Tarceva® erlotinib tablets

Tarceva® (erlotinib) tablets is NOW APPROVED as first-line therapy for metastatic non–small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) mutations.

Tarceva efficacy was demonstrated in the phase III, randomized, open-label EURTAC trial (N=174). EURTAC was designed to assess the efficacy and safety of Tarceva vs. standard chemotherapy in the first-line treatment of metastatic NSCLC containing EGFR exon 19 deletions or exon 21 (L858R) substitution mutations.[1,2]

Pivotal EURTAC trial demonstrated significant benefit in NSCLC with EGFR mutations.[1,2]

- Tarceva demonstrated a median investigator assessed progression-free survival (PFS) of 10.4 months (n=86) compared to 5.2 months with chemotherapy (n=88) (HR=0.34 [95% CI, 0.23-0.49] $P<0.001$).
- The most frequent (≥30%) adverse reactions in Tarceva-treated patients were diarrhea, asthenia, rash, cough, dyspnea, and decreased appetite.

Select codes for your reference[3,4]		
ICD-9 Codes	162.2-162.9 Malignant neoplasm of bronchus and lung	
NDC 10-Digit Codes	50242-062-01	25 mg (30 tablets)
	50242-063-01	100 mg (30 tablets)
	50242-064-01	150 mg (30 tablets)
NDC 11-Digit Codes	50242-0062-01	25 mg (30 tablets)
	50242-0063-01	100 mg (30 tablets)
	50242-0064-01	150 mg (30 tablets)

- Tarceva will be transitioning to a specialty pharmacy distribution model on July 1, 2013. Customers will be able to acquire Tarceva through select specialty pharmacies and authorized distributors for hospitals and physician purchasers for in-office dispensing pharmacies if a patient is covered by a commercial health plan as of this date.
  - To find out which specialty pharmacies are in the network, visit Tarceva.com/HCP or contact Access Solutions at 1-888-249-4918.
  - Prior to July 1, 2013, Tarceva is available at any retail or specialty pharmacy, as well as hospitals and physician purchasers for in-office dispensing pharmacies.
- Tarceva Access Solutions offer services to help you navigate the access and reimbursement process, and our dedicated, in-house specialists help bring patient treatment and practice solutions together. For information on patient access support, please contact Tarceva Access Solutions by calling 1-888-249-4918 or by visiting Genentech-Access.com/Tarceva.

For more information, please contact your Field Reimbursement Manager or visit http://www.gene.com/contact-us/email-us.

NCCN guidelines include erlotinib as first-line therapy for patients with EGFR mutation–positive advanced NSCLC (Category 1 recommendation).[4]

INDICATIONS AND USAGE

Non-Small Cell Lung Cancer

Tarceva 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) substitution mutations as detected by an FDA-approved test.
- 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 whose tumors have EGFR mutations other than exon 19 deletions or exon 21 (L858R) substitution.

For Important Safety Information, please see reverse and accompanying full prescribing information.

IMPORTANT SAFETY INFORMATION

DOSE MODIFICATIONS

- **Reduce Tarceva dose by 50 mg decrements:**
  - If severe reactions occur with concomitant use of strong CYP3A4 inhibitors [such as atazanavir, clarithromycin, indinavir, itraconazole, ketoconazole, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin, troleandomycin (TAO), voriconazole, or grapefruit or grapefruit juice] or when using concomitantly with an inhibitor of both CYP3A4 and CYP1A2 (e.g., ciprofloxacin). Avoid concomitant use if possible.
  - When restarting therapy following withholding treatment for a dose-limiting toxicity that has resolved to baseline or grade ≤1.
- **Increase Tarceva dosage by 50 mg increments as tolerated for:**
  - Concomitant use with CYP3A4 inducers such as rifampin, rifabutin, rifapentine, phenytoin, carbamazepine, phenobarbital, or St. John's wort. Increase doses by 50 mg increments at 2 week intervals to a maximum of 450 mg. Avoid concomitant use if possible.
  - Concurrent cigarette smoking. Increase by 50 mg increments at 2 week intervals to a maximum of 300 mg. Immediately reduce the dose of Tarceva to the recommended dose (150 mg) upon cessation of smoking.
- **For drugs affecting gastric pH:**
  - Avoid concomitant use of Tarceva with proton pump inhibitors if possible. Separation of doses may not eliminate the interaction since proton pump inhibitors affect the pH of the upper GI tract for an extended period.
  - If treatment with an H2-receptor antagonist is required, Tarceva must be taken 10 hours after the H2-receptor antagonist dosing and at least 2 hours before the next dose of the H2-receptor antagonist.
  - Although the effect of antacids on erlotinib pharmacokinetics has not been evaluated, the antacid dose and the Tarceva dose should be separated by several hours, if an antacid is necessary.

CONTRAINDICATIONS: None

WARNINGS AND PRECAUTIONS:

- **Interstitial Lung Disease (ILD):**
  - Cases of serious ILD, including fatal cases, can occur with Tarceva treatment.
  - Withhold Tarceva for acute onset of new or progressive unexplained pulmonary symptoms such as dyspnea, cough, and fever pending diagnostic evaluation. If ILD is confirmed, permanently discontinue Tarceva.
- **Renal Failure:**
  - Hepatorenal syndrome, severe acute renal failure including fatal cases, and renal insufficiency can occur with Tarceva treatment. Renal failure may arise from exacerbation of underlying baseline hepatic impairment or severe dehydration.
  - Withhold Tarceva in patients developing severe renal impairment until renal toxicity is resolved. Perform periodic monitoring of renal function and serum electrolytes during Tarceva treatment.
- **Hepatotoxicity with or without Hepatic Impairment:**
  - Hepatic failure and hepatorenal syndrome, including fatal cases, can occur with Tarceva treatment in patients with normal hepatic function; the risk of hepatic toxicity is increased in patients with baseline hepatic impairment.
  - Perform periodic liver testing (transaminases, bilirubin, and alkaline phosphatase) during treatment with Tarceva. Increased frequency of monitoring of liver function is required for patients with pre-existing hepatic impairment or biliary obstruction.
  - Withhold Tarceva in patients without pre-existing hepatic impairment for total bilirubin >3 x ULN and/or transaminases >5 x ULN. Withhold Tarceva in patients with pre-existing hepatic impairment or biliary obstruction for doubling of bilirubin or tripling of transaminases value over baseline.
  - Discontinue Tarceva in patients whose abnormal liver tests meeting the above criteria do not improve significantly or resolve within 3 weeks.
- **Gastrointestinal Perforation:**
  - Gastrointestinal perforation, including fatal cases, can occur with Tarceva treatment. Patients receiving concomitant anti-angiogenic agents, corticosteroids, NSAIDs, or taxane-based chemotherapy, or who have prior history of peptic ulceration or diverticular disease may be at increased risk of perforation.
  - Permanently discontinue Tarceva in patients who develop gastrointestinal perforation.
- **Bullous and Exfoliative Skin Disorders:**
  - Bullous, blistering and exfoliative skin conditions, including cases suggestive of Stevens-Johnson syndrome/toxic epidermal necrolysis, which in some cases were fatal, can occur with Tarceva treatment.
  - Discontinue Tarceva treatment if the patient develops severe bullous, blistering or exfoliating conditions
- **Myocardial Infarction (MI)/Ischemia:**
  - In the pancreatic carcinoma trial, MI/ischemia was reported in patients, including fatal cases of MI. In the pooled incidence in the 3 monotherapy lung studies cases of MI/ischemia were reported.
- **Cerebrovascular Accident:**
  - In the pancreatic carcinoma trial, cerebrovascular accident was reported in patients, including a fatal case. In the pooled incidence in the 3 monotherapy lung studies cases of cerebrovascular accident were reported.
- **Microangiopathic Hemolytic Anemia with Thrombocytopenia:**
  - In the pooled incidence of 3 monotherapy lung cancer studies and the pancreatic carcinoma trial, cases of microangiopathic hemolytic anemia with thrombocytopenia were reported.
- **Ocular Disorders:**
  - Corneal perforation or ulceration can occur with Tarceva treatment, including abnormal eyelash growth, keratoconjunctivitis sicca or keratitis.
  - Interrupt or discontinue Tarceva therapy if patients present with acute/worsening ocular disorders such as eye pain.
- **Hemorrhage in patients taking Warfarin:**
  - Severe and fatal hemorrhage associated with International Normalized Ratio (INR) elevations can occur when Tarceva and warfarin are administered concurrently.
  - Regularly monitor prothrombin time and INR during Tarceva treatment in patients taking warfarin or other coumarin-derivative anticoagulants.
- **Embryo-Fetal Toxicity:**
  - Tarceva is pregnancy category D. Based on its mechanism of action, Tarceva can cause fetal harm when administered to a pregnant woman. If Tarceva is used during pregnancy, or if the patient becomes pregnant while taking Tarceva, the patient should be apprised of the potential hazard to a fetus.
  - Advise females of reproductive potential to use highly effective contraception during therapy and for at least 2 weeks after the last dose of Tarceva. Advise patients to contact their healthcare provider if they become pregnant, or if pregnancy is suspected, while taking Tarceva.

MOST COMMON ADVERSE REACTIONS

- **NSCLC – First-Line With EGFR Mutations:**
  - Diarrhea, asthenia, rash, cough, dyspnea, and decreased appetite.
  - Grade 3/4 (NCI-CTC Version 3.0) adverse reactions were rash (14%) and diarrhea (5%). In Tarceva-treated patients, the most frequently reported adverse reactions leading to dose modification were rash (13%), diarrhea (10%), and asthenia (3.6%).
- **NSCLC – Maintenance:**
  - Rash and diarrhea.
  - Grade 3/4 (NCI-CTC Version 3.0) adverse reactions were rash (9%) and diarrhea (2%). Rash and diarrhea resulted in dose reductions or interruption (5% and 3%, respectively) and discontinuation (1% and 0.5%, respectively) of Tarceva-treated patients.
- **NSCLC – Second/Third Line:**
  - Rash and diarrhea.
  - Grade 3/4 (NCI-CTC Version 2.0) adverse reactions were rash (9%) and diarrhea (6%). Rash and diarrhea each resulted in dose reductions (6% and 1%, respectively) and discontinuation in 1% of Tarceva-treated patients.

You may report side effects to the FDA at (800) FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Genentech at (888) 835-2555.

For additional Important Safety Information, please see accompanying full prescribing information.

References: 1. Tarceva® [package insert]. Farmingdale, NY: OSI Pharmaceuticals, LLC, an affiliate of Astellas Pharma US, Inc.; 2013. **2.** Rosell R, Carcereny E, Gervais R, et al; on behalf of the Spanish Lung Cancer Group in collaboration with the Groupe Français de Pneumo-Cancérologie and the Associazione Italiana Oncologia Toracica. Erlotinib versus standard chemotherapy as first-line treatment for European patients with advanced EGFR mutation-positive non-small-cell lung cancer (EURTAC): a multicentre, open-label, randomised phase 3 trial. *Lancet Oncol*. 2012;13(3):239-246. **3.** ICD9Data. Malignant neoplasm of bronchus and lung, unspecified. http://www.icd9data.com/2012/Volume1/140-239/160-165/162/162.9.htm. Accessed February 14, 2013. **4.** NCCN Clinical Practice Guidelines in Oncology: Non-Small Cell Lung Cancer V.2.2013. Available at: http://www.nccn.org. Accessed March 19, 2013. ©National Comprehensive Cancer Network, 2013. To view the most recent and complete version of the Guideline, go online to www.nccn.org.

013C-071-7476 TAR0001724400 5/13

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