Report LENVIMA® lenvatinib - EC

Product & Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
Substance: lenvatinib **Brand Name:** Lenvima **Originator/licensee:** Eisai GmbH **Classification:** NI **ATC code:** L01EX08 **Orphan Status:** **Eu:** No **Us:** No **Mechanism of action:** Lenvatinib is a RTK inhibitor that selectively inhibits the activities of VEGF receptor kinase VEGFR1 (FLT1), VEGFR2 (KDR) and VEGFR3 (FLT4), in addition to other RTKs related to proangiogenic and oncogenic agents, including FGF receptors FGFR1, 2, 3, 4, PDGFRα, KIT and RET [1].	**Authorized Indication:** **EMA:** lenvatinib, in combination with pembrolizumab, is indicated for the treatment of adult pts with advanced or recurrent EC who have disease progression on or following prior treatment with a platinum-containing therapy in any setting and are not candidates for curative surgery or radiation. [2]. **FDA**: lenvatinib, in combination with pembrolizumab, is indicated for the treatment of pts with advanced EC that is not MSI-H or dMMR, who have disease progression following prior systemic therapy and are not candidates for curative surgery or radiation [1]. **Route of administration:** os **Licensing status** **EU CHMP P.O. date:** 14/10/2021 **FDA M.A. date:** 17/09/2019 **EU Speed Approval Pathway:** Yes **FDA Speed Approval Pathway:** Yes --- **ABBREVIATIONS:** **CHMP:** Commettee for Medicinal Products for Human Use **EC**: Endometrial Cancer **dMMR:** Mismatch Repair Deficient **FGF:** Fibroblast Growth Factor **FGFR**: Fibroblast Growth Factor Receptor **MA:** Marketing Authorization **MSI-H:** Microsatellite Instability-High **os**: Oral Administration **OS**: Overall Survival **PDGFRα**: Platelet Derived Growth Factor Receptor Alpha **PFS**: Progression Free Survival **PO**: Positive Opinion **pts**: Patients **RTK**: Tyrosine Kinase Receptor **TPC**: Treatment of Physician's Choice **TRAEs:** Treatment Related Adverse Events **VEGF**: Vascular Endothelial Growth Factor **VEGFR**: Vascular Endothelial Growth Factor Receptor **vs**.: Versus	**Summary of clinical EFFICACY:** **Study KEYNOTE-775/Study 309 (NCT03517449):** multicenter, randomized, open-label, active-controlled phase III trial designed to evaluate the investigational use of pembrolizumab in combination with lenvatinib for the treatment of advanced EC, following at least one prior platinum-based regimen. Pts (*n*=827) were randomized 1:1 to receive either pembrolizumab 200 mg by IV infusion on Day one of each 21-day cycle plus lenvatinib 20 mg orally QD during each 21-day cycle for up to 35 cycles (*n*=411), or TPC of either doxorubicin at 60 mg/m^2 dose by IV every three weeks for up to a maximum cumulative dose of 500 mg/m^2 or paclitaxel at a 80 mg/m^2 dose by IV on a 28-day cycle (*n*=416). The dual primary endpoints were OS and PFS. Pembrolizumab and lenvatinib reduced the risk of disease progression or death by 44% (HR=0.56 [95% CI: 0.47-0.66]; p<0.0001), with a median PFS of 7.2 months (95% CI: 5.7-7.6; number of events=281) vs. 3.8 months (95% CI: 3.6-4.2; number of events=286) for pts who received TPC. Additionally, pembrolizumab and lenvatinib reduced the risk of death by 38% (HR=0.62 [95% CI: 0.51-0.75]; p<0.0001), with a median OS of 18.3 months (95% CI: 15.2-20.5; number of events=188) vs. 11.4 months (95% CI: 10.5-12.9; n. of events=245) for pts who received TPC [4]. **Summary of clinical SAFETY:** Any-grade TEAEs occurred in all pts in the experimental arm vs. 98% in the comparator arm. The most common (≥25% of pts) TEAEs of any grade in the pembrolizumab + lenvatinib arm were: hypertension (64% vs. 5%), hypothyroidism (57% vs. 1%), diarrhoea (54% vs. 19%), nausea (50% vs. 46%), decreased appetite (45% vs. 21%), vomiting (37% vs. 20%), weight decrease (34% vs. 6%), fatigue (33% vs. 28%), arthralgia (31% vs. 8%), proteinuria (29% vs. 3%), anemia (26% vs. 47%), constipation (26% vs. 25%) and urinary tract infections (26% vs. 10%). Grade 3 TRAEs occurred in 89% of pts in the pembrolizumab + lenvatinib arm vs. 73% of pts in the TPC arm. Grade 5 TEAEs of any cause occurred in 6% of pts in the experimental vs. 5% in the TPC arm. Death occurred in 184 (45%) pts in the experimental arm vs. 236 (61%) in the TPC arm [4]. **Ongoing studies:** ● ***For the same indication:*** Yes ● ***For other indications:*** Yes **Discontinued studies (for the same indication):** Yes --- **References:** 1.https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/206947s011lbl.pdf 2.https://www.ema.europa.eu/en/medicines/human/summaries-opinion/lenvima 3.https://clinicaltrials.gov/ct2/show/results/NCT03517449?term=NCT03517449&draw=2&rank=1&view=results 4. https://gallery.farmadati.it/Home.aspx 5. https://www.aiom.it/i-numeri-del-cancro-in-italia/ 6. https://clinicaltrials.gov/ct2/home	**Cost of therapy:** The Italian price for a three-week cycle with lenvatinib 20 mg is 5,585.18 €* [4]. **Retail price including VAT* **Epidemiology:** In Italy, there were an estimated 8,300 new cases of EC in 2020 (slightly less than 5% of all female cancers. It is the third most common malignancy in women in the 50-69 age group) [5]. --- **POSSIBLE PLACE IN THERAPY** The first-line treatment for advanced/metastatic EC is represented by the combination of carboplatin and paclitaxel. In pts progressing to the first-line there is no defined standard of second-line: the most active drugs are represented by doxorubicin and weekly paclitaxel. The combination of lenvatinib and pembrolizumab has recently been shown to increase PFS and OS compared with chemotherapy in the second-line treatment after platinum of endometrial cancers without MSI [5]. **OTHER INDICATIONS IN DEVELOPMENT:** Yes (Adenocarcinoma, Adrenal Cancer, Biliary Cancer, Gastrointestinal Cancer) [6]. **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT:** No [6]. **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION:** Yes **(**Atezolizumab, Abemaciclib + Letrozolo) [6]. *Service reorganization Y/N: No *Possible off label use Y/N: Yes

Issued on: 15/11/2021