vandetanib (Caprelsa®)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO223

Description

Vandetanib (Caprelsa) is an orally administered kinase inhibitor, with activity at VEGF, EGFR, and RET kinases.

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity Limits

Product Name	Dosage Form	Indication	Quantity Limit
vandetanib (Caprelsa)	100 mg tablets	Locally advanced or metastatic medullary thyroid cancer	60 tablets/30 days
	300 mg tablets		30 tablets/30 days

Initial Evaluation

I. Vandetanib (Caprelsa) may be considered medically necessary when the following criteria are met:
   A. Member is 18 years of age or older; **AND**
   B. Medication is prescribed by, or in consultation with, an oncologist or endocrinologist; **AND**
   C. A diagnosis of **unresectable locally advanced or metastatic (stage III or IV) medullary thyroid cancer** when the following is met:
      1. Medication is not used in combination with any other oncology therapy.

II. Vandetanib (Caprelsa) is considered investigational when used for all other conditions, including but not limited to:
   A. Anaplastic Thyroid Carcinoma
   B. Biliary tract cancer
   C. Breast cancer
   D. Follicular Thyroid Carcinoma
   E. Glioblastoma
   F. Ovarian cancer
   G. Renal cell carcinoma
   H. Urothelial cancer
   I. Non-small cell lung cancer

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. Initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Medication is prescribed by, or in consultation with, an oncologist or endocrinologist; **AND**
IV. Will not be used with any other oncology therapy; **AND**
V. Disease response to treatment defined by stabilization of disease or decrease in tumor size or tumor spread.

Supporting Evidence

I. Vandetanib (Caprelsa) is a kinase inhibitor with activity at multiple kinases. *In vitro* studies show that vandetanib (Caprelsa) inhibits the activity of epidermal growth factor receptor (EGFR) family, vascular endothelial growth factor (VEGF) receptors, rearranged during transfection (RET), protein tyrosine kinase 6, TIE2, members of the EPH receptors kinase family, and members of the Src family of tyrosine kinases. In mouse models, vandetanib (Caprelsa) reduced tumor cell growth and metastasis.
II. Vandetanib (Caprelsa) was studied in a Phase 3, double blind, placebo controlled, randomized trial (ZETA) in 331 patients with symptomatic or progressive unresectable locally advanced or metastatic medullary thyroid cancer. There is currently no evidence that it is safe and effective in treating other types of cancer.
III. The ZETA trial evaluated treatment with vandetanib (Caprelsa) as monotherapy versus placebo. Patients in the trial had either hereditary, sporadic, or unknown, or metastatic disease type. Fifty nine percent of patients had a RET positive mutation while 40% had unknown RET mutation. Patients were excluded from treatment if they had significant cardiac, hematopoietic, hepatic, or renal dysfunction, were treated with chemotherapy and/or radiation therapy within four weeks of treatment with vandetanib (Caprelsa) or were taking any concomitant medications that may have affected QTc or induced CYP3A4 function.
IV. The primary endpoint evaluated in the ZETA trial was progression free survival (PFS). There was a statistically significant improvement in PFS for patients randomized to vandetanib (Caprelsa). The number of events in vandetanib (Caprelsa) arm was 59 (26%) and 41 (41%) in the placebo arm with a Hazard Ratio (HR) = 0.35; 95% Confidence Interval (CI) = 0.24-0.53; p<0.001. The median survival in months for the placebo arm was 16.4 while for the vandetanib (Caprelsa) arm the median survival was not reached at the time of analysis;, however, the predicted median

survival was 30.5 months. The mature data for overall survival (OS) was studied as a secondary endpoint and was similar between both treatment arms at 81.6 months for vandetanib (Caprelsa) and 80.4 months for placebo arm. However, OS survival data was not powered and was confounded by patients from the placebo arm that were eligible to start treatment with vandetanib (Caprelsa) after conclusion of the study. Other secondary endpoints evaluated included objective response rate (ORR) and disease control rate, both of which reached statistical significance when compared to placebo. Quality of life and pain reduction outcomes were not reported or could not be evaluated.

V. Fifty-five percent (55%) of the patients on the vandetanib (Caprelsa) arm experienced grade 3 or 4 adverse events. Adverse reactions resulting in death occurred in five patients treated with vandetanib (Caprelsa) due to respiratory failure, respiratory arrest, aspiration pneumonia, cardiac failure with arrhythmia, and sepsis. Causes of discontinuation in vandetanib (Caprelsa)-treated patients in >1 patient included asthenia, fatigue, rash, arthralgia, diarrhea, hypertension, prolonged QT interval, increase in creatinine, and pyrexia. Serious adverse events in vandetanib (Caprelsa) treated patients in >2% of patients included diarrhea, pneumonia, and hypertension. Patients receiving vandetanib (Caprelsa) experienced a mean prolongation of their QT interval of 35ms, and sudden death and torsades des pointes have been observed with vandetanib (Caprelsa). A Risk Evaluation and Mitigation Strategy (REMS) is used to decrease the risk of these adverse events.

VI. Vandetanib (Caprelsa) has a Category 1 recommendation by the National Comprehensive Cancer Network (NCCN) guidelines for the treatment of recurrent or persistent medullary thyroid carcinoma and joins cabozantinib (Cabometyx) and selpercatinib (Retevmo) in the list of preferred systemic regimens. It is also recommended as the first line treatment option by the American Thyroid Association Guidelines. Vandetanib (Caprelsa) should be prescribed in consultation with, or by, an oncologist or endocrinologist for the treatment of symptomatic or progressive medullary thyroid cancer in patients with unresectable locally advanced or metastatic disease. Use of vandetanib (Caprelsa) in patients with indolent, asymptomatic, or slowly progressive disease should only be considered after examining the treatment related risks of this agent.

Investigational or Not Medically Necessary Uses

I. Vandetanib (Caprelsa) has not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:
   A. Anaplastic Thyroid Carcinoma
   B. Biliary tract cancer
   C. Breast cancer
   D. Follicular Thyroid Carcinoma
   E. Glioblastoma

F. Ovarian cancer
G. Renal cell carcinoma
H. Urothelial cancer
I. Non-small cell lung cancer

References

1. Caprelsa (vandetanib) [package insert]. Cambridge, MA: Sanofi Genzyme; December 2016.
2. Wells, SA, Jr., Robinson, BG, Gagel, RF, et al. Vandetanib in patients with locally advanced or metastatic medullary thyroid cancer: a randomized, double-blind phase III trial. J Clin Oncol. 2012 Jan 10;30(2):134-41. PMID: 22025146
3. Haddad RI, Bischoff L, Bernet V, et al. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines). Thyroid Carcinoma. Available at https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf. Accessed January 3, 2021.
4. Wells SA Jr, Asa SL, Dralle H, et al. Revised American Thyroid Association guidelines for the management of medullary thyroid carcinoma. Thyroid. 2015;25(6):567-610. doi:10.1089/thy.2014.0335
5. Thornton K, Kim G, Maher VE, et al. Vandetanib for the treatment of symptomatic or progressive medullary thyroid cancer in patients with unresectable locally advanced or metastatic disease: U.S. Food and Drug Administration drug approval summary. Clin Cancer Res. 2012;18(14):3722-3730. doi:10.1158/1078-0432.CCR-12-0411

Policy Implementation/Update:

Action and Summary of Changes	Date
Policy was updated and transitioned from an old criteria to a new format Removal of criteria requirements that are managed by provider (drug-drug interactions, REMS program, monitoring of CrCl, QT prolongation, hepatic impairments, hypertension, and other aspects from labeled warnings and precautions)	02/2021
Criteria created	02/2012