Submitted by:
Ellen Yang, PharmD
Medical Communications, Medical Affairs
Genentech, Inc.
1 DNA Way
South San Francisco, CA 94080
Phone: (650) 467-0637
Email: mcmc-d@gene.com
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NCCN Guidelines Panel: Non-Small Cell Lung Cancer (NSCLC)

On behalf of Genentech, Inc., I respectfully request the NCCN NSCLC Guideline Panel to review the enclosed recently presented key data from the 2014 American Society of Clinical Oncology (ASCO) Annual Meeting for:

- **Tarceva® (erlotinib):** NSCLC

Kelly K, Altorki NK, Eberhardt WEE, et al. A randomized double blind Phase 3 trial of adjuvant erlotinib vs. placebo following complete tumor resection with or without adjuvant chemotherapy in patients with Stage IB-IIIA EGFR positive (IHC/FISH) non-small cell lung cancer: RADIANT results. Presented at the American Society of Clinical Oncology 2014 Annual Meeting in Chicago, IL; May 30 - June 3, 2014. ASCO Oral presentation.

O'Brien MER, Eberhardt WEE, Altorki NK, et al. Analysis of treatment duration and safety of adjuvant erlotinib (E) vs placebo (P) after surgery in patients (pts) with non-small cell lung cancer (NSCLC): RADIANT trial. Presented at the American Society of Clinical Oncology 2014 Annual Meeting in Chicago, IL; May 30 - June 3, 2014. ASCO Poster #7535.

Shepherd FA, Altorki NK, Eberhardt WEE, et al. Adjuvant erlotinib vs placebo in non-small cell lung cancer (NSCLC) patients with tumors carrying EGFR sensitizing mutations from the RADIANT trial. Presented at the American Society of Clinical Oncology 2014 Annual Meeting in Chicago, IL; May 30 - June 3, 2014. ASCO Poster #7513.

Pennell NA, Neal JW, Chaft JE, et al. SELECT: a multicenter Phase II trial of adjuvant erlotinib in resected early-stage EGFR mutation-positive NSCLC. Presented at the American Society of Clinical Oncology 2014 Annual Meeting in Chicago, IL; May 30 - June 3, 2014. ASCO Poster #7514.

Please go to www.asco.org to view the abstracts for the above conference proceedings.

Specific Changes:
There are no specific changes being requested. We are providing data on Tarceva in NSCLC for your review and consideration.

FDA Clearance: Tarceva is FDA-approved for 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, maintenance treatment of patients with locally advanced or metastatic NSCLC whose disease has not progressed after four

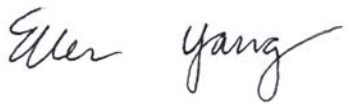
cycles of platinum-based first-line chemotherapy, and treatment of locally advanced or metastatic NSCLC after failure of at least one prior chemotherapy regimen.

Please refer to the enclosed prescribing information for the full FDA-approved indications and safety information.

Rationale:

The RADIANT trial, a Phase III, randomized, double-blind trial, evaluated the safety and efficacy of Tarceva vs placebo in the adjuvant setting following surgical resection, showed that disease-free survival (DFS) was not significantly improved with Tarceva treatment in patients with EGFR expressing tumors as determined by FISH or IHC. There was also no benefit seen in overall survival in this overall study population. With respect to the pre-specified subgroup analysis of patients with EGFR activating mutations, DFS favored Tarceva treatment with a hazard ratio of HR=0.61 (95% CI 0.384-0.981) and nominal p-value of 0.0391, however, this observation was not statistically significant due to hierarchical testing outlined in the statistical methods. In the overall study population, there was a higher rate of Grade 3/4 rash in the Tarceva vs. placebo arms (22.3% vs 0.3%). Additional studies have evaluated Tarceva in the adjuvant NSCLC setting, including the SELECT trial which specifically enrolled patients with EGFR activating mutations.[1-3] There are other ongoing trials of tyrosine kinase inhibitors in the adjuvant EGFR mutation-positive patient population listed on ClinicalTrials.gov.[4-13]

Respectfully submitted,



Supplemental References

1. Waterhouse DM, Hainsworth JD, Greco FA, et al. Adjuvant carboplatin, docetaxel, bevacizumab, and erlotinib versus chemotherapy alone in patients with resected non-small cell lung cancer: a randomized Phase II study of the Sarah Cannon Research Institute (SCRI). Presented at the American Society of Clinical Oncology 2012 Annual Meeting in Chicago, IL; June 1-5, 2012. ASCO Abstract #7035. http://www.asco.org.
2. Gold KA, Lee JJ, Rice D, et al. Pilot phase II study of neoadjuvant docetaxel (T) and cisplatin (P) followed by adjuvant erlotinib (E) in patients with stage I-III non-small cell lung cancer (NSCLC). J Thorac Oncol 2009;4:S784-S785.IASLC Abstract #P2.137.
3. Pennell NA, Neal JW, Chaft JE, et al. SELECT: a multicenter Phase II trial of adjuvant erlotinib in resected early-stage EGFR mutation-positive NSCLC. Presented at the American Society of Clinical Oncology 2014 Annual Meeting in Chicago, IL; May 30 - June 3, 2014. ASCO Poster #7514.
4. National Institutes of Health. Erlotinib Versus Vinorelbine/Cisplatin as Adjuvant Treatment in Stage IIIA NSCLC Patients With EGFR Mutations. Available at: http://clinicaltrials.gov/ct2/show/NCT01410214. Accessed June 6, 2014.
5. National Institutes of Health. Icotinib Versus Placebo as Adjuvant Therapy in EGFR-mutant Lung Adenocarcinoma. Available at: http://clinicaltrials.gov/ct2/show/NCT02125240. Accessed June 6, 2014.
6. National Institutes of Health. Gefitinib Versus Vinorelbine/Platinum as Adjuvant Treatment in Stage II-IIIA(N1-N2) NSCLC With EGFR Mutation (ADJUVANT). Available at: http://clinicaltrials.gov/ct2/show/NCT01405079. Accessed June 6, 2014.
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8. National Institutes of Health. Adjuvant Afatinib in Stage I-III NSCLC With EGFR Mutation. Available at: http://clinicaltrials.gov/ct2/show/NCT01746251. Accessed June 6, 2014.

9. National Institutes of Health. Icotinib as an Adjuvant Therapy for Patients With Stage IIA-IIIA (N0-1) Adenocarcinoma With EGFR Mutation. Available at: http://clinicaltrials.gov/ct2/show/NCT02044328. Accessed June 6, 2014.
10. National Institutes of Health. Erlotinib in Post Radical Operation NSCLC Patients With EGFR Mutation. Available at: http://clinicaltrials.gov/ct2/show/NCT01683175. Accessed June 6, 2014.
11. National Institutes of Health. Erlotinib in Patients With Resected, Early Stage NSCLC With Confirmed Mutations in the EGFR. Available at: http://clinicaltrials.gov/ct2/show/NCT00567359. Accessed June 6, 2014.
12. National Institutes of Health. Icotinib Following Chemotherapy Versus Chemotherapy as Adjuvant Therapy in Stage IIA-IIIA NSCLC With EGFR Mutation (ICTAN). Available at: http://clinicaltrials.gov/ct2/show/NCT01996098. Accessed June 6, 2014.
13. National Institutes of Health. Preoperative Gefitinib for EGFR Mutant II-IIIa NSCLC. Available at: http://clinicaltrials.gov/ct2/show/NCT01833572. Accessed June 6, 2014.