Clinical Policy: Erlotinib (Tarceva)
Reference Number: ERX.SPA.06
Effective Date: 04.01.17
Last Review Date: 02.18

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

Description
Erlotinib (Tarceva®) is a kinase inhibitor.

FDA Approved Indication(s)
Tarceva is indicated for the 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) substitution mutations as detected by an FDA-approved test receiving first-line, maintenance, or second or greater line treatment after progression following at least one prior chemotherapy regimen.
- Patients with locally advanced, unresectable or metastatic pancreatic cancer, in combination with gemcitabine as first-line.

Limitation(s) of use:
- Safety and efficacy of Tarceva have not been established in patients with NSCLC whose tumors have other EGFR mutations.
- Tarceva is not recommended for use in combination with platinum based chemotherapy.

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that 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 NSCLC;
      2. Age ≥ 18 years;
      3. Tumor is positive for an EGFR exon 19 deletion or EGFR exon 21 (L858R) substitution mutation;
         a. Tarceva will be used in one of the following ways for metastatic disease:
            i. As first-line therapy;
            ii. As maintenance therapy after initial treatment with chemotherapy;
            iii. As second- or greater-line therapy after progression following one or more chemotherapy regimens;
      4. 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: Length of Benefit

   B. Pancreatic Cancer (must meet all):
      1. Diagnosis of pancreatic cancer;
      2. Disease is locally advanced, unresectable, or metastatic;
      3. Age ≥ 18 years;
      4. Tarceva will be used in combination with gemcitabine;
      5. Request meets one of the following (a or b):
         a. Dose does not exceed 450 mg per day;
II. Continued Therapy
A. All Indications in Section I (must meet all):
   1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
   2. Member is responding positively to therapy (e.g., no disease progression);
   3. If request is for a dose increase, request meets one of the following (a or b):
      a. New dose does not exceed 450mg per day;
      b. New does is supported by practice guideline or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).
   Approval duration: Length of Benefit

B. Other diagnoses/indications (must meet 1 or 2):
   1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
      Approval duration: Duration of request or 6 months (whichever is less); or
   2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 or evidence of coverage documents;

B. Use in combination with platinum-based chemotherapy;

C. Use of Tarceva for the treatment of NSCLC without documentation of EGFR exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

EGFR: epidermal growth factor receptor
NCCN: National Comprehensive Cancer Network
FDA: Food and Drug Administration
NSCLC: non-small cell lung cancer

Appendix B: Therapeutic Alternatives

<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><strong>NSCLC - EGFR mutation:</strong> 40 mg PO QD</td>
<td>40 mg/day</td>
</tr>
<tr>
<td>cisplatin (Platinol-AQ®)</td>
<td><strong>NSCLC</strong> Various doses</td>
<td>Number of cycles varies</td>
</tr>
<tr>
<td>carboplatin (Paraplatin®)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>paclitaxel (Taxol®)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>docetaxel (Taxotere®)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>vinorelbine (Navelbine®)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>gemcitabine (Gemzar®)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>etoposide (Toposar®, Vepesid®)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>irinotecan (Camptosar®)</td>
<td></td>
<td></td>
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<tr>
<td>vinblastine (Velban®)</td>
<td></td>
<td></td>
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<tr>
<td>mitomycin (Mitosol®)</td>
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<td></td>
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<tr>
<td>ifosfamide (Ifex®)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alimta® (pemetrexed - 2nd line)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>gemcitabine (Gemzar®)</td>
<td><strong>Pancreatic cancer</strong> Various doses</td>
<td>Number of cycles varies</td>
</tr>
<tr>
<td>gemcitabine (Gemzar®)+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>cisplatin (Platinol-AQ®)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>gemcitabine(Gemzar®) + oxaliplatin (Eloxatin®)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-FU (Efudex®)</td>
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</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: General Information

- National Comprehensive Cancer Network (NCCN) Practice Guidelines for NSCLC recommend platinum-based chemotherapy regimens for first-line therapy for advanced NSCLC.
- Per NCCN guidelines (category 2A), Tarceva is recommended as first line therapy in patients with advanced, recurrent, or metastatic nonsquamous NSCLC who have known active EGFR mutation or gene amplification regardless of their performance status. This recommendation is based on the results of a phase III trial in which patients with EGFR mutations who received gefitinib had increased progression free survival (25% vs. 7%), response rate (71%) and quality of life and fewer side effects when compared to those receiving chemotherapy (carboplatin/paclitaxel).
- Results from 2 placebo-controlled, randomized, phase III trials showed no clinical benefit with concurrent administration of Tarceva with platinum-based chemotherapy.
- Contraindications to platinum-based chemotherapy regimens may include pre-existing neuropathy, and other complicating comorbidities (e.g., transplant patients, patients with chronic renal insufficiency).
• NCCN Practice Guidelines do not recommend systemic, cytotoxic chemotherapy for patients of any age with a Performance Status (PS) score of 3-4 for NSCLC except Tarceva for EGFR mutation positive patients.

**ECOG Performance Status Scale**

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal activity</td>
</tr>
<tr>
<td>1</td>
<td>Symptoms but nearly fully ambulatory</td>
</tr>
<tr>
<td>2</td>
<td>Ambulatory but bedtime required during normal daytime (&lt; 50%)</td>
</tr>
<tr>
<td>3</td>
<td>Confined to bed &gt; 50% of waking hours</td>
</tr>
<tr>
<td>4</td>
<td>Unable to get out of bed</td>
</tr>
</tbody>
</table>

• Tarceva monotherapy for pancreatic cancer has not been studied.
• Colorectal, head, neck, prostate, and ovarian cancer are class III recommendations in Micromedex.
• NCCN recommends Tarceva (2A) as single agent therapy for recurrent chordoma and for relapsed or surgically unresectable stage IV kidney cancer with non-clear cell histology.
• In the IUNO trial examining the use of Tarceva as maintenance therapy in patients with NSCLC without exon 19 deletions or exon 21 (L858R) substitution mutations and without disease progression after four cycles of chemotherapy, Tarceva did not differentiate from placebo on median overall survival or median progression-free survival rates.

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
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<tbody>
<tr>
<td>NSCLC</td>
<td>150 mg PO QD on an empty stomach</td>
<td>150 mg/day</td>
</tr>
<tr>
<td>Pancreatic cancer</td>
<td>150 mg PO QD in combination with gemcitabine</td>
<td></td>
</tr>
<tr>
<td>Chordoma</td>
<td>150 mg PO QD</td>
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</tr>
<tr>
<td>Kidney cancer</td>
<td>150 mg PO QD</td>
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</tr>
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</table>

VI. Product Availability

Tablets: 25 mg, 100 mg, 150 mg

VII. References


<table>
<thead>
<tr>
<th>Reviews, Revisions, and Approvals</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Policy created</td>
<td>12.01.16</td>
<td>02.17</td>
</tr>
<tr>
<td>1Q18 annual review:</td>
<td>11.14.17</td>
<td>02.18</td>
</tr>
<tr>
<td>Added criteria for bone cancer, central nervous system cancers, and kidney caners. Added age requirements for NSCLC and pancreatic cancer. Added additional FDA indication criteria for NSCLC. Updated maximum dose to from 100mg/150mg to 450 mg per clinical pharmacology. Approval durations modified to length of benefit.</td>
<td></td>
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</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.

This Clinical Policy is not intended to dictate 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.

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