

November 30th, 2015

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NCCN Guidelines® Panel: Non-Small Cell Lung Cancer (NSCLC)

Dear Ms. McClure and Panel Members,

On behalf of Eli Lilly and Company, we respectfully request the NCCN Panel consider modifying the listing of ramucirumab plus docetaxel for the treatment of metastatic NSCLC, regardless of histology, with disease progression on or after platinum-based chemotherapy, to distinguish the combination of ramucirumab plus docetaxel as a preferred or superior treatment choice over docetaxel alone. In addition, we request that the NCCN Panel consider using safety language for ramucirumab in the NCCN guidelines that is consistent with the label.

On December 12th, 2014, following priority review, CYRAMZA® (ramucirumab) was approved by the US FDA in combination with docetaxel for treatment of patients with metastatic NSCLC with disease progression on or after platinum-based chemotherapy.^{1,2} Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving CYRAMZA®.¹

Specific Change: We request that NCCN guidelines list ramucirumab plus docetaxel for the treatment of metastatic NSCLC with disease progression on or after platinum-based chemotherapy, regardless of histology, as a preferred or superior treatment choice over docetaxel alone (pages NSCL-19 and NSCL-20). As currently listed in the guidelines, one may draw the conclusion that there is equivalence between ramucirumab plus docetaxel and docetaxel given as a single agent. Our request is based on the following scientific evidence:

1. The indication was based on the REVEL study, a large (N=1253), randomized, double-blind, Phase III registration trial that enrolled patients with either non-squamous (73%) or squamous (26%) histology, stage IV metastatic NSCLC.^{2,3}
2. In the REVEL trial, ramucirumab+docetaxel demonstrated robust and consistent improvements over docetaxel single agent across the three efficacy endpoints of overall survival, progression-free survival, and objective response rate.³
3. Ramucirumab+docetaxel treatment did not have a negative impact on global quality-of-life scores vs. docetaxel alone.³

Specific Change: We request that the NCCN guidelines use language consistent with the FDA label when describing warnings and precautions for the use of ramucirumab with docetaxel. While the label for ramucirumab does include boxed warnings related to risks for hemorrhage, gastrointestinal perforation, and impaired wound healing, it does not include *contraindications* as currently stated in the NCCN Guidelines version 2.2016 MS-30. We also note the label contains additional warnings and precautions for: arterial thromboembolic events, hypertension, infusion-related reactions, clinical deterioration in patients with cirrhosis, reversible posterior leukoencephalopathy syndrome, proteinuria including nephrotic syndrome, thyroid dysfunction, and embryofetal toxicity.¹

The CYRAMZA® Prescribing Information is included for your review in support of the proposed specific change.

Thank you in advance for your consideration and please do not hesitate to contact us for additional information.

Sincerely,

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References:

1. CYRAMZA Prescribing Information
2. Link to FDA press release of REVEL approval.
<http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm426720.htm>
3. The Lancet 384(9944):665-673, 2014.