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July 19, 2019

NCCN Guidelines Review Panel: Cervical/Uterine Cancer

On behalf of Amgen Inc., I respectfully request the NCCN panel members to review the recently published data on MVASI™ (bevacizumab-awwb), the first therapeutic oncology biosimilar approved by the US Food and Drug Administration (FDA), and the totality of evidence supporting demonstration of biosimilarity to US-licensed AVASTIN® (bevacizumab).

Specific Changes: Based on demonstration of biosimilarity to AVASTIN®, please consider the addition of bevacizumab-awwb as an appropriate substitute to bevacizumab within the NCCN Guidelines, NCCN Patient Guidelines, and the associated “NCCN Drugs and Biologics Compendium™” for the following five cancer types per the FDA-approved MVASI™ label: metastatic colorectal cancer, metastatic non-squamous non-small cell lung cancer, metastatic renal cell carcinoma, recurrent glioblastoma, and cervical cancer.

Rationale: Biosimilars offer the potential to expand treatment options and mitigate cost barriers for payers. FDA approval of MVASI™ was based on a totality of evidence – comparisons of extensive structural and functional product characterization, animal data, pharmacokinetic (PK) and pharmacodynamic data (PD), immunogenicity, safety, and efficacy – demonstrating that MVASI™ is highly similar to AVASTIN® and that there are no clinically meaningful differences between the products.

- The extensive analytical characterization and comparison of the structural and functional properties of MVASI to AVASTIN demonstrated that they are highly similar.
- The PK profile of MVASI was similar to that of AVASTIN in healthy subjects following a single dose and in patients with advanced non–small cell lung cancer (NSCLC) following multiple dosing.
- Clinical comparability data in patients with NSCLC demonstrated clinical similarity (PK, efficacy, safety, immunogenicity) between MVASI and AVASTIN.
 - Sensitive endpoints and patient populations were chosen to identify any potential clinically meaningful differences with the reference biologic, which may differ from those of the pivotal clinical studies for the reference product.
 - Conducting biosimilar studies in a sensitive patient population provides scientific evidence supporting extrapolation to less sensitive and homogenous populations.

In addition to demonstration of biosimilarity, scientific justification was provided to support extrapolation to all available FDA-approved indications of AVASTIN:

- The mechanism of action (MOA) of bevacizumab, regardless of tumor type or location, is the binding and neutralization of VEGF.
- Comparative PK data, combined with the knowledge of the PK profiles of AVASTIN in different patient populations, indicate that MVASI will retain a PK profile similar to AVASTIN in all available FDA-approved indications.
- The immunogenicity was similar in that the treatment of subjects with NSCLC with either MVASI or AVASTIN; few subjects developing binding antidrug antibody (4 [1.4%] and 7 [2.5%] patients, respectively) and no patients developing neutralizing antibodies.

A summary of the totality of evidence and scientific justification for extrapolation is provided in the enclosed Table.

FDA Status: MVASI™ (bevacizumab-awwb) is FDA-approved for use in: metastatic colorectal cancer, metastatic non-squamous non-small cell lung cancer, metastatic renal cell carcinoma, recurrent glioblastoma, and cervical cancer.

Enclosed, please find the following:

- Table. Scientific Justification for Indications of Use for MVASI™
- Thatcher N, Goldschmidt JH, Thomas M, et al. Efficacy and safety of the biosimilar ABP 215 compared with bevacizumab in patients with advanced nonsquamous non-small cell lung cancer (MAPLE): a randomized, double-blind, phase III study. *Clin Cancer Res.* 2019;25:2088-2095.
- Markus R, Chow V, Pan Z, Hanes V. A phase I, randomized, single-dose study evaluating the pharmacokinetic equivalence of biosimilar ABP 215 and bevacizumab in healthy adult men. *Cancer Chemother Pharmacol.* 2017;80:755-763.
- Seoa N, Polozovab A, Zhangb M, et al. Analytical and functional similarity of Amgen biosimilar ABP 215 to bevacizumab. *mAbs.* 2018;10:678-691.

Amgen is providing you with the attached reprint. Please note that if you are a covered recipient as defined by the Affordable Care Act (ACA), Amgen's cost to obtain such reprint may need to be disclosed and reported in accordance with the requirements under the ACA, state law, and related disclosure obligations by Amgen. If you are a non-covered recipient requesting information on behalf of or for the benefit of a covered recipient (physician or teaching hospital), the same requirements may apply.

Should you have any questions or require additional materials, please feel free to contact me directly at +1 (805) 313-4438. Thank you in advance for your prompt attention to this matter and I look forward to your response.

Sincerely,



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