



August 18, 2015

Joan McClure, MS
National Comprehensive Cancer Network
500 Old York Road, Suite 250
Jenkintown, PA 19046

Dear Ms. McClure,

Recently the NCCN Colon/Rectal Cancer Guidelines were updated with the following information: "When an angiogenic agent is used in second-line therapy, bevacizumab is preferred over ziv-aflibercept and ramucirumab, based on toxicity and cost." We request that the panel reconsider the inclusion of the statement on toxicity as there are currently no head-to-head comparative clinical data between ziv-aflibercept and bevacizumab to support this statement. In addition, we request that the panel review the enclosed economic data on ziv-aflibercept and bevacizumab. An economic model factoring costs of agents as well as costs associated with published adverse events and palliative care was developed to evaluate the 1-year projected incremental budget impact with the addition of ziv-aflibercept to FOLFIRI chemotherapy in patients with metastatic colorectal cancer who have progressed following treatment with an oxaliplatin-containing regimen. The model includes five treatment regimens: FOLFIRI alone, ziv-aflibercept + FOLFIRI, bevacizumab + FOLFIRI, cetuximab + FOLFIRI, and panitumumab + FOLFIRI. This model was presented as a poster at the American Society of Clinical Oncology 2015 Gastrointestinal Cancers Symposium.

The enclosed submission contains a copy of the referenced economic data, VELOUR registration study and Zaltrap prescribing information for your review. A presentation of the budget impact model is available upon request.

We appreciate the opportunity to provide this information for consideration by the NCCN Colon/Rectal Cancer Panel. If you have any questions or require additional information, please do not hesitate to contact us at (800) 633-1610, option 1 or via e-mail at medinfo@sanofi.com. Thank you for your time and consideration.

Sincerely,

A handwritten signature in black ink, appearing to read "Julia Petses".

Julia Petses, PharmD
Director, Oncology Medical Information Services
Sanofi U.S.

A handwritten signature in black ink, appearing to read "Ed Drea".

Ed Drea, PharmD
Director, Outcomes Liaisons
Sanofi U.S.

Enclosures: Submission with copy of referenced primary literature

AFL-07243



Name: Julia Petses/ Ed Drea
Company/Organization: Sanofi U.S.
Address: 55 Corporate Drive, Bridgewater, NJ 08807
Phone: (800) 633-1610, option 1
Email: MED.INFO@sanofi.com
Date of request: August 18, 2015
NCCN Guidelines Panel: Colon/Rectal Cancer

On behalf of Sanofi U.S, we respectfully request the NCCN Colon/Rectal Cancer Panel to reevaluate the statement in the guidelines regarding bevacizumab as a preferred agent compared to ziv-aflibercept based on toxicity. In addition, we ask the panel to review the enclosed economic data regarding the cost of ziv-aflibercept and bevacizumab.

Specific Changes: In regards to the use of ziv-aflibercept, removal of the statement "Bevacizumab is the preferred anti-angiogenic agent based on toxicity and cost" in sections COL-11/REC-11, COL-C/REC-E (1 of 9, 3 of 9, and 5 of 9) of the Colon/Rectal Cancer Guidelines and MS-44 in the Colon Cancer Guidelines.

FDA Status: Ziv-aflibercept was approved by the FDA on August 3, 2012, in combination with 5-fluorouracil, leucovorin, irinotecan-(FOLFIRI), for patients with metastatic colorectal cancer (mCRC) that is resistant to or has progressed following an oxaliplatin-containing regimen.

Rationale: There are no head-to-head comparative clinical trials between ziv-aflibercept and bevacizumab and conclusions regarding the toxicity profile of ziv-aflibercept in comparison to bevacizumab cannot be made; in addition, an economic model provides United States managed health plans with an objective and transparent platform to evaluate the 1-year economic impact of the utilization of FOLFIRI alone, ziv-aflibercept + FOLFIRI, bevacizumab + FOLFIRI, cetuximab + FOLFIRI, and panitumumab + FOLFIRI, factoring agent costs as well as the costs associated with published adverse events and palliative care.

References

1. Huff KD, Drea E, Hennessy DD, et al. Budgetary impact of adding ziv-aflibercept to a United States health plan formulary as a post-oxaliplatin biologic option for patients with metastatic colorectal cancer (mCRC) [poster]. Presented at the 2015 Gastrointestinal Cancers Symposium (ASCO-GI), San Francisco, CA, USA, January 15-17, 2015.
2. Van Cutsem E, Tabernero J, Lakomy R, et al. Addition of aflibercept to fluorouracil, leucovorin, and irinotecan improves survival in a phase III randomized trial in patients with metastatic colorectal cancer previously treated with an oxaliplatin-based regimen. *J Clin Oncol.* 2012; 30 (28):3499-3506.
3. Zaltrap [package insert]. Bridgewater, NJ: sanofi-aventis U.S.; 2014.

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