23 July 2026

Etcamah (camizestrant) in combination with a CDK4/6 inhibitor approved in the EU for 1st-line advanced ER-positive breast cancer

Approval based on SERENA-6 Phase III trial results which showed combination reduced the risk of disease progression or death by 56% in patients with an emergent ESR1 tumour mutation

First and only next-generation oral SERD and complete ER antagonist approved in 1st-line and only option in combination with all widely approved CDK4/6 inhibitors

Etcamah is 11th new AstraZeneca medicine of the 20 expected to launch by 2030

AstraZeneca's *Etcamah* (camizestrant) in combination with a cyclin-dependent kinase (CDK) 4/6 inhibitor (palbociclib, ribociclib or abemaciclib) has been approved in the European Union (EU) for the treatment of adult patients with estrogen receptor (ER)-positive, HER2-negative locally advanced or metastatic breast cancer upon detection of *ESR1* mutation and without disease progression during 1st-line endocrine therapy in combination with a CDK4/6 inhibitor.

The approval by the European Commission follows the positive opinion of the Committee for Medicinal Products for Human Use and was based on the positive results from the pivotal SERENA-6 Phase III trial published in *The New England Journal of Medicine*.[1]

In a planned interim analysis, the *Etcamah* combination reduced the risk of disease progression or death by 56% versus standard-of-care treatment with an aromatase inhibitor (AI) (anastrozole or letrozole) in combination with a CDK4/6 inhibitor (based on a hazard ratio [HR] of 0.44; 95% confidence interval [CI]:0.31-0.60; p<0.00001; median progression-free survival (PFS) 16.0 versus 9.2 months).

In Europe, breast cancer remains the leading cause of cancer death among women, with more than 140,000 deaths in 2024 and more than 540,000 patients diagnosed in the same year.[2] Hormone receptor (HR)-positive breast cancer, characterised by the expression of estrogen or progesterone receptors, or both, is the most common subtype of breast cancer with 70% of tumours considered HR-positive and HER2-negative.[3] More than 97% of HR-positive breast cancer tumours are ER-positive.[4,5] Across the UK, France, Germany, Spain and Italy, approximately 37,000 patients with HR-positive metastatic breast cancer are treated with a medicine in the 1st-line setting; most frequently with endocrine therapies paired with CDK4/6 inhibitors.[6-8] However, many patients have tumours that develop resistance to these therapies, at which point treatment options are limited and survival rates are low, with only approximately 36% of patients anticipated to live beyond five years after diagnosis.[3,8] Mutations in the *ESR1* gene are a key driver of endocrine resistance and are associated with poor outcomes, emerging during treatment of the disease and becoming more prevalent as the disease progresses.[9,10] Approximately 30% of patients with endocrine sensitive HR-positive disease develop *ESR1* mutations during 1st-line treatment before disease progression.[6]

François-Clément Bidard MD, PhD, Professor of Medical Oncology at Institut Curie & Versailles University (Paris/Saclay) France and co-principal investigator for the trial, said: "Today's approval is welcome news for the one in three patients in Europe with this form of advanced breast cancer whose tumours develop *ESR1* mutations before disease progression and are in urgent need of new options that both delay this progression and extend the benefit of 1st-line treatments. As the first pivotal trial to demonstrate the clinical value of monitoring circulating tumour DNA in the 1st-line breast cancer setting, SERENA-6 represents a significant advance in clinical practice and it is now important to identify patients who may be able to benefit from this combination and intervene promptly before their disease progresses."

Dave Fredrickson, Executive Vice President, Oncology Haematology Business Unit, AstraZeneca, said: "The approval of the *Etcamah* combination marks an important shift in the 1st-line treatment paradigm for patients with ER-positive, HER2-negative advanced breast cancer in Europe, providing a new standard-of-care to address emerging resistance ahead of disease progression. It also reflects the

strength of AstraZeneca's oncology pipeline and our commitment to translate innovative science into practice-changing treatment options for patients."

Data for the key secondary endpoints of time to second disease progression (PFS2) and overall survival (OS) were immature at the time of the interim analysis of the SERENA-6 trial, however, a subsequent pre-planned analysis demonstrated a statistically significant and clinically meaningful PFS2 benefit of 25.7 months versus 19.1 months in favour of the *Etcamah* combination (HR: 0.63; 95% CI: 0.46-0.86; p=0.00373) and OS continued to mature in favour of the *Etcamah* combination (HR: 0.87; 95% CI: 0.57-1.30). The trial will continue to assess OS as a key secondary endpoint.

The safety profile of *Etcamah* in combination with palbociclib, ribociclib or abemaciclib in the SERENA-6 trial was consistent with the known safety profile of each medicine. No new safety concerns were identified, and discontinuations were very low and similar in both arms.[1]

SERENA-6 is the first global, double-blind, registrational Phase III trial to use a circulating tumour DNA (ctDNA)-guided approach to detect the emergence of endocrine resistance and inform a switch in therapy before disease progression. The innovative trial design used ctDNA monitoring via a blood test at the time of routine tumour scans every two to three months to identify patients for early signs of endocrine resistance via the emergence of *ESR1* mutations. Following detection of an *ESR1* mutation without disease progression, the endocrine therapy of patients was switched to *Etcamah* from ongoing treatment with an AI, while continuing combination with the same CDK4/6 inhibitor.

Etcamah is also approved in Japan, the United Arab Emirates and Saudi Arabia based on the SERENA-6 Phase III trial. Regulatory applications for *Etcamah* in this setting are currently under review in several other countries including the US where the US Food and Drug Administration recently extended the Prescription Drug User Fee Act date to review the updated results from the trial.

Notes

HR-positive breast cancer

Breast cancer is the second most common cancer and one of the leading causes of cancer-related deaths worldwide.[11] More than two million patients were diagnosed with breast cancer in 2024, with more than 690,000 deaths globally.[11] While survival rates are high for those diagnosed with early breast cancer, only about 30% of patients diagnosed with or who progress to metastatic disease are expected to live five years following diagnosis.[3]

Globally, approximately 200,000 patients with HR-positive breast cancer are treated with a medicine in the 1st-line setting; most frequently with endocrine therapies that target ER-driven disease, which are often paired with CDK4/6 inhibitors.[6-8]

The optimisation of endocrine therapy and overcoming resistance to enable patients to continue benefiting from these treatments, as well as identifying new therapies for those who are less likely to benefit, are active areas of focus for breast cancer research.

SERENA-6

SERENA-6 is a Phase III, double-blind, randomised trial evaluating the efficacy and safety of *Etcamah* in combination with a CDK4/6 inhibitor (palbociclib, ribociclib or abemaciclib) versus treatment with an AI (anastrozole or letrozole) in combination with a CDK4/6 inhibitor (palbociclib, ribociclib or abemaciclib) in patients with HR-positive, HER2-negative advanced breast cancer (patients with either locally advanced disease, or metastatic disease) whose tumours have an emergent *ESR1* mutation.

The global trial enrolled 315 adult patients with histologically confirmed HR-positive, HER2-negative advanced breast cancer, undergoing treatment with an AI in combination with a CDK4/6 inhibitor as 1st-line treatment. The primary endpoint of the SERENA-6 trial is PFS as assessed by investigator, with secondary endpoints including OS, and PFS2 by investigator assessment.

Etcamah
Etcamah (camizestrant) is a potent, next-generation oral selective estrogen receptor degrader (SERD) and complete ER antagonist, administered orally, once daily. The recommended dose of *Etcamah* in combination with a CDK4/6 inhibitor is 75mg.

Etcamah in combination with a CDK4/6 inhibitor (palbociclib, ribociclib or abemaciclib) is approved in the EU, Japan and several other countries for the treatment of adult patients with HR-positive (or ER-positive), HER2-negative locally advanced or metastatic breast cancer upon detection or emergence of *ESR1* mutation and without disease progression during 1st-line endocrine therapy based on the results from the SERENA-6 trial.

The broad, robust and innovative *Etcamah* clinical development programme, including the SERENA-4, CAMBRIA-1 and CAMBRIA-2 Phase III trials, is evaluating the safety and efficacy of *Etcamah* when used as a monotherapy or in combination with CDK4/6 inhibitors to address a number of areas of unmet need in HR-positive, HER2-negative breast cancer.

Etcamah has demonstrated anti-cancer activity across a range of preclinical models, including those with ER-activating mutations. In the SERENA-2 Phase II trial, camizestrant demonstrated a statistically significant and clinically meaningful improvement in PFS versus *Faslodex* (fulvestrant) in the overall trial population, including in patients with *ESR1* tumour mutations irrespective of prior treatment with CDK4/6 inhibitors in patients with ER-positive locally advanced or metastatic breast cancer, previously treated with endocrine therapy. The SERENA-1 Phase I trial demonstrated that camizestrant is well tolerated and has a promising anti-tumour profile when administered alone or in combination with palbociclib, ribociclib and abemaciclib; three widely used CDK4/6 inhibitors.

AstraZeneca in breast cancer
Driven by a growing understanding of breast cancer biology, AstraZeneca is challenging, and redefining, the current clinical paradigm for how breast cancer is classified and treated to deliver even more effective treatments to patients in need - with the bold ambition to one day eliminate breast cancer as a cause of death.

AstraZeneca has a comprehensive portfolio of approved and promising compounds in development that leverage different mechanisms of action to address the biologically diverse breast cancer tumour environment.

With *Enhertu* (trastuzumab deruxtecan), a HER2-directed antibody drug conjugate (ADC), AstraZeneca and Daiichi Sankyo are aiming to improve outcomes in previously treated HER2-positive, HER2-low and HER2-ultralow metastatic breast cancer and are exploring its potential in earlier lines of treatment and in new breast cancer settings.

In HR-positive breast cancer, AstraZeneca continues to improve outcomes with foundational medicines *Faslodex* and *Zoladex* (goserelin) and aims to reshape the HR-positive space with first-in-class AKT inhibitor, *Truqap* (capivasertib), the TROP-2-directed ADC, *Datroway* (datopotamab deruxtecan) and next-generation oral SERD, *Etcamah*.

PARP inhibitor *Lynparza* (olaparib) is a targeted treatment option that has been studied in early and metastatic breast cancer patients with an inherited *BRCA* mutation. AstraZeneca with MSD (Merck & Co., Inc. in the US and Canada) continue to research *Lynparza* in these settings. AstraZeneca is also exploring the potential of saruparib, a potent and selective inhibitor of PARP1, in combination with *Etcamah* in *BRCA*-mutated, HR-positive, HER2-negative advanced breast cancer.

To bring much-needed treatment options to patients with triple-negative breast cancer, an aggressive form of breast cancer, AstraZeneca is collaborating with Daiichi Sankyo to evaluate the potential of *Datroway* alone and in combination with immunotherapy *Imfinzi* (durvalumab).

AstraZeneca in oncology
AstraZeneca is leading a revolution in oncology with the ambition to provide cures for cancer in every form, following the science to understand cancer and all its complexities to discover, develop and deliver life-changing medicines to patients.

The Company's focus is on some of the most challenging cancers. It is through persistent innovation that AstraZeneca has built one of the most diverse portfolios and pipelines in the industry, with the potential to catalyse changes in the practice of medicine and transform the patient experience.

AstraZeneca has the vision to redefine cancer care and, one day, eliminate cancer as a cause of death.

AstraZeneca
AstraZeneca (LSE/STO/NYSE: AZN) is a global, science-led biopharmaceutical company that focuses on the discovery, development, and commercialisation of prescription medicines in Oncology, Rare Disease, and BioPharmaceuticals, including Cardiovascular, Renal & Metabolism, and Respiratory & Immunology. Based in Cambridge, UK, AstraZeneca's innovative medicines are sold in more than 125 countries and used by millions of patients worldwide. Please visit astrazeneca.com and follow the Company on Social Media @AstraZeneca.

Contacts
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