label, active-controlled, multicenter trial (EMERALD) | overall survival addendum as of 2nd September 2022. 2023/10/27.
10. Menarini Stemline. Clinical Study Report v.2: Elacestrant monotherapy vs. standard of care for the treatment of patients with ER+/HER2- advanced breast cancer following CDK4/6 inhibitor therapy: A phase 3 randomized, open-label, active-controlled, multicenter trial (EMERALD). Clinical Study Report. 2023 2023/01/06
11. Radius. Module 5.3.5.1. RAD1901-308 Confidential Overall Survival Final version. Table 14.2.2.1.1: Overall Survival for Elacestrant vs SOC, in ESR1-mut Subjects. Database cut-off date: 02SEP2022, Database extraction date: 13OCT2022.
12. Bardia A, Cortés J, Bidard F-C, Neven P, Garcia-Sáenz J, Aftimos P*, et al.* Elacestrant in ER+, HER2- Metastatic Breast Cancer with ESR1-Mutated Tumors: Subgroup Analyses from the Phase III EMERALD Trial by Prior Duration of Endocrine Therapy plus CDK4/6 Inhibitor and in Clinical Subgroups. Clin Cancer Res. 2024;30(19):4299-309.
13. Menarini Stemline. Data on File EMERALD post hoc subgroup additional analyses. All patients with ESR1-mut and ≥12 months of prior ET + CDK4/6i.

14. Cortés J, Bidard FC, Bardia A, Kaklamani VG, Vlachaki I, Tonini G*, et al.* 188O EMERALD trial analysis of patient-reported outcomes (PROs) in patients with ER+/HER2− advanced or metastatic breast cancer (mBC) comparing oral elacestrant vs standard of care (SOC) endocrine therapy. ESMO Open. 2023;8(1):101377.
15. Rugo HS, Kaklamani V, McArthur H, Wander SA, Gradishar W, Mahtani R*, et al.* Real-World Outcomes of Elacestrant in ER+, HER2-, ESR1-Mutant Metastatic Breast Cancer. Clin Cancer Res. 2026;32(1):179-87.
16. Lloyd MR, Weipert CM, Ali A, Solomon SR, Saha J, Lipsyc-Sharf MD*, et al.* Clinical and Genomic Factors Associated with Elacestrant Outcomes in ESR1-Mutant Metastatic Breast Cancer. Clin Cancer Res. 2026;32(1):169-78.
17. Flatiron. Clinico-Genomic Data is a Game Changer for Precision Oncology.
18. Rugo, Tolaney S, Jhaveri K, Moscetti L, Brufsky A. GS3-09 - Clinical and biomarker subgroup analysis of evERA Breast Cancer: A Phase III trial of giredestrant plus everolimus in patients with estrogen receptor-positive, HER2-negative advanced breast cancer previously treated with a CDK4/6 inhibitor. Presented at San Antonion Breast Cancer Symposium (SABCS), December 2025.
19. Felizzi F, Fenu E, Kloss S, Laizet V, Nouveau PL, Moreno S. RWD130 Elacestrant vs Everolimus + Exemestane in Patients With ER+/HER2- ESR1-Mutated Advanced/Metastatic Breast Cancer (mBC) With Prior Endocrine Therapy + CDK4/6 Inhibitor ≥12 Months: Combining Real-World and Clinical Trial Data. Value in Health. 2024;27(12):S598.
20. Lloyd A, Nafees B, Narewska J, Dewilde S, Watkins J. Health state utilities for metastatic breast cancer. Br J Cancer. 2006;95(6):683-90.
21. Gennari A, André F, Barrios CH, Cortés J, Azambuja dE, DeMichele A, et al. ESMO Clinical Practice Guideline for the diagnosis, staging and treatment of patients with metastatic breast cancer. Annals of Oncology. 2021;32(12):1475-95. ESMO Metastatic Breast Cancer Living Guideline, v1.2 April 2025.
22. National Institute for Health and Care Excellence (NICE). Advanced breast cancer: diagnosis and treatment CG81. Published 23 February 2009. Last updated 19 February 2025. Available at: www.nice.org.uk.
23. NICE. Early and locally advanced breast cancer: diagnosis and management NICE guideline NG101. Last updated: 14 April 2025. Available at: www.nice.org.uk.

This assessment is based on data submitted by the applicant company up to and including 17 July 2026.

**Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal:*https://www.scottishmedicines.org.uk/about-us/policies-publications/

Medicine prices are those available at the time the papers were issued to SMC for consideration. SMC includes Scottish national contract prices in its decision-making. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document.

Patient Access Schemes (PAS): A PAS is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a medicine and enable patients to receive access to cost-effective innovative medicines. The Patient Access Scheme Assessment Group (PASAG), established under the auspices of Public Services Delivery Scotland, reviews and advises NHS Scotland on the feasibility and acceptability on implementing proposed schemes. PASAG operates separately from SMC to maintain the integrity and independence of the assessment process of the

SMC. When SMC accepts a medicine for use in NHS Scotland on the basis of a PAS that has been considered acceptable for implementation by PASAG, a set of guidance notes on the operation of the scheme will be circulated to health boards' Area Drugs and Therapeutics Committees prior to publication of SMC advice.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.