Report CABOMETYX® - Cabozantinib

Product & Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
Substance: Cabozantinib **Brand Name:** Cabometyx **Originator/licensee:** Ipsen Pharma **Classification:** NI **ATC code:** L01EX07 **Orphan Status:** **Eu:** No **Us:** Yes **Mechanism of action:** Cabozantinib is a tyrosine kinase inhibitor. It blocks the activity of enzymes known as tyrosine kinases. These enzymes can be found in certain receptors in cancer cells, where they are involved in activating processes that include cell division and the growth of new blood vessels to supply the cancer. By blocking the activity of these enzymes in cancer cells, the medicine reduces the growth and spread of the tumor[1].	**Authorized Indication:** **EMA**: Cabozantinib is indicated for the treatment of adults with unresectable or metastatic, well differentiated epNET and pNET who have progressed following at least one prior systemic therapy other than somatostatin analogues [1]. **FDA:** Cabozantinib is indicated for the treatment of adult and pediatric pts. ≥12 years of age with previously treated, unresectable, locally advanced or metastatic, well-differentiated pNET and epNET [2]. **Route of administration:** OS **Licensing status** **EU CHMP P.O. date:** 19/06/2025 **FDA M.A. date:** 26/03/2025 **EU Speed Approval Pathway:** Yes **FDA Speed Approval Pathway:** Yes --- **ABBREVIATIONS:** **AE**: Adverse Event **BICR**: Blinded independent central review **CHMP**: Committee for Medicinal Products for Human Use **CI**: Confidential Interval **ECOG**: Eastern Cooperative Oncology Group **epNET**: Extra-pancreatic neuroendocrine tumours **HR**: Hazard Ratio **M.A.**: Marketing Authorization **OS**: Oral administration **PFS**: Progression-Free Survival **PI**: Proteasome inhibitor **pNET**: Pancreatic neuroendocrine tumours **PO**: Positive Opinion **PS**: Performance Status **Pts**: Patients **RECIST**: Response Evaluation Criteria in Solid Tumours **SAE**: Serious adverse events **TRAE**: Treatment related AE **WHO**: World Health Organization	**Summary of clinical EFFICACY:** **CABINET (NCT03375320)** was a multicentre, double-blind, randomized, controlled, phase III trial in pts. with progressive epNET or pNET. Eligible pts. were aged ≥18 years with histologically confirmed, locally advanced or metastatic well- or moderately differentiated epNET or pNET and WHO tumour grade of 1 to 3. Pts. had to have progressive disease according to RECIST v1.1 and ECOG PS score of 0 to 2. Pts. were required to have disease progression after prior treatment with ≥1 FDA approved therapy (everolimus or lutetium Lu 177 dotatate for pts. with epNET; everolimus, sunitinib or lutetium Lu 177 dotatate for pts. with pNET), other than somatostatin analogues. Pts. were enrolled in two independent cohorts: those with epNET (n=203) and those with pNET (n=95). Pts. were randomly assigned in a 2:1 ratio to receive cabozantinib 60 mg orally once daily or placebo. Randomization was stratified according to concurrent somastatin analogue use and primary tumour site in the epNET cohort and according to concurrent somastatin analogue use and previous sunitinib therapy in pNET cohort. The primary endpoint was PFS as assessed by BICR according to RECIST v1.1 in the ITT. In the epNET cohort, 134 pts. received cabozantinib and 69 were allocated in the placebo arm. After a median follow-up of 10.2 months, the median PFS with cabozantinib was 8.4 months vs 3.9 months with placebo (stratified HR for progression or death, 0.38; 95% CI 0.25 to 0.59; P<0.001). In the pNET cohort, 64 pts. received cabozantinib and 31 placebo. After a median follow-up of 13.8 months, the median PFS was 13.8 months with cabozantinib and 4.4 with placebo (HR for disease progression or death, 0.23 (95% CI, 0.12–0.42) P<0.001 by log-rank test) [3]. **Summary of clinical SAFETY:** The safety population in the epNET cohort consisted of 132 pts., who were treated with cabozantinib and 67, who received placebo. The incidence of AEs was 98% in the cabozantinib arm and 82% in the placebo arm, with an incidence of grade ≥3 TRAEs of 62% with cabozantinib and 27% with placebo. The most common grade 3 or 4 TRAE with cabozantinib were hypertension (in 21% of the pts.), fatigue (in 13%), and diarrhoea (in 11%). Grade 5 events occurred in nine pts. (7%) in the cabozantinib group and four pts. (6%) in the placebo group. Four pts. in the cabozantinib group had a grade 5 event that was deemed to be at least possibly related to treatment — gastric haemorrhage in one pt., cardiac arrest in one pt., and cause of death not specified in two pts. The safety population in the pNET cohort consisted of 63 pts., who were treated with cabozantinib and 31, who received placebo. The incidence of AEs any grade attributed to cabozantinib was 98% and to placebo was 84%, with an incidence of grade 3 or 4 TRAEs of 65% with cabozantinib and 23% with placebo. The most common grade 3 or 4 TRAEs with cabozantinib were hypertension (in 22% of the pts.), fatigue (in 11%), and thromboembolic events (in 11%). No grade 5 events were noted in the pNET cohort. **Ongoing studies:** ● ***For the same indication:*** Yes ● ***For other indications:*** Yes **Discontinued studies (for the same indication):** No --- **References:** [1] https://www.ema.europa.eu/en/medicines/human/EPAR/cabometyx [2] https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/208692s017lbl.pdf [3] https://www.nejm.org/doi/full/10.1056/NEJMoa2403991 [4] https://gallery.farmadati.it/ [5] https://bmccancer.biomedcentral.com/articles/10.1186/s12885-019-6412-8 [6] https://link.springer.com/chapter/10.1007/978-3-662-45215-8_3 [7] https://www.sciencedirect.com/science/article/pii/S0923753420363948?via%3Dihub	**Cost of therapy:** In Italy, 30 tablets of CABOMETYX® 20 mg cost € 5,821.13 (ex-factory price) [4]. **Epidemiology:** NETs are considered rare tumours, responsible for approximately 0.5% of all cancers. The estimated incidence is 1-5 per 100,000 inhabitants. Gastrointestinal tract is the most common site and is responsible for two-thirds of NETs [5,6]. --- **POSSIBLE PLACE IN THERAPY**: For pts. with well differentiated NET the first line treatment is represented by surgery, in case of local or locoregional disease. When surgery is not indicated, systemic therapy can be considered to control the tumour-associated clinical symptoms and the tumour growth. Somatostatin analogues are an anti-proliferative therapy in metastatic NETs. Other treatments include mTOR inhibitors (everolimus), RTK inhibitors (sunitinib), chemotherapy or radiotherapy [7]. The addition of Cabozantinib to these regimens could represent a new opportunity for these pts. **OTHER INDICATIONS IN DEVELOPMENT:** Differentiated Thyroid Cancer (NCT03690388); Advanced Medullary Thyroid Cancer (NCT00704730); Prostate Cancer (NCT01605227, NCT01522443); NSCLC (NCT04471428). **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT**: - **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION:** Surufatinib (NCT02589821). *Service reorganization: No *Possible off label use: Yes

Issued in June 2025