

Submitted by:  
Ellen Yang, PharmD  
Medical Communications, Medical Affairs  
Genentech, Inc.  
1 DNA Way  
South San Francisco, CA 94080  
Phone: (650) 467-0637  
Email: [elleny@gene.com](mailto:elleny@gene.com)  
Date of request: April 16, 2014  
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 recent key publications for:

- **Avastin (bevacizumab):** Maintenance therapy for NSCLC

Barlesi F, Scherpereel A, Rittmeyer A, et al. Randomized Phase III trial of maintenance bevacizumab with or without pemetrexed after first-line induction with bevacizumab, cisplatin, and pemetrexed in advanced nonsquamous non-small-cell lung cancer: AVAPERL (MO22089). *J Clin Oncol* 2013;31:3004-3011

Barlesi F, Scherpereel A, Gorbunova V, et al. Maintenance bevacizumab–pemetrexed after first-line cisplatin–pemetrexed–bevacizumab for advanced nonsquamous non–small cell lung cancer: updated survival analysis of the AVAPERL (MO22089) randomized phase III trial. *Annals of Onc.* 2014 Feb 27; [epub ahead of print]

Rittmeyer A, Gorbunova V, Vikström A, et al. Health-related quality of life in patients with advanced nonsquamous non-small-cell lung cancer receiving bevacizumab or bevacizumab-plus-pemetrexed maintenance therapy in AVAPERL (MO22089). *J Thorac Oncol.* E-pub Date: [published online ahead of print] 2013. DOI # 10.1097/JTO.0b013e3182a46bcf.

**Specific Changes:**

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

**FDA Clearance:**

- Avastin is Off-label for Maintenance Therapy for NSCLC

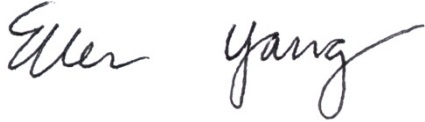
Please refer to the enclosed prescribing information for the full FDA-approved indications and safety information.

**Rationale:**

- **Avastin:** In the randomized, Phase III AVAPERL trial evaluating the safety and efficacy of Avastin maintenance with or without pemetrexed in nonsquamous non–small cell lung cancer (NSCLC), progression-free survival (PFS) was significantly prolonged with Avastin–pemetrexed. In an independent updated analysis of survival outcomes from AVAPERL, overall survival was found to be numerically, but not significantly longer for the Avastin-pemetrexed combination. Health-Related Quality Outcomes remained relatively stable throughout maintenance and was generally similar in both arms. The original full publication, along with publications of updated survival and quality of life

analyses have been submitted for your review and consideration. Additional Phase III data on the use of Avastin with pemetrexed in NSCLC have been reported.<sup>1-4</sup>

Respectfully submitted,

Handwritten signature of Ellen Yang in black ink.

#### Supplemental References

1. Patel JD, Socinski MA, Garon EB, et al. PointBreak: a randomized Phase III study of pemetrexed plus carboplatin and bevacizumab followed by maintenance pemetrexed and bevacizumab versus paclitaxel plus carboplatin and bevacizumab followed by maintenance bevacizumab in patients with Stage IIIB or IV nonsquamous non-small-cell lung cancer. *J Clin Oncol* 2013;31:4349-4357.
2. Socinski MA, Patel JD, Garon EB, et al. A Phase III study of pemetrexed (Pem) plus carboplatin(Cb) plus bevacizumab (Bev) followed by maintenance pem plus bev versus paclitaxel (Pac) plus cb plus bev followed by maintenance bev in Stage IIIB or IV nonsquamous non-small cell lung cancer (NS-NSCLC): overall and age group results. Presented at the American Society of Clinical Oncology 2013 Annual Meeting in Chicago, Illinois; May 31 - June 4, 2013. ASCO Abstract #8004.
3. Reynolds CH, Patel JD, Garon EB, et al. Randomized Phase III trial of pemetrexed (Pem)+carboplatin (Cb)+bevacizumab (Bev) followed by maintenance Pem+Bev (Pem arm) versus paclitaxel (Pac)+Cb+Bev followed by maintenance Bev (Pac arm) in patients (pts) with Stage IIIB/IV nonsquamous non-small cell lung cancer (nsNSCLC) (POINTBREAK): African American (AA) subset. Presented at the American Society of Clinical Oncology 2013 Annual Meeting in Chicago, Illinois; May 31 - June 4, 2013. ASCO Abstract #e19150.
4. Schuette W, Nagel S, Schneider C-P, et al. 65 plus: a randomized Phase III trial of pemetrexed and bevacizumab versus pemetrexed, bevacizumab, and carboplatin as first-line treatment for elderly patients with advanced nonsquamous, non-small cell lung cancer (NSCLC). Presented at the American Society of Clinical Oncology 2013 Annual Meeting in Chicago, Illinois; May 31 - June 4, 2013. ASCO Abstract #8013.