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Submitted by:
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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 updated prescribing information (PI) for:

- **Tarceva® (erlotinib)**: NSCLC

Specific Changes:
Please consider the updated labeling information regarding blood-based epidermal growth factor receptor (EGFR) mutation testing as an option for patients with challenges related to tissue biopsy for your updating purposes.

FDA Clearance:
- Section 2.1 of the Tarceva label has been updated with the following additional language: "Select patients for the first-line treatment of metastatic NSCLC with TARCEVA based on the presence of EGFR exon 19 deletions or exon 21 (L858R) substitution mutations in tumor or plasma specimens. If these mutations are not detected in a plasma specimen, test tumor tissue if available."
- Tarceva is a kinase inhibitor indicated for first-line treatment of patients with NSCLC whose tumors have 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. 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.

Please refer to the product prescribing information for the full FDA-approved indications and safety information.
- Full Tarceva prescribing information available at:
  http://www.gene.com/download/pdf/tarceva_prescribing.pdf
- Information on the cobas® EGFR Mutation Test v2 can be found at the following links
  http://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm504540.htm
  http://molecular.roche.com/assays/Pages/cobasEGFRMutationTestv2.aspx

Rationale:
- The update to the PI was based on a multicenter, open-label, randomized, Phase III study (ENSURE) conducted to evaluate the efficacy and safety of Tarceva versus gemcitabine plus cisplatin as first-line treatment for stage IIIB/IV NSCLC patients. In this study, patients whose plasma results were positive for EGFR exon 19 deletion and/or L858R mutation treated with Tarceva had improved progression-free survival compared to those treated with chemotherapy.
- Additional data on the use of the plasma test is available[1].

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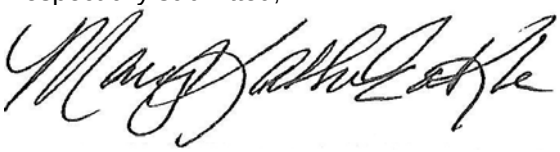
Respectfully submitted,



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Supplemental References

1. Mok T, Wu YL, Lee JS, et al. Detection and Dynamic Changes of EGFR Mutations from Circulating Tumor DNA as a Predictor of Survival Outcomes in NSCLC Patients Treated with First-line Intercalated Erlotinib and Chemotherapy. Clin Cancer Res. E-pub Date: July 2015. DOI # 10.1158/1078-0432.CCR-14-2594. http://www.ncbi.nlm.nih.gov/pubmed/25829397

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