Clinical Policy: Osimertinib (Tagrisso)
Reference Number: CP.PHAR.294
Effective Date: 12.01.16
Last Review Date: 05.20
Line of Business: Commercial, HIM, Medicaid

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Osimertinib (Tagrisso®) is a tyrosine kinase inhibitor.

FDA Approved Indication(s)
Tagrisso 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

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

It is the policy of health plans affiliated with Centene Corporation® that Tagrisso is medically necessary when the following criteria are met:

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. Request meets one of the following (a, b or c):*
         a. Dose does not exceed 80 mg (1 tablet) per day;
         b. Dose does not exceed 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).
   *Prescribed regimen must be FDA-approved or recommended by NCCN
Approval duration:
Medicaid/HIM – 6 months
Commercial – Length of Benefit

B. Other diagnoses/indications
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy
A. Non-Small Cell Lung Cancer (must meet all):
   1. Currently receiving medication via Centene benefit, 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. New dose does not exceed 80 mg (1 tablet) per day;
      b. New dose does not exceed 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).

*Prescribed regimen must be FDA-approved or recommended by NCCN

Approval duration:
Medicaid/HIM – 12 months
Commercial – Length of Benefit

B. Other diagnoses/indications (must meet 1 or 2):
   1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
      Approval duration: Duration of request or 6 months (whichever is less); or
   2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:
   A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information
   Appendix A: Abbreviation/Acronym Key
   EGFR: epidermal growth factor receptor
   FDA: Food and Drug Administration
Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gilotrif® (afatinib)</td>
<td>Metastatic NSCLC 40 mg PO QD</td>
<td>40 mg/day 50 mg/day when on chronic concomitant therapy with a P-gp inducer</td>
</tr>
<tr>
<td>Iressa® (gefitinib)</td>
<td>Metastatic NSCLC 250 mg PO QD</td>
<td>250 mg/day 500 mg/day when used with a strong CYP3A4 inducer</td>
</tr>
<tr>
<td>Tarceva® (erlotinib)</td>
<td>Metastatic NSCLC 150 mg PO QD</td>
<td>150 mg/day 450 mg/day when used with a strong CYP3A4 inducer or 300 mg/day when used with a moderate CYP1A2 inducer</td>
</tr>
<tr>
<td>Vizimpro® (dacomitinib)</td>
<td>Metastatic NSCLC 45 mg PO QD</td>
<td>45 mg/day</td>
</tr>
</tbody>
</table>

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

None reported.

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSCLC</td>
<td>80 mg PO QD</td>
<td>80 mg/day 160 mg/day when used with a strong CYP3A4 inducer</td>
</tr>
</tbody>
</table>

VI. Product Availability

Tablets: 40 mg, 80 mg

VII. References

## Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Description</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>New policy.</td>
<td>11.16</td>
<td>12.16</td>
</tr>
<tr>
<td>Converted to new template. Initial: added age restriction per PI/safety approach; modified max dose requirement to include QL; increased approval duration from 3 to 6 months. Re-auth: added requirement for positive response to therapy; removed requirement related to reasons to discontinue per safety approach-retained no disease progression or unacceptable toxicity as examples of positive response; added max dose; increased approval duration from 6 to 12 months. Updated references.</td>
<td>08.03.17</td>
<td>11.17</td>
</tr>
<tr>
<td>Policies combined for commercial and Medicaid lines of business. Criteria added for new FDA indication: first-line therapy in EGFR sensitizing exon 19 or exon 21 L858R-mutated, metastatic NSCLC; for commercial and Medicaid: added prescriber specialty requirement, removed requirement that mutation must be detected by an FDA approved test, added COC language for continuation criteria; for commercial: added age restriction, added max dosing requirement for use with a strong CYP3A4 inducer; references reviewed and updated.</td>
<td>05.29.18</td>
<td>08.18</td>
</tr>
<tr>
<td>4Q 2018 annual review; no significant changes; references reviewed and updated.</td>
<td>08.07.18</td>
<td>11.18</td>
</tr>
<tr>
<td>2Q 2019 annual review: NCCN designation of advanced added to NSCLC; sensitizing EGFR mutations restated as examples; Vizimpro added as a trial option for prior NSCLC therapy per NCCN; references reviewed and updated.</td>
<td>02.19.19</td>
<td>05.19</td>
</tr>
<tr>
<td>2Q 2020 annual review: added HIM line of business; references reviewed and updated.</td>
<td>02.12.20</td>
<td>05.20</td>
</tr>
</tbody>
</table>

### Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.
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This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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