SANOFI GENZYME

May 15, 2017

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

Dear Ms. McClure and Panel Chairs:

We are writing in regards to the NCCN Colon/Rectal Cancer Guidelines and specifically the following statement: "When an angiogenic agent is used in second-line therapy, bevacizumab is preferred over ziv-aflibercept, based on toxicity and/or cost." We are requesting that the panel reconsider the inclusion of the statement on comparative toxicity as there are currently no head-to-head comparative clinical data between ziv-aflibercept and bevacizumab to support this statement. Recently the 5th interim report (year 4) of the ongoing global Aflibercept Safety and Quality-of-Life Program (ASQoP) was presented at the European Society of Medical Oncology (ESMO) 2016 Meeting and no new safety signals were reported.[1] These data are corroborated by the results of the 2nd interim analysis of QoLiTrap[2] presented at the American Society of Clinical Oncology Gastrointestinal Cancers Symposium (ASCO-GI) 2016 as well as the retrospective analysis conducted via the Gallego Research Group Digestive Tumors (GITUD)[3] and presented at the World Congress on Gastrointestinal Cancer (July 2016).

We also request that the panel reconsider the statement that "bevacizumab is preferred over ziv-aflibercept based on cost". When addressing the cost for ziv-aflibercept, it is important to reference the actual cost to clinicians and payer organizations. The average sales price (ASP) plus 6% is the Centers for Medicare and Medicaid Services (CMS)-derived 'ASP Payment Limit' and is the most accurate actual cost basis for clinicians and payers. For ziv-aflibercept, the CMS-established 'ASP Payment Limit' is $8.122 per 1 mg as of April 6th 2017.[4] The CMS-published Payment Limit ASP and a table of the costs of second-line colorectal cancer therapies based on FDA-indicated dosing and the CMS Payment Limit ASP are enclosed (Table 1).[4]

A population-based economic model factoring costs of agents as well as costs associated with adverse events and palliative care was developed to evaluate the 1-year projected incremental economic 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.[5] The model is an objective, referenced, and transparent platform to evaluate the 1-year economic impact of the utilization of five treatment regimens: FOLFIRI alone, FOLFIRI + ziv-aflibercept, FOLFIRI + bevacizumab, FOLFIRI + cetuximab, and FOLFIRI + panitumumab. Modest cost savings are derived for the use of ziv-aflibercept over bevacizumab. This model was presented as a poster at the Academy of Managed Care and Specialty Pharmacy 2016 Annual Meeting.

The enclosed submission contains copies of all referenced publications as well as the ASP Payment Limit per treatment cycle of each agent for a 70kg patient and an objective graphic that illustrates the range of weight-based dosing (Table 1 and Chart 1).

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 contact us at (800) 633-1610, option 1 or via e-mail at med.info@sanofi.com. Thank you for your time and consideration of this request.

Sincerely,

Ed Drea, PharmD
Director, Medical Managed Care – Oncology
Sanofi-Genzyme U.S.

Rebecca Falcone, PharmD
Senior Manager, Medical Information
Sanofi-Genzyme U.S.

Enclosures: ASQoP 5th Interim Report Poster, QoLiTrap Poster, GITUD Poster, Ziv-aflibercept Budget Impact Model Poster, CMS.gov ASP Payment Limits - Table 1 and Chart 1

Name: Ed Drea/ Rebecca Falcone
Company/Organization: Sanofi-Genzyme U.S.
Address: 55 Corporate Drive, Bridgewater, NJ 08807
Phone: (800) 633-1610, option 1
Email: MED.INFO@sanofi.com
Date of request: May 15, 2017

NCCN Guidelines Panel: Colon/Rectal Cancer

On behalf of Sanofi-Genzyme U.S, we respectfully request the NCCN Colon/Rectal Cancer Panel to evaluate the statement in the guidelines regarding bevacizumab as a preferred agent compared to ziv-aflibercept based on "toxicity and/or cost" (Colon Cancer v2.2017, MS-50). In support of this request, we ask the panel to review the enclosed 5th interim report of the ongoing (now 4 year) real world global Aflibercept Safety and Quality-of-Life (ASQoP) study[1] and additionally published safety data.[2,3] Published cost data[4] and a published economic model for the cost of ziv-aflibercept in comparison to bevacizumab[5] is also included.

Specific Changes: Specific to ziv-aflibercept,

- Removal of the statement "Bevacizumab is the preferred anti-angiogenic agent based on toxicity and/or cost" in sections REC-11 footnote bb, REC-E (2 of 10, 5 of 10, and 6 of 10 footnote 9) of the Rectal Cancer Guidelines and, COL-C 2 of 10, COL-C 5 of 10, and reference to footnote 9 on COL-C 6 of 10, and MS-50 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.[6,7] The FDA-approved dose is 4 mg/kg every 2 weeks by intravenous infusion.[7]

Rationale: As there are no head-to-head comparative clinical trials between ziv-aflibercept and bevacizumab or ramucirumab, ongoing monitoring of real world safety via the published ASQoP safety study[1], the QoLiTrap[2] and GITUD[3] studies provide no new ziv-aflibercept safety signal; in addition, based on the CMS-published ASP Payment Limit[4], a published economic model for FDA-approved biologics for second-line management of metastatic colorectal cancer[5], and ziv-aflibercept dosed per FDA-approved indication and relative to bevacizumab[8] and ramucirumab[9] FDA-approved dosing (Table 1), ziv-aflibercept is less costly or comparable in cost to bevacizumab across the spectrum of dosing based on patient weight (Chart 1); this rationale appears to be supported by the NCCN Evidence Blocks of COL-C EB-2 and REC-E EB-2.

References

1. Riechelmann R, Srimuninnimit V, Kavan P, Di Bartolomeo M, Maiello E, Cicin I, Garcia-Alfonso P, Chau I, Fernandez-Martos C, Ter-Ovanesov M, Peeters M, Picard P, Bordonaro R. Aflibercept plus FOLFIRI for 2nd line treatment of metastatic colorectal cancer (mCRC): Long-term safety observation from the global Aflibercept Safety and Quality-of-Life (QOL) Program (ASQoP) [poster]. Presented at the European Society of Medical Oncology (ESMO) Meeting, Copenhagen, Denmark, October 7-11, 2016.
2. Hofheinz R-D, Thaler J, von Moos R. Analysis of the quality of life (QoL) and therapy management in patients treated with aflibercept and FOLFIRI for metastatic colorectal cancer (mCRC) – Interim results from the non-interventional QoLiTrap study [poster]. Presented at Gastrointestinal Cancers Symposium (ASCO). San Francisco, CA. January 21-23, 2016.
3. Fernandez Montes A, Martinez Lago N, Covela Rua M, D la Camara Gomez J, Gonzalez Villaroel P, Mendez Mendez C. Efficacy and toxicity of FOLFIRI/aflibercept in second line colorectal cancer in real life population, retrospective study. Dos first line matters? Presented at the 18th World Congress on Gastrointestinal Cancer. Barcelona, Spain. June 29 – July 2, 2016.
4. APR17 ASP Pricing File 031017 at https://www.cms.gov accessed April 6, 2017.
5. Huff KD, Drea EJ, Thompson SF, Dhawan R. 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 2016 Academy of Managed Care and Specialty Pharmacy (AMCP) Annual Meeting, San Francisco, CA, USA, April 19-22, 2016.
6. 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.
7. Zaltrap Prescribing Information. sanofi-aventis: Bridgewater, NJ, US; 6/2016.
8. Avastin Prescribing Information. Genentech: South San Francisco, CA, US; 12/2016.
9. Cyramza Prescribing Information. Eli Lilly: Indianapolis, IN, US; 3/2017

Sincerely,

Ed Drea, PharmD
Director, Medical Managed Care – Oncology
Sanofi-Genzyme U.S.

Rebecca Falcone, PharmD
Senior Manager, Medical Information
Sanofi-Genzyme U.S.