RXADVANCE
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Clinical Policy Title:	ceritinib
Policy Number:	RxA.582
Drug(s) Applied:	Zykadia®
Original Policy Date:	03/06/2020
Last Review Date:	12/07/2020
Line of Business Policy Applies to:	All lines of business

Background

Ceritinib (Zykadia®) is a tyrosine kinase inhibitor. Ceritinib is indicated for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
ceritinib (Zykadia®)	ALK-positive NSCLC	450 mg PO once daily	450 mg/day

Dosage Forms

- Tablets and Capsules: 150 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

I. Initial Approval Criteria

A. Non-Small Cell Lung Cancer (must meet all):

1. Diagnosis of recurrent, advanced or metastatic NSCLC;
2. Prescribed by or in consultation with an oncologist;
3. Age 18 years of age or older;
4. Meets one of the following (a or b):
   a. Disease is ALK positive;
   b. Disease is ROS1 positive and Zykadia® is prescribed as first-line therapy;
5. Request meets one of the following (a or b):
   a. Dose does not exceed 450 mg per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence)*.

Approval Duration

Commercial: 6 months

Medicaid: 6 months
HIM: 6 months

B. Inflammatory Myofibroblastic Tumor (off-label) (must meet all)**:**

1. Diagnosis of inflammatory myofibroblastic tumor (a soft tissue sarcoma);
2. Prescribed by or in consultation with an oncologist;
3. Age 18 years of age or older;
4. Disease is ALK positive;
5. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence)*.

Approval Duration
Commercial: 6 months
Medicaid: 6 months
HIM: 6 months

II. Continued Therapy Approval

A. All Indications in Section I (must meet all):

1. Currently receiving medication that has been authorized by RxAdvance, or documentation supports that member is currently receiving Zykadia® for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):
    a. New dose does not exceed 450 mg per day;
    b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence)*.

Approval Duration
Commercial: 12 months
Medicaid: 12 months
HIM: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
ALK: anaplastic lymphoma kinase
FDA: Food and Drug Administration
NCCN: National Comprehensive Cancer Network
NSCLC: non-small cell lung cancer
ROS1: ROS proto-oncogene 1

APPENDIX B: Therapeutic Alternatives
Not applicable

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
    - None reported

- Boxed Warning(s):

- None reported

APPENDIX D: General Information

- Targets of ceritinib inhibition identified in either biochemical or cellular assays at clinically relevant concentrations include ALK, insulin-like growth factor 1 receptor (IGF-1R), insulin receptor (InsR), and ROS1. Among these, ceritinib is most active against ALK. Ceritinib inhibited autophosphorylation of ALK, ALK-mediated phosphorylation of the downstream signaling protein STAT3, and proliferation of ALK-dependent cancer cells in in vitro and in vivo assays.
- Ceritinib inhibited the in vitro proliferation of cell lines expressing EML4-ALK and NPM-ALK fusion proteins and demonstrated dose-dependent inhibition of EML4-ALK-positive NSCLC xenograft growth in mice and rats. Ceritinib exhibited dose-dependent anti-tumor activity in mice bearing EML4-ALK-positive NSCLC xenografts with demonstrated resistance to crizotinib, at concentrations within a clinically relevant range.

References

1. Zykadia® Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; March 2019. Available at: www.zykadia.com. Accessed September 04, 2020.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed January 24, 2019.
3. National Comprehensive Cancer Network Guidelines. Non-Small Cell Lung Cancer Version 6.2020. Available at www.nccn.org. Accessed September 04, 2020.
4. National Comprehensive Cancer Network Guidelines. Central Nervous System Cancers Version 2.2020. Available at www.nccn.org. Accessed September 04, 2020.
5. National Comprehensive Cancer Network Guidelines. Soft Tissue Sarcoma Version 2.2020. Available at www.nccn.org. Accessed September 04, 2020.
6. Ceritinib, Lexi-Drug. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Accessed with subscription at: http://online.lexi.com. Accessed September 04, 2020.
7. Clinical Pharmacology [database online] powered by ClinicalKey. Tampa, FL: Elsevier, 2020. Accessed with subscription at: http://www.clinicalkey.com. Updated January 14, 2020. Accessed September 04, 2020.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Policy title table was updated: Line of business policy applies was updated to All lines of business. 2. Initial Approval Criteria A.5a was updated as "Dose does not exceed 450 mg per day". 3. Continued Therapy Approval Criteria A.3a was updated as “New dose does not exceed 450 mg per day”. 4. Continued therapy criteria II.A.1 was rephrased to “Currently receiving medication that has been authorized by RxAdvance…”. 5. Commercial approval duration was updated	09/04/2020	12/07/2020

from Length of benefit to 6 months for initial therapy, and to 12 months for continued approval criteria. 6. Appendix D was added. 7. References were updated.		