RXADVANCE
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Clinical Policy Title:	osimertinib
Policy Number:	RxA.502
Drug(s) Applied:	Tagrisso®
Original Policy Date:	03/06/2020
Last Review Date:	12/07/2020
Line of Business Policy Applies to:	All lines of business

Background

Osimertinib (Tagrisso®) is a tyrosine kinase inhibitor. It is indicated:

- For the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test.
- For the treatment of patients with metastatic EGFR T790M mutation-positive NSCLC, as detected by an FDA-approved test, whose disease has progressed on or after EGFR tyrosine kinase inhibitor (TKI) therapy.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
Osimertinib (Tagrisso®)	NSCLC	80 mg orally once daily	80 mg/day 160 mg/day when used with a strong CYP3A4 inducer

Dosage Forms

- Tablets: 40 mg, 80 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;
4. Disease is positive for either of the following (a or b):
   a. Sensitizing EGFR mutation (e.g., exon 19 deletion or insertion; exon 21 point mutation - L858R, L861Q; exon 18 point mutation - G719X; exon 20 point mutation - S768I);
   b. T790M mutation with progression on or after an EGFR TKI therapy (e.g., Tarceva®, Gilotrif®, Iressa®, Vizimpro®);

**Prior authorization may be required for EGFR TKI therapies.*

5. Dose does not exceed one of the following (a, b or c):
   a. 80 mg (1 tablet) per day;
   b. 160 mg (2 tablets) per day if co-administered with a strong CYP3A4 inducer (e.g., phenytoin, rifampin, carbamazepine, St. John's wort).
   c. 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

B. Leptomeningeal Metastases (Off-label) (must meet all)**:**

1. Diagnosis of Leptomeningeal metastases from NSCLC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Member is EGFR mutation-positive and meets one of the following (a, b or c):
   a. Tagrisso is used as primary treatment and the member has good risk status (KPS ≥60, no major neurologic deficits, minimal systemic disease, and reasonable systemic treatment options if needed);
   b. Tagrisso is used as maintenance treatment and the member has negative CSF cytology or is clinically stable with persistently positive CSF cytology;
   c. The member has positive cerebrospinal fluid (CSF) cytology that have progressed after receiving prior treatment
5. Dose does not exceed one of the following (a or b):
   a. 160 mg (2 tablets) 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

C. Brain Metastases (Off-label) (must meet all)**:**

1. Diagnosis of Brain metastases from NSCLC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. EGFR T790M mutation-positive;
5. Dose does not exceed one of the following (a, b or c):
   a. 80 mg (1 tablet) per day;
   b. 160 mg (2 tablets) per day if co-administered with a strong CYP3A4 inducer (e.g., phenytoin, rifampin, carbamazepine, St. John's wort).
   c. 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

II. Continued Therapy Approval

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

1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy, or documentation supports that member is currently receiving Tagrisso® for NSCLC 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, b or c):
   a. 80 mg (1 tablet) per day;
   b. 160 mg (2 tablets) per day if co-administered with a strong CYP3A4 inducer (e.g., phenytoin, rifampin, carbamazepine, St. John's wort).
   c. 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

B. Leptomeningeal Metastases (must meet all)(Off label use):
1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy, or documentation supports that member is currently receiving Tagrisso® for NSCLC and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. Dose does not exceed one of the following (a or b):
   a. 160 mg (2 tablets) 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: 12 months
Medicaid: 12 months

C. Brain Metastases (must meet all)(Off label use):
1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy, or documentation supports that member is currently receiving Tagrisso® for NSCLC and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. Dose does not exceed one of the following (a, b or c):
   a. 80 mg (1 tablet) per day;
   b. 160 mg (2 tablets) per day if co-administered with a strong CYP3A4 inducer (e.g., phenytoin, rifampin, carbamazepine, St. John's wort).
   c. 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

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
EGFR: epidermal growth factor receptor
FDA: Food and Drug Administration
NSCLC: non-small cell lung cancer

TKI: tyrosine kinase inhibitor

APPENDIX B: Therapeutic Alternatives

Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Gilotrif®(afatinib)	Metastatic NSCLC 40 mg orally once daily	40 mg/day; 50 mg/day when on chronic concomitant therapy with a P-glycoprotein inducer
Iressa®(gefitinib)	Metastatic NSCLC 250 mg orally, once daily	250 mg/day; 500 mg/day when used with a strong CYP3A4 inducer
Drug Name	**Dosing Regimen**	**Dose Limit/ Maximum Dose**
Tarceva® (erlotinib)	Metastatic NSCLC: 150 mg orally, on empty stomach, once daily.	150 mg/day; 450 mg/day when used with a strong CYP3A4 inducer or 300 mg/day when used with a moderate CYP1A2 inducer
Vizimpro®(dacomitinib)	Metastatic NSCLC 45 mg orally once daily	45 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None reported.

- Boxed Warning(s):
  - None reported.

APPENDIX D: General Information

- None

References

1. Tagrisso® Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP; June 2020. Available at: https://www.tagrisso.com/. Accessed December 3, 2020.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed December 3, 2020.
3. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer. Version 8.2020. Available at https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed December 3, 2020.
4. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2019. Available at: http://www.clinicalpharmacology-ip.com/. Accessed December 3, 2020.
5. Ahn M-J, Chiu C-H, Cheng Y, et al. Osimertinib for patients with leptomeningeal metastases associated with egfr t790m-positive advanced nsclc: the aura leptomeningeal metastases analysis. Journal of Thoracic

Oncology. 2020;15(4):637-648. Available at : https://www.jto.org/article/S1556-0864(19)33854-7/fulltext. Accessed December 02, 2020.
6. National Comprehensive Cancer Network. Central Nervous System Cancer. Version 3.2020. Available at https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf. Accessed December 3, 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. 2. Line of Business Policy Applies to was update to all lines of business. 3. Initial Approval criteria: Commercial approval duration was updated from length of benefit to 6 months. 4. Continued Therapy Approval criteria: Commercial approval duration was updated from length of benefit to 12 months. 5. Initial Approval criteria and Continued Therapy Approval criteria updated to include criteria for Leptomeningeal Metastases. 6. Initial Approval criteria and Continued Therapy Approval criteria updated to include criteria for Brain Metastases. 7. Continued therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance…". 8. Appendix B: Therapeutic Alternatives statement was rephrased to "Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements". 9. References were updated.	12/03/2020	12/07/2020