



August 3, 2012

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

Clinical Evidence in Support of Ziv-aflibercept in Combination with 5-Fluorouracil, Leucovorin, Irinotecan-(FOLFIRI) in Patients with Metastatic Colorectal Cancer

Dear Ms. McClure,

On August 3, 2012, Sanofi U.S. received FDA approval on Zaltrap® (ziv-aflibercept) Injection for Intravenous Infusion. Zaltrap is indicated 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. As the NCCN Colon/Rectal Cancer Panel reviews emerging evidence we have enclosed data supporting this indication.

We believe that this clinical evidence warrants a review by the panel for consideration in the Colon/Rectal Cancer NCCN Clinical Practice Guidelines in Oncology and the NCCN Drugs & Biologics Compendium—Colon/Rectal Cancer chapter.

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 me at (866) 662-6411, 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 "JP", is positioned above the printed name of the sender.

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

Enclosures: Submission with copies of referenced primary literature



Name: Julia Petses
Company/Organization: Sanofi U.S.
Address: 55 Corporate Drive, Bridgewater, NJ 08807
Phone: (866) 662-6411, option 1
Email: medinfo@sanofi.com
Date of request: August 3, 2012
NCCN Guidelines Panel: Colon/Rectal Cancer

On behalf of Sanofi U.S, I respectfully request the NCCN Colon/Rectal Cancer Panel to review the enclosed data for inclusion of ziv-aflibercept in combination with 5-fluorouracil, leucovorin, irinotecan-(FOLFIRI) for the treatment of mCRC in patients previously treated with an oxaliplatin-containing regimen.

Specific Changes: Addition of ziv-aflibercept as treatment in mCRC after treatment with an oxaliplatin-containing regimen in the Continuum of Care – Chemotherapy for Advanced or Metastatic Disease section (COL-C and REC-E) of the colon and rectal cancer guidelines.

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

Rationale: Ziv-aflibercept demonstrated significantly longer overall survival and progression free survival compared with placebo, with predictable and manageable adverse events, in patients previously treated with an oxaliplatin-containing regimen.

The following references are submitted in support of this proposed change.

1. Zaltrap® (ziv-aflibercept) Injection for Intravenous Infusion [package insert]. Bridgewater, NJ: Regeneron Pharmaceuticals, Inc./sanofi-aventis U.S. LLC; 2012.
2. Van Cutsem E, Tabernero J, Lakomy R, et al. Intravenous (IV) ziv-aflibercept versus placebo in combination with irinotecan/5-FU (FOLFIRI) for second-line treatment of metastatic colorectal cancer (mCRC): results of a multinational phase III trial (EFC10262-VELOUR) [abstract]. *Ann Oncol*. 2011;22(suppl 5):v18. Abstract O-0024.
3. Van Cutsem E, Tabernero J, Lakomy R, et al. Intravenous (IV) ziv-aflibercept versus placebo in combination with irinotecan/5-FU (FOLFIRI) for second-line treatment of metastatic colorectal cancer (mCRC): results of a multinational phase III trial (EFC10262-VELOUR). Presented at the 13th European Society for Medical Oncology World Congress on Gastrointestinal Cancer. Barcelona, Spain, June 22-25, 2011. Abstract O-0024.
4. Tabernero J, Van Cutsem E, Lakomy R, et al. Results from VELOUR, a phase 3 study of ziv-aflibercept versus placebo in combination with FOLFIRI for the treatment of patients with previously treated metastatic colorectal cancer [abstract]. *Eur J Cancer*. 2011;47(suppl 2):5-5. Abstract 6LBA.
5. Tabernero J, Van Cutsem E, Lakomy R, et al. Results from VELOUR, a phase 3 study of ziv-aflibercept versus placebo in combination with FOLFIRI for the treatment of patients with previously treated metastatic colorectal cancer: results from respecified subgroup analyses. Presented at the 2011 European Multidisciplinary Cancer Congress. Stockholm, Sweden, September 23-27, 2011. Abstract LBA6.
6. Allegra C, Tabernero J, Lakomy J et al. Effects of prior bevacizumab use on outcomes from the VELOUR study: a phase 3 study of ziv-aflibercept and FOLFIRI in patients with metastatic colorectal cancer after failure of an oxaliplatin regimen. Presented at: 48th Annual American Society of Clinical Oncology Meeting, Chicago, IL, USA, June 1-5, 2012. Abstract 3505.
7. Allegra CJ, Lakomy R, Tabernero J, et al. Effects of prior bevacizumab (B) use on outcomes from the VELOUR study: a phase III study of ziv-aflibercept (Afl) and FOLFIRI in patients (pts) with metastatic colorectal cancer (mCRC) after failure of an oxaliplatin regimen [abstract]. *J Clin Oncol*. 2012;30(15 suppl). Abstract 3505.