PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Erlotinib Prior Authorization Policy
- Tarceva® (erlotinib tablets – Genentech, generic)

REVIEW DATE: 02/07/2024

OVERVIEW

Erlotinib, a tyrosine kinase inhibitor, is indicated for the following uses:[1]

- **Non-Small Cell Lung Cancer (NSCLC)**, treatment of patients 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. Limitations of use: The safety and efficacy of erlotinib have not been established in patients with NSCLC whose tumors have other *EGFR* mutations. Erlotinib is not recommended for use in combination with platinum-based chemotherapy.
- **Pancreatic Cancer**, in combination with gemcitabine as first-line treatment of patients with locally advanced, unresectable, or metastatic pancreatic cancer.

Guidelines

Erlotinib has been addressed in National Comprehensive Cancer Network (NCCN) guidelines.[2-7]

- **Bone Cancer:** Guidelines (version 1.2024 – August 7, 2023) note erlotinib (category 2A) as a treatment option under "Useful in Certain Circumstances" for patients with chordoma.[3] The efficacy of erlotinib was demonstrated in patients with advanced chordoma resistant to imatinib.
- **Kidney Cancer:** Guidelines (version 2.2024 – January 3, 2024) note erlotinib monotherapy as a treatment option for patients with recurrent or advanced renal cell carcinoma of non-clear cell histology (category 2A) under "Useful in Certain Circumstances".[6] The combination of bevacizumab with erlotinib is a treatment option (category 2A) for selected patients with non-clear cell and papillary cell histology, including hereditary leiomyomatosis and renal cell carcinoma under "Useful in Certain Circumstances".
- **Non-Small Cell Lung Cancer:** Guidelines (version 1.2024 – December 21, 2023) recommend erlotinib and other *EGFR* tyrosine kinase inhibitors as first-line treatment for patients with advanced or metastatic NSCLC with *EGFR* exon 19 deletions, exon 21 (L858R) substitution mutations (category 1 for both exon 19 and exon 21), L861Q, G719X, and S768I (category 2A for these three mutations).
- **Pancreatic Adenocarcinoma:** Guidelines (version 1.2024 – December 13, 2023) recommend the combination of gemcitabine and erlotinib as first-line treatment option (category 2A) for patients with locally advanced or metastatic disease under "Other Recommended Regimens".[5] In addition, the combination is recommended as a subsequent therapy option (category 2A) for locally advanced, metastatic, or recurrent disease under "Other Recommended Regimens".
- **Vulvar Cancer:** Guidelines (version 3.2024 – December 21, 2023) recommend erlotinib (category 2B) as a second-line or subsequent treatment option for patients with advanced, recurrent, or metastatic vulvar cancer under "Other Recommended Regimens".[7]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of erlotinib. All approvals are provided for the duration noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of erlotinib is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Non-Small Cell Lung Cancer.** Approve for 1 year if the patient meets the following (A, B, and C):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has advanced or metastatic disease; AND
   - **C)** Patient has *EGFR* mutation-positive non-small cell lung cancer as detected by an approved test. Note: Examples of *EGFR* mutation-positive non-small cell lung cancer include the following: exon 19 deletions, exon 21 (L858R) substitution mutations, L861Q, G719X, and S768I.

2. **Pancreatic Cancer.** Approve for 1 year if the patient meets the following (A, B, and C):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has locally advanced, metastatic, or recurrent disease; AND
   - **C)** The medication is used in combination with gemcitabine.

Other Uses with Supportive Evidence

3. **Bone Cancer.** Approve for 1 year if the patient meets the following (A, B, and C):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has chordoma; AND
   - **C)** Patient has tried at least one previous therapy.

4. **Renal Cell Carcinoma.** Approve for 1 year if the patient meets the following (A and B):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient meets one of the following (i or ii):
     - **i.** Patient has recurrent or advanced renal cell carcinoma of non-clear cell histology; OR
     - **ii.** Patient meets both of the following (a and b):
       - **a)** Patient has hereditary leiomyomatosis and renal cell carcinoma; AND
       - **b)** The medication is used in combination with bevacizumab.

5. **Vulvar Cancer.** Approve for 1 year if the patient meets the following (A and B):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has advanced, recurrent, or metastatic disease.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of erlotinib is not recommended in the following situations:

1. **Breast Cancer.** One Phase II, non-randomized, open-label, bi-institutional trial did not demonstrate a beneficial effect of erlotinib plus bevacizumab in patients with metastatic breast cancer with stage IV disease that was stable or had progressed after treatment with one or two chemotherapy regimens. If the patient's tumor was human epidermal growth factor receptor-2 (HER-2) positive, prior therapy with trastuzumab was required (n = 38).[8] As single-agent therapy, erlotinib had minimal activity in unselected, previously treated women with locally advanced or metastatic breast cancer in one multicenter, Phase II study (n = 69).[9] Metronomic (frequent low-dose) capecitabine tablets and cyclophosphamide plus bevacizumab and erlotinib was effective in patients with untreated advanced metastatic HER-2 negative, estrogen receptor-negative, and progesterone receptor-poor advanced breast cancer (n = 26).[10] Among 24 patients assessable for response, 4% of patients had a complete response (CR) [n = 1], 58% of patients had partial response (PR) [n = 14], 21% of patients had stable disease (SD) > 9 weeks duration (n = 5) and 4% of patients (n = 1) had early progression of disease. The overall clinical benefit (CR + PR + SD > 24 weeks) was 75% (95% confidence interval [CI]: 53, 90). Median time to progression was 43 weeks (95% CI: 21, 69). Overall survival was 108 months (95% CI: 70, 110). NCCN Breast Cancer guidelines (version 1.2024 – January 25, 2024) do not mention erlotinib.[11]

2. **Colon Cancer, Advanced**. NCCN Colon Cancer guidelines (version 1.2024 – January 29, 2024) note several drug combinations, including bevacizumab plus erlotinib, produced negative results in phase III trials involving patients with advanced colorectal cancer and these regimens are not recommended.[12] In addition, the panel recommends against the use of several medications, including erlotinib, for the treatment of patients who progressed after treatment with standard therapies.

3. **Glioblastoma Multiforme (GBM).** In one Phase II study, concurrent radiation therapy (RT) and temozolomide in combination with erlotinib in patients newly diagnosed with glioblastoma (n = 27) was not efficacious.[13] In two Phase II studies, erlotinib plus temozolomide given during and after RT produced favorable median survival, and progression free survival (PFS), as well as 12- or 14-month survival rates in patients with newly diagnosed GBM or gliosarcoma.[14,15] In patients with newly diagnosed (untreated; could have had resection) GBM or gliosarcoma who received erlotinib plus temozolomide during and after radiation, median survival was longer with erlotinib plus temozolomide vs. historical controls (19.3 months vs. 14.1 months, respectively; hazard ratio for survival 0.64; 95% confidence interval [CI]: 0.45, 0.91; P = 0.01) in one open-label, single-center, Phase II trial (n = 65).[14] The historical controls were comparable in patients from two prospective, Phase II trials (n = 128); the first trial included the use of Thalomid® (thalidomide capsules) in combination with temozolomide during and after radiotherapy; the second included the use of *cis*-retinoic acid with temozolomide during and after radiotherapy. In one open-label, Phase I/II trial, treatment with erlotinib plus temozolomide during and after RT resulted in favorable survival rate (61% of patients were alive at 1 year) and median PFS (7.2 months) in patients with newly diagnosed GBM (following resection); however, there was no significant difference in overall survival with the addition of erlotinib compared with the temozolomide/RT arm of a historical control trial (15.3 months vs. 15 months, respectively).[24] Erlotinib has failed to demonstrate benefit in recurrent glioblastomas.[16-19] In a recent study involving patients with recurrent gliobastoma, the combination regimen of sorafenib and erlotinib failed to meet the predetermined efficacy endpoint and the study was terminated.[20] NCCN Central Nervous System guidelines (version 1.2023 – March 24, 2023) do not mention erlotinib as a treatment option for patients with glioblastoma.[21]

4. **Head and Neck Cancer, Squamous Cell, Recurrent and/or Metastatic.** Two Phase II studies assessed the use of erlotinib and bevacizumab in different settings and showed promising results.[22,23] One multicenter, Phase II trial assessed the addition of bevacizumab and erlotinib to chemoradiation as first-line treatment for previously untreated patients with locally advanced squamous cell carcinoma of the head and neck (SCCHN) [n = 60].[22] After a median follow-up of 32 months the estimated 3-year progression free survival (PFS) and overall survival rates were 71% and 82%, respectively. After induction therapy, 65% of patients had major responses; after completion of therapy, 95% of patients had either partial or complete radiographic responses. One multi-institutional Phase I/II study enrolled patients with recurrent or metastatic SCCHN (previously treated with ≤ 1 prior regimen for recurrent disease) to receive erlotinib and bevacizumab (n = 56).[23] The median overall survival and PFS durations were 7.1 months (95% confidence interval [CI]: 5.7, 9.0) and 4.1 months (95% CI: 2.8, 4.4), respectively. Treatment with erlotinib monotherapy produced few partial responses in unselected (*EGFR* status not known at baseline) patients with locally recurrent and/or metastatic SCCHN in one open-label, Phase II clinical trial (n = 115); 38.3% of patients achieved stable disease for a median of 16.1 weeks.[24] In one Phase II study, 204 patients with locally advanced SCCHN were randomized to receive cisplatin in combination with radiation therapy (RT) with or without erlotinib.[25] Complete response rates evaluated by central review were reported in 40% of patients (n = 42/105) on cisplatin/RT vs. 52% of patients (n = 51/99) on cisplatin/RT/erlotinib (P = 0.08). At a median follow-up of 26 months and 54 progression events, there was no difference in PFS between the two treatment arms (hazard ratio 0.0; P = 0.71). In a Phase II study, patients with recurrent SCCHN were treated with erlotinib for 12 months (n = 31). The overall survival was 61% at 1 year and 56% at 2 years.[26] Disease-free survival was 54% at 1 year and 45% at 2 years. The mean time to recurrence (n = 16) was 8.7 months. Only 8 patients completed the full 12-month course of erlotinib; the median duration of erlotinib therapy was 5 months. NCCN Head and Neck Cancer guidelines (version 2.2024 – December 8, 2023) do not mention erlotinb.[27]

5. **Hepatocellular Carcinoma, Advanced**. NCCN Hepatocellular Carcinoma guidelines (version 2.2023 – September 14, 2023) note the combination regimen of sorafenib and erlotinib did not significantly improve survival compared with sorafenib monotherapy in the treatment of patients with advanced hepatocellular carcinoma (sorafenib is one of several agents recommended for first-line treatment).[28] In addition, the disease control rate was significantly lower for patients who received the combination vs. those who received sorafenib monotherapy; treatment duration was also shorter for those received sorafenib and erlotinib. .

6. **Renal Cell Carcinoma, Advanced – Clear Cell Histology.** NCCN Kidney Cancer guidelines (version 2.2024 – January 3, 2024) do not note erlotinib as a treatment option for advanced clear-cell renal cell carcinoma.[6]

7. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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