EXPRESS SCRIPTS®

PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Zykadia™ (ceritinib capsules – Novartis Pharmaceuticals)

TAC APPROVAL DATE: 05/23/2018

OVERVIEW

Zykadia, a kinase inhibitor, is indicated for the treatment of patients with anaplastic lymphoma kinase (*ALK*)-positive metastatic non-small cell lung cancer (NSCLC), as detected by an FDA-approved test.[1] Using biochemical or cellular assays at clinically relevant concentrations, it has been noted that Zykadia inhibits *ALK*, insulin-like growth factor 1 receptor (IGF-1R), insulin receptor (InsR), and c-ros oncogene 1 (ROS1). Among these, Zykadia is most effective against *ALK*.

GUIDELINES

According to the National Comprehensive Cancer Network (NCCN) NSCLC guidelines (version 4.2018), Xalkori® (crizotinib capsules), Zykadia, and Alecensa® (alectinib capsules) [preferred] are the recommended first-line therapies for ALK-positive NSCLC (all category 1).[2] For subsequent therapy with progression on Xalkori, local therapy can be considered, Xalkori can be continued, or therapy can be switched to Zykadia, (if not previously given) Alecensa (if not previously given), or Alunbrig™ (brigatinib tablets) [category 2A] for asymptomatic progression or symptomatic progression to the brain. If there is rapid radiographic progression or threatened organ function, continuing Xalkori therapy is not recommended and instead alternate therapies should be considered. The guidelines also refer to NCCN guidelines for CNS Cancers for additional therapies. For symptomatic progression with systemic isolated lesion, local therapy can be considered in addition to continuing Xalkori. For multiple systemic lesions, Zykadia (if not previously given and progression on Xalkori initial therapy), Alecensa (if not previously given and progression on Xalkori initial therapy), or Alunbrig (all category 2A) are recommended or other cytotoxic therapy options (i.e., chemotherapy) can be used. For progression on Alecensa or Zykadia, local therapy should be considered along with continuing Zykadia or Alecensa (category 2A) if it is asymptomatic or symptomatic progression to brain or if it is an isolated lesion. For multiple systemic lesions, initial cytotoxic therapy options for adenocarcinoma or squamous cell carcinoma should be considered (category 2A). Xalkori or Zykadia are recommended as first-line therapy for ROS1 rearrangement-positive NSCLC (both category 2A). Of the two choices, Xalkori is preferred. Xalkori is also recommended as an emerging targeted therapy in patients with high level *MET* amplification or *MET* exon 14 skipping mutation in lung cancer (category 2A).

POLICY STATEMENT

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

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indications

1. **Non-Small Cell Lung Cancer (NSCLC).** Approve for 3 years if the patient has metastatic anaplastic lymphoma kinase (*ALK*)-positive NSCLC as detected by an approved test.

Other Uses with Supportive Evidence

2. **Non-Small Cell Lung Cancer (NSCLC) with ROS1 Rearrangement – First-Line Therapy.** Approve for 3 years.

   A multicenter, open-label, Phase II study evaluated the efficacy of Zykadia in patients with ROS1-rearranged NSCLC (n = 32).[6] All patients, except two, were Xalkori treatment-naïve. Patients received Zykadia at the recommended dose of 750 mg/day. The overall objective response rate (ORR) was 62% (95% CI: 45%, 77%); in Xalkori-naïve patients the ORR was 67%. The median PFS was 9.3 months and the median PFS for Xalkori-naïve patients was 19.3 months (95% CI: 1, 37). The median OS was 24 months (95% CI: 5, 43) with a 6-month OS rate of 84% and a 12-month OS rate of 56%. Only eight patients had brain metastases at baseline. The overall intracranial ORR was 25% (n = 2/8) and the DCR was 63% (n = 5/8). The NCCN NSCLC guidelines recommend Xalkori (preferred) or Zykadia as first-line options for ROS1-positive NSCLC (both category 2A).

3. **Soft Tissue Sarcoma Inflammatory Myofibroblastic Tumor (IMT) with ALK Translocation.** Approve for 3 years.

   The NCCN guidelines for soft tissue sarcoma (version 2.2018) recommend Zykadia as a single-agent therapy for the treatment of IMT with ALK translocation (category 2A recommendation).[4-5]

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Zykadia 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. 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. Zykadia™ [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals; December 2017.
2. The NCCN Non-Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (Version 4.2018). © 2018 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on May 18, 2018.
3. Soria JC, Tan DSW, Chiari R, et al. First-line ceritinib versus platinum-based chemotherapy in advanced ALK-rearranged non-small-cell lung cancer (ASCEND-4): a randomized, open-label, Phase 3 study. *Lancet.* 2017;389:917-929.
4. The NCCN Soft Tissue Sarcoma Clinical Practice Guidelines in Oncology (version 2.2018). ©2018 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on May 18, 2018.
5. The NCCN Drugs & Biologics Compendium. © 2018 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on May 18, 2018. Search terms: ceritinib.

6. Lim SM, Kim HR, Lee JS, et al. Open-label, multicenter, Phase II study of ceritinib in patients with non-small cell lung cancer harboring ROS1 rearrangement. *J Clin Oncol*. 2017;35:2613-2618.

HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
Annual revision	No criteria changes	06/17/2015
Annual revision	Added new approval criteria under Other Uses with Supportive Evidence in patients with soft tissue sarcoma inflammatory myofibroblastic tumor with ALK translocation based on NCCN soft tissue sarcoma guidelines.	07/13/2016
Selected revision	Added new approval criteria under Other Uses with Supportive Evidence for Zykadia use in the first-line setting. Deleted Non-Small Cell Lung Cancer ALK-positive, Xalkori treatment-naïve from Conditions Not Recommended for Approval.	04/05/2017
Early annual revision	Zykadia has FDA approval in first-line use. Deleted all criteria for "After Xalkori Therapy". Also deleted wording "First-Line Therapy" since it's not needed.	06/07/2017
Selected revision	Added approval criteria for ROS1 positive non-small cell lung cancer based on guideline recommendations under Other Uses with Supportive Evidence. Deleted NSCLC - ALK status is negative or unknown from Conditions Not Recommended for Approval since patients without ALK positive or ROS1 testing would not get approval anyways based on current criteria.	01/17/2018
Annual revision	No criteria changes	05/23/2018

TAC – Therapeutic Assessment Committee; * For a further summary of criteria changes, refer to respective TAC minutes available at: http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx; ALK – Anaplastic lymphoma kinase; NCCN – National Comprehensive Cancer Network; NSCLC – Non-small cell lung cancer.