

## PRIOR AUTHORIZATION POLICY

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

**TAC APPROVAL DATE:** 04/17/2019

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### 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.<sup>1</sup> 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 1.2019 – March 28, 2019) lists surgery as the main treatment option for MTC.<sup>2-3</sup> Postoperative levothyroxine is recommended in all patients to normalize thyroid stimulating hormone (TSH) levels. For recurrent or persistent disease after surgery, the choice of therapy is as follows: for *locoregional* disease, surgical resection is the preferred treatment modality. Caprelsa (category 1) or Cometriq™ (cabozantinib capsules) [category 1] are recommended for unresectable locoregional disease that is symptomatic or structurally progressive. For recurrent or persistent *symptomatic disease* with distant metastases, the guidelines recommend the following treatment options: 1) Caprelsa [category 1]; 2) Cometriq [category 1]; 3) clinical trial; 4) consider other small molecule kinase inhibitors (Nexavar® [sorafenib tablets], Sutent® [sunitinib capsules], Lenvima™ [lenvatinib capsules] or Votrient® [pazopanib tablets] ) if clinical trials, Caprelsa or Cometriq are not available or appropriate, or if the patient progresses on Caprelsa or Cometriq; or 5) dacarbazine-based systemic chemotherapy. Kinase inhibitor therapy may not be appropriate for patients with stable or slowly progressive indolent disease. The guidelines and compendium recommend the use of Caprelsa for differentiated thyroid carcinoma, along with several other small molecule inhibitors, if clinical trials are not available or appropriate.

### 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<sup>®</sup> (erlotinib tablets) in patients (n = 1,240) with advanced NSCLC who have had treatment failure with one or two prior cytotoxic chemotherapy regimens.<sup>6</sup> 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.<sup>7</sup> 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 NSCLC after progression following platinum-based first-line chemotherapy.<sup>8</sup> 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<sup>®</sup> (pemetrexed disodium injection) for the second-line treatment of patients with advanced NSCLC.<sup>9</sup> 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 1.2019 – March 28, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed April 15, 2019.
3. The NCCN Drugs and Biologics Compendium. © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed April 15, 2019. 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.

## HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
Annual revision	Approval for differentiated thyroid carcinoma added under Other Uses with Supportive Evidence based on NCCN guidelines.	03/04/2015
Annual revision	Changed Medullary and differentiated thyroid carcinoma criteria to make it simpler and to be consistent with other policies.	03/16/2016
Annual revision	Added new approval indication for Non-Small Cell Lung Cancer with RET Gene Rearrangements based on guidelines. Added clarification to Non-Small Cell Lung Cancer under “Conditions Not Recommended for Approval” that it applies to patients “(Without RET Gene Rearrangements)”.	03/15/2017
Annual revision	Deleted the following conditions from Conditions Not Recommended for Approval section due to lack of data in past few years: breast cancer, hepatocellular cancer, ovarian cancer, prostate cancer, and urothelial cancer.	04/11/2018
Annual revision	No criteria changes	04/17/2019

TAC – Therapeutic Assessment Committee; DEU – Drug Evaluation Unit; \* For a summary of criteria changes, refer to respective TAC minutes available at: <http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx>.