

Annex No. 1 to Art. 7a, para. 2	
Marketing Authorisation Holder	AstraZeneca AB, Sweden
Name of medicine	Etcamah 75 mg film-coated tablet
ATC code	L02BA05
International non-proprietary name/INN	camizestrant
Therapeutic indications and ICD code or Orphanet code	
Suggested	Etcamah in combination with a CDK4/6 inhibitor (palbociclib, ribociclib, or abemaciclib) is indicated for the treatment of adult patients with ER-positive, HER2-negative, locally advanced or metastatic breast cancer upon detection of ESR1-mutation and without disease progression during first-line endocrine therapy in combination with a CDK4/6 inhibitor. In pre- or peri-menopausal women and in men, Etcamah plus a CDK4/6 inhibitor should be combined with a luteinizing hormone releasing hormone (LHRH) agonist or antagonist.
ICD	C50.0-C50.9 „Malignant neoplasm of breast“
Line of therapy	Early, biomarker-guided change in the endocrine component within first-line treatment. Patients are receiving first-line endocrine treatment in combination with a CDK4/6 inhibitor and are found to have an ESR1 mutation, without evidence of disease progression. Camizestrant is not positioned as a standard second-line treatment after progression, but as an early switch to the endocrine component before progression, while maintaining the same CDK4/6 inhibitor.
Patient population and subgroups	Adult patients with ER-positive, HER2-negative local advanced or metastatic breast cancer who are receiving first-line endocrine therapy in combination with a CDK4/6 inhibitor, in whom an ESR1 mutation is identified and there is no disease progression. In pre- or perimenopausal women, as well as in men. Clinically relevant subgroups include patients according to the concomitant CDK4/6 inhibitor (palbociclib, ribociclib, or abemaciclib), according to the previous endocrine component (most often letrozole or anastrozole), according to menopausal status, as well as according to the presence/type of ESR1 mutation.
Dosage form	Film-coated tablet - the tablet is a beige, round, biconvex film-coated tablet with a concave relief marking "CM" over "75" on one side and plain on the other, with an approximate diameter of 9 mm.
Quantity of active substance	75 mg
Final packaging	28 x 1 film-coated tablets in perforated unit dose aluminium/aluminium blisters; 2 blisters of 14 film-coated tablets.

Posology	The recommended dose of Etcamah in combination with a CDK4/6 inhibitor is 75 mg once daily. The CDK4/6 inhibitor should be continued at the same dose at the time of initiation with Etcamah as when the ESR1m was detected. If the CDK4/6 inhibitor is permanently discontinued, Etcamah should also be discontinued. Etcamah should be continued until a clinical effect is observed or until unacceptable toxicity occurs.
Method of administration	Oral use. The tablet should be swallowed whole with water and may be taken with or without food, at approximately the same time each day. Etcamah should not be ingested if it is broken, cracked, or otherwise not intact. The tablet should not be chewed, crushed, dissolved, or divided because these methods have not been studied in clinical studies.
Mechanism of action	Camizestrant is an oral selective oestrogen receptor degrader (SERD). It binds to the ligand-binding domain of ERα, antagonising the activity of ERα encoded by both wild-type ESR1 and mutated ESR1, and inducing proteasome-dependent degradation of ERα without agonising ERα. Through this mechanism, camizestrant addresses a key mechanism of endocrine resistance occurring during aromatase inhibitor treatment.
Companion diagnostic	Treatment requires detection of an ESR1 mutation before disease progression. Patients should be selected for treatment based on the presence of ESR1 mutations in a plasma or tumor sample taken every 3 months until an ESR1 mutation is detected. The assessment should be performed with a medical device with CE marked in vitro diagnostic (IVD) for the appropriate intended use; if a CE marked IVD is not available, an alternative validated test should be used. In SERENA-6, ESR1m was detected by ctDNA testing, allowing early therapeutic switch before clinical or radiological progression.
Current therapeutics approaches	Endocrine therapy with an aromatase inhibitor in combination with CDK4/6 inhibitor (palbociclib, ribociclib or abemaciclib) continued until progression or unacceptable toxicity. After progression, treatment choices depend on biomarker profile, prior exposure and clinical status and may include fulvestrant-based regimens, targeted combinations for PIK3CA/AKT1/PTEN alterations, elacestrant for ESR1m after progression, everolimus-based regimens, PARP inhibitors for BRCA1/2 mutation, antibody-drug conjugates for appropriate indications and chemotherapy in visceral crisis or later lines of treatment. The present proposal addresses the period before progression, when ESR1m is already detectable but the patient is still clinically controlled.
Comparative therapeutic alternatives	Direct comparative alternatives: anastrozole + palbociclib; anastrozole + ribociclib; anastrozole + abemaciclib; letrozole + palbociclib; letrozole + ribociclib; letrozole + abemaciclib.

	In the camizestrant scenario, patients switch from anastrozole/letrozole to camizestrant while maintaining the same CDK4/6 inhibitor: camizestrant + palbociclib; camizestrant + ribociclib; camizestrant + abemaciclib.
Name of the clinical trial, used in the dossier for marketing authorization application	SERENA-6 double-blind, randomized ctDNA-targeted study to evaluate the efficacy and safety of switching to Etcamah in combination with a CDK4/6 inhibitor versus continuing application of aromatase inhibitor (letrozole or anastrozole) + CDK4/6 inhibitor in patients with HR+/HER2- locally advanced or metastatic breast cancer with a detectable ESR1 mutation without disease progression during 1L aromatase inhibitor + CDK4/6 inhibitor.
Clinical trial number	NCT04964934; Study ID D8534C00001. Additionally: EudraCT 2021-000546-17; CTIS 2023-503990-39-00.
Clinical trial phase	Phase III, registrational, randomized, double-blind, 2-arm, placebo-matched, multicenter international study
Start date and expected end date of the clinical trial	Start date 2021-06-30 Initial completion date 2025-06-30 End date 2028-09-01, with ongoing follow-up of long-term endpoints, including overall survival.
Current phase of clinical development of the medicinal product	Phase 3 - The SERENA-6 study has completed the primary assessment/primary analysis and is continuing with follow-up. The available data support the positive CHMP opinion. The available SPC presents updated efficacy results at DCO3 (2 January 2026): median PFS 16.76 months for Etcamah + CDK4/6 inhibitor vs 9.23 months for AI + CDK4/6 inhibitor; HR 0.45 (95% CI 0.34; 0.59); $p < 0.00001$. Overall survival is immature, at 30% of the planned follow-up time, with a median of 41.20 months vs 40.21 months and a HR 0.87 (95% CI 0.57; 1.30).
Claimed status of orphan medicinal product (yes/no)	No
Registration procedure	Centralized procedure through EMA/European Commission.
Expected regulatory approval date (CHMP date and date of regulatory approval)	CHMP Opinion 2026-05-21 European Commission decision – pending
Expected date of start of pricing and reimbursement procedure	National price and reimbursement dossier submission planned for the fourth quarter of 2026. Expected reimbursement 2028-01.

Suggested average dose	Camizestrant 75 mg once daily orally, continuously. Camizestrant replaces the aromatase inhibitor as the endocrine component, while the CDK4/6 inhibitor is retained according to the patient's previous regimen and according to the dose at the time of ESR1m determination.
Expected place in the therapeutic pathway, listed in pharmacotherapeutic guidelines	Camizestrant is a biomarker-guided early switch to endocrine therapy in first-line HR+/HER2- locally advanced or metastatic breast cancer when ESR1m is detected by a plasma or tumor sample with an appropriate CE-marked IVD or alternative validated test, before progression. In practice, camizestrant replaces the aromatase inhibitor (anastrozole/letrozole) in the current AI + CDK4/6i regimen, with the aim of prolonging disease control, delaying progression and delaying the need for subsequent lines, including chemotherapy.
Expected cost (range from-to) for a patient per year or for a patient per episode/cycle if shorter than a year	Preliminary information has been submitted, it is confidential.
Influence on current NHIF expenses	Camizestrant will increase direct drug costs for endocrine treatment. At the same time, the clinical value is associated with delaying progression and transition to subsequent lines, reducing or postponing costs for treatment of advanced disease, subsequent therapies, hospitalizations, emergency care, complications and palliative care. The study data showed a longer median PFS with Etcamah + CDK4/6 inhibitor compared to AI + CDK4/6 inhibitor (16.76 months vs. 9.23 months; HR 0.45).
Influence on patients and patients caregivers	The potential for early, biomarker-guided breakthrough of endocrine resistance before clinical progression. In SERENA-6, switching to Etcamah plus a CDK4/6 inhibitor prolonged progressionfree survival compared with continuing on AI + CDK4/6 inhibitor and supported longer disease control. From a patient perspective, this potentially translates into longer progression-free survival, delay of subsequent lines of treatment, including chemotherapy, and reduced burden on family and caregivers. The oral formulation further supports convenience of administration.
Estimated number (range from-to) of Bulgarian patients eligible for treatment with the assessed therapy	It will be determined when localizing the budget model and based on current national epidemiological data.
Estimated 5-year budget impact (range from-to) plus budget model, if applicable	A budget impact will be presented with the national dossier planned for the fourth quarter of 2026, after finalizing the pricing strategy and localization of the model.