PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Caprelsa® (vandetanib tablets – AstraZeneca)

DATE REVIEWED: 05/13/2020

OVERVIEW

Caprelsa is a kinase inhibitor indicated for the treatment of symptomatic or progressive medullary thyroid cancer (MTC) in patients with unresectable locally advanced or metastatic disease.[1] Due to the treatment related risks of Caprelsa, its use in patients with indolent, asymptomatic, or slowly progressing disease should be carefully considered. Caprelsa has a black box warning regarding the increased risk of QT prolongation, Torsades de pointes, and sudden death. It is available only through the restricted distribution program called the Caprelsa Risk Evaluation and Mitigation Strategy (REMS) program. Only prescribers and pharmacies certified with the program are able to prescribe or dispense Caprelsa.

Guidelines

The National Comprehensive Cancer Network (NCCN) guidelines for thyroid carcinoma (version 2.2019 – September 16, 2019) lists surgery as the main treatment option for MTC.[2-3] For *locoregional* , recurrent or persistent disease, or for distant metastases Caprelsa (category 1) or Cometriq™ (cabozantinib capsules) (category 1) are recommended for unresectable locoregional disease that is symptomatic or structurally progressive. The guidelines recommend that Caprelsa be considered if clinical trials or other systemic therapies are not available or appropriate for the treatment of progressive and/or symptomatic iodine refractory thyroid cancer that is unresectable recurrent or persistent locoregional disease or that is distant metastatic disease.[2-3] This recommendation is for follicular, Hürthle cell, and papillary cancer subtypes (all category 2A).

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Caprelsa. All approvals are provided for the duration noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Caprelsa is recommended in those who meet the following criteria:

Food and Drug Administration (FDA)-Approved Indications

1. **Medullary Thyroid Cancer (MTC).** Approve for 3 years.

Other Uses with Supportive Evidence

2. **Differentiated (i.e., papillary, follicular, and Hürthle) Thyroid Carcinoma.** Approve for 3 years if the disease is refractory to radioactive iodine therapy.

3. **Non-Small Cell Lung Cancer with RET Gene Rearrangements.** Approve for 3 years.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Caprelsa has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. **Non-Small Cell Lung Cancer (NSCLC) [Without RET Gene Rearrangements].** The efficacy of Caprelsa for the treatment of NSCLC was evaluated in four Phase III studies; three of these studies did not show any statistically significant improvement with Caprelsa with regards to progression free survival (PFS) or overall survival. In the ZEST (Zactima Efficacy Study versus Tarceva) study, Caprelsa was compared with Tarceva® (erlotinib tablets) in patients (n = 1,240) with advanced NSCLC who have had treatment failure with one or two prior cytotoxic chemotherapy regimens.[6] There was no significant improvement in PFS in patients treated with Caprelsa vs. Tarceva (median PFS 2.6 months vs. 2.0 months, respectively; P = 0.721). In the second Phase III study (ZEPHYR), Caprelsa was assessed for overall survival benefit in patients with locally advanced or metastatic NSCLC who have had treatment failures with one or two previous chemotherapy regimens, including an EGFR tyrosine kinase inhibitor.[7] Patients (n = 924) were randomized 2:1 to receive either Caprelsa 300 mg/day or placebo. There was no statistically significant difference in the primary end point of overall survival in patients receiving Caprelsa or placebo. The median overall survival was 8.5 months for Caprelsa and 7.8 months with placebo (P = 0.527). The estimated percentage of patients alive after 1 year was 35.5% vs. 31.7% for Caprelsa and placebo, respectively. In the ZODIAC (Zactima in cOmbination with Docetaxel In non-smAll cell lung Cancer) Phase III study, Caprelsa in combination with docetaxel was compared with placebo and docetaxel in patients (n = 1,391) with locally advanced or metastatic NCSLC after progression following platinum-based first-line chemotherapy.[8] PFS was statistically significant in the Caprelsa group compared with the placebo group for the overall population (median PFS 4.0 months with Caprelsa vs. 3.2 months with placebo; P < 0.0001). There were no significant differences between the two groups for the secondary endpoint of overall survival. In the ZEAL (Zactima Efficacy with Alimta in Lung cancer) study the efficacy of Caprelsa was assessed in combination with Alimta® (pemetrexed disodium injection) for the second-line treatment of patients with advanced NSCLC.[9] The primary efficacy endpoint of PFS was not statistically significantly different between the treatment groups. The median PFS was 17.6 weeks for Caprelsa and 11.9 weeks for placebo (P = 0.108). There were also no significant differences between the two groups for overall survival.

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Caprelsa® [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; July 2016.
2. The NCCN Thyroid Carcinoma Clinical Practice Guidelines in Oncology (Version 2.2019 – September 16, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed May 11, 2020.
3. The NCCN Drugs and Biologics Compendium. © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed May 11, 2020. Search term: vandetanib.
4. Natale RB, Thongprasert S, Greco FA, et al. Phase III trial of vandetanib compared with erlotinib in patients with previously treated advanced non-small-cell lung cancer. *J Clin Oncol.* 2011;29:1059-1066.

5. Lee JS, Hirsh V, Park K, et al. Vandetanib versus placebo in patients with advanced non-small-cell lung cancer after prior therapy with an epidermal growth factor receptor tyrosine kinase inhibitor: a randomized, double-blind Phase III trial (ZEPHYR). *J Clin Oncol.* 2012;30:1114-1121.
6. Herbst RS, Sun Y, Eberhardt WEE, et al. Vandetanib plus docetaxel versus docetaxel as second-line treatment for patients with advanced non-small-cell lung cancer (ZODIAC): a double-blind, randomised, phase 3 trial. *Lancet Oncol.* 2010;11:619-626.
7. De Boer RH, Arrieta O, Yang CH, et al. Vandetanib plus pemetrexed for the second-line treatment of advanced non-small-cell lung cancer: a randomized, double-blind phase III trial. *J Clin Oncol.* 2011;29:1067-1074.