On behalf of Genentech, Inc., I respectfully request the NCCN NSCLC Guideline Panel to review the enclosed recent key publications for:

- **Avastin® (bevacizumab). Tarceva® (erlotinib):** NSCLC


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

**FDA Clearance:** Avastin is FDA-approved for first-line treatment of non-squamous NSCLC in combination with carboplatin and paclitaxel in patients with unresectable, locally advanced, recurrent or metastatic disease. Tarceva is a kinase inhibitor indicated for first-line treatment of patients with 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. 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 enclosed prescribing information for the full FDA-approved indications and safety information.

**Rationale:**
In an open-label, randomized, Phase II trial evaluating the safety and efficacy of Avastin in combination with Tarceva vs. Tarceva alone in non-squamous NSCLC, progression-free survival (PFS) was significantly prolonged with the combination of Avastin and Tarceva (p=0.0015). There was no significant difference in overall response rate, or duration of response. There was a significant difference for disease...
control rate (p=0.0177). Overall survival data is not yet mature. In a pre-specified biomarker analysis, there was a significant correlation between improved PFS and patients with the mutation sub-type EGFR exon 19 deletion (p=0.0011). There was no significant correlation between improved PFS and the EGFR exon 21-L858R substitution. There were significantly more patients with Grade ≥3 proteinuria and hypertension in the Avastin plus Tarceva arm than in the Tarceva alone arm. Additional data on the use of Avastin in combination with Tarceva in NSCLC with subset analyses on EGFR+ patients have been reported.1-7 There are also two ongoing trials with Avastin in combination with Tarceva in EGFR positive NSCLC patients specifically.8-9

Please refer to the following ASCO link to view this abstract:
http://abstracts.asco.org/144/AbstView_144_127760.html

Respectfully submitted,

Supplemental References

Tarceva is co-promoted by Genentech, Inc. and Astelles Oncology