Clinical Policy: Erlotinib (Tarceva)
Reference Number: ERX.SPMN.119
Effective Date: 03/14
Last Review Date: 09/16

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

Policy/Criteria
It is the policy of health plans affiliated with Envolve Pharmacy Solutions® that erlotinib (Tarceva®) 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 non-small cell lung cancer (NSCLC);
      2. Member meets a or b:
         a. FDA approved use: (i, ii, or iii)
            i. Initial treatment of metastatic disease in members whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test;
            ii. Maintenance treatment of locally advanced or metastatic disease that has not progressed after four cycles of platinum chemotherapy;
            iii. Subsequent treatment locally advanced or metastatic disease after failure of at least one prior chemotherapy regimen;
         b. Off-label NCCN recommended use: (i, ii, or iii)
            i. Initial treatment for recurrent disease in patients with a known sensitizing EGFR mutation;
            ii. Maintenance treatment in member recurrent who have achieved tumor response or stable disease following chemotherapy;
            iii. Treatment in member with history of progression on erlotinib for asymptomatic disease, symptomatic brain lesions or isolated symptomatic systemic lesions and disease is recurrent or metastatic.

      Approval duration: 3 months

   B. Pancreatic Cancer (must meet all):
      1. Diagnosis of pancreatic cancer;
      2. Disease is locally advanced, unresectable, or metastatic;
      3. Tarceva will be used as first-line therapy in combination with gemcitabine;
      4. Prescribed daily dose of Tarceva does not exceed 100 mg.

      Approval duration: 3 months

   C. Other diagnoses/indications: Refer to ERX.SPMN.16 - Global Biopharm Policy.
1. Off-label NCCN compendial uses for erlotinib, meeting NCCN categories 1, 2a or 2b, are approved for the following indications per the USS.SPMN.16 Global Biopharm policy:
   a. Bone cancer – chordoma;
   b. Central nervous system cancers – leptomeningeal metastases from NSCLC;
   c. Kidney cancer.

II. Continued Approval
   A. All Indications (must meet all):
      1. Currently receiving medication via health plan benefit or member has previously met all initial approval criteria;
      2. If diagnosis is pancreatic cancer, prescribed daily dose of Tarceva does not exceed 100 mg.

   B. Other diagnoses/indications (must meet 1 or 2):
      1. Currently receiving medication via health plan benefit and documentation supports positive response to therapy; or
      2. Refer to ERX.SPMN.16 - Global Biopharm Policy.

Background
Description/Mechanism of Action:
Erlotinib is a kinase inhibitor that reversibly inhibits the kinase activity of epidermal growth factor receptor (EGFR), preventing autophosphorylation of tyrosine residues associated with the receptor and thereby inhibiting further downstream signaling. EGFR is expressed on the cell surface of both normal and cancer cells. In some tumor cells, signaling through this receptor plays a role in tumor cell survival and proliferation irrespective of EGFR mutation status. Erlotinib binding affinity for EGFR exon 19 deletion or exon 21 (L858R) mutations is higher than its affinity for the wild type receptor. Erlotinib inhibition of other tyrosine kinase receptors has not been fully characterized.

Formulations:
   Tablet, Oral:
      Tarceva: 25 mg, 100 mg, 150 mg

FDA Approved Indications:
Tarceva is a tyrosine kinase inhibitor/oral tablet formulation indicated for:
   ● Non-small cell lung cancer (NSCLC):
      o The first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whole tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test.
      o The maintenance treatment of patients with locally advanced or metastatic NSCLC whose disease has not progressed after four cycles of platinum-based first-line chemotherapy.
The treatment of patients with locally advanced or metastatic NSCLC after failure of at least one prior chemotherapy regimen.

Limitations of use:
- Tarceva is not recommended for use in combination with platinum-based chemotherapy.
- Safety and efficacy of Tarceva have not been evaluated as first-line treatment in patients with metastatic NSCLC whole tumors have EGFR mutations other than exon 19 deletions or exon 21 (L858R) substitution.

- Pancreatic cancer:
  - Tarceva in combination with gemcitabine is indicated for the first-line treatment of patients with locally advanced, unresectable, or metastatic pancreatic cancer.

Appendices
Appendix A: Abbreviation Key
EGFR: epidermal growth factor receptor
NSCLC: non-small cell lung cancer

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Reviews, Revisions, and Approvals

| Policy created. | 02/14 | 03/14 |
| Policy converted to new template. | 08/16 | 09/16 |

- NSCLC: FDA approved use criteria is made slightly less specific to incorporate NCCN compendial uses that are similar but less restrictive (i.e., added “recurrent” to first-line and maintenance therapies, added “locally advanced” to maintenance therapy, removed specific types of EGFR mutations from first-line therapy, removed “platinum” and specific number of chemotherapy cycles from maintenance therapy, added “or other systemic therapies” to second-line therapy to account for the NCCN recommended use of erlotinib after immune checkpoint inhibitors). This left one additional “off-label” NSCLC use under Section I.A.2.b. “NCCN recommended use”.
- Pancreatic cancer: FDA and NCCN indications overlap here and are presented as one criteria set; max dosing criteria added per PI.
- Additional NCCN uses: all additional NCCN recommended uses are listed under Section C – “other diagnoses/indications”.

Page 3 of 4
References

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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 policy is the property of Envolve Pharmacy Solutions. Unauthorized copying, use, and distribution of this Policy or any information contained herein is strictly prohibited. By accessing this policy, you agree to be bound by the foregoing terms and conditions, in addition to the Site Use Agreement for Health Plans associated with Envolve Pharmacy Solutions.

©2016 Envolve Pharmacy Solutions. All rights reserved. All materials are exclusively owned by Envolve Pharmacy Solutions and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Envolve Pharmacy Solutions. You may not alter or remove any trademark, copyright or other notice contained herein.