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Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

Retired
Effective Date: 02/02/2023

Zaltrap[®] (ziv-aflibercept)

HCPCS: J9400

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Criteria:

- a. Diagnosis of metastatic colorectal, anal, small bowel, or appendiceal adenocarcinomas
 - i. Resistant to or progressed following treatment with oxaliplatin-based therapy
- b. Must be used in combination with FOLFIRI in a FOLFIRI naïve patient
- c. Neutrophils at treatment initiation must be $\geq 1.5 \times 10^9/L$
- d. Prescribed by or in consultation with an oncologist
- e. Should not be used if prior treatment failure has occurred with Zaltrap

B. Quantity Limitations, Authorization Period and Renewal Criteria

- a. Quantity Limits: Align with FDA recommended dosing
- b. Authorization Period: Aligns with FDA recommended or guideline supported treatment duration and provided for up to 6 months at a time
- c. Renewal Criteria: Clinical documentation must be provided to confirm that current criteria are met and that the medication is providing clinical benefit

***Note: Coverage may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at <http://www.cms.hhs.gov/>. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Zaltrap is a vascular endothelial growth factor inhibitor indicated in combination with fluorouracil, leucovorin, and irinotecan (FOLFIRI) for the treatment of patients with metastatic colorectal cancer that is resistant to or has progressed following an oxaliplatin-containing regimen.

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- Current National Comprehensive Cancer Network (NCCN) 2022 treatment guidelines for colon cancer state that appendiceal adenocarcinoma may be treated with systemic chemotherapy according to colon cancer recommendations.
- The 2022 NCCN anal cancer guidelines state adenocarcinoma of the anus should be treated following the 2022 NCCN rectal cancer treatment guidelines. They recommend use of Zaltrap with FOLFIRI for metastatic anal cancer following an oxaliplatin-containing regimen.
- Small bowel adenocarcinomas are rare cancers and the limited data for therapy consists mainly of small retrospective reports and case series. While new NCCN treatment guidelines for small bowel adenocarcinoma do not recommend use of Zaltrap, older versions of the NCCN colon cancer guidelines state small bowel adenocarcinomas may be treated with systemic chemotherapy according to colon cancer recommendations.
- Treatment guidelines state that Zaltrap has only shown activity when given in conjunction with FOLFIRI in FOLFIRI naïve patients. Additionally, NCCN reports a lack of data to suggest activity of FOLFIRI with Zaltrap in individuals who progressed on FOLFIRI plus bevacizumab or vice-versa, and no data to suggest activity of single agent zivafibercept. NCCN recommends adding Zaltrap as a second-line treatment option in combination with FOLFIRI or irinotecan only following progression on therapy not containing irinotecan.
- There are no studies to support use of Zaltrap following failure of its use. NCCN guidelines also do not recommend use of Zaltrap following a previous failure.
- Safety and efficacy was evaluated in the VELOUR trial, a multinational, randomized, double-blind study of 1,226 patients with metastatic colorectal cancer who progressed on oxaliplatin-based combination chemotherapy, or whose cancer was removed by surgery but returned within 6 months after receiving oxaliplatin-based combination chemotherapy for post-surgery (adjuvant) treatment. Participants received treatment until their cancer progressed or side effects became unacceptable. The study was designed to measure overall survival (OS). Patients who were assigned to receive the Zaltrap plus FOLFIRI combination lived an average of 13.5 months compared to an average of 12 months for those on the FOLFIRI plus placebo arm. The PFS for patients receiving the Zaltrap plus FOLFIRI combination was 6.9 months compared with 4.7 months for those receiving FOLFIRI plus placebo.

References:

1. Zaltrap [prescribing information]. Bridgewater, NJ: Sanofi-Aventus, U.S. LLC; December 2020.
2. National Comprehensive Cancer Network. Colon cancer (Version 1.2022). 2022 Feb 25. Available at: https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Accessed on August 24, 2022.
3. National Comprehensive Cancer Network. Anal carcinoma (Version 1.2022). 2022 March 2. Available at: https://www.nccn.org/professionals/physician_gls/pdf/anal.pdf. Accessed on August 24, 2022.
4. National Comprehensive Cancer Network. Rectal cancer (Version 1.2022). 2022 Feb 25. Available at: https://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf. Accessed on August 24, 2022.
5. National Comprehensive Cancer Network. Small bowel adenocarcinoma (Version 1.2022). 2022 March 9. Available at: https://www.nccn.org/professionals/physician_gls/pdf/small_bowel.pdf. Accessed on August 24, 2022.
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 - 506.

Policy History												
#	Date	Change Description										
2.2	Effective Date: 02/02/2023	Retiring policy as drug will no longer be part of the prior authorization program										
2.1	Effective Date: 10/06/2022	Updated approval length to allow for FDA recommended dosing or up to 6 months at a time										
2.0	Effective Date: 10/07/2021	Annual review of criteria was performed, no changes were made										
1.9	Effective Date: 12/01/2020	UM medical management system update for BCBS <table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>Yes</td></tr><tr><td>BCNA</td><td>Yes</td></tr></table>	Line of Business	PA Required in Medical Management System (Yes/No)	BCBS	Yes	BCN	Yes	MAPPO	Yes	BCNA	Yes
Line of Business	PA Required in Medical Management System (Yes/No)											
BCBS	Yes											
BCN	Yes											
MAPPO	Yes											
BCNA	Yes											
1.8	Effective Date: 10/08/2020	Annual Review										
1.7	Effective Date: 01/01/2020	UM medical management system update for BCNA and MAPPO <table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>No</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>Yes</td></tr><tr><td>BCNA</td><td>Yes</td></tr></table>	Line of Business	PA Required in Medical Management System (Yes/No)	BCBS	No	BCN	Yes	MAPPO	Yes	BCNA	Yes
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BCBS	No											
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BCNA	Yes											
1.6	Effective Date: 11/07/2019	Annual Review of Medical Policy										
1.5	Effective Date: 08/01/2019	UM medical management system update for BCN <table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>No</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>No</td></tr><tr><td>BCNA</td><td>No</td></tr></table>	Line of Business	PA Required in Medical Management System (Yes/No)	BCBS	No	BCN	Yes	MAPPO	No	BCNA	No
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BCBS	No											
BCN	Yes											
MAPPO	No											
BCNA	No											
1.4	Effective Date: 11/01/2018	Updated criteria per oncology vendor										
1.3	Effective Date: 08/09/2018	Annual Review of Medical Policy										
1.2	Effective Date: 08/10/2017	Annual Review of Medical Policy										
1.1	Effective Date: 08/11/2016	Annual Review of Medical Policy										

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1.0	Effective Date: 11/08/2012	New Policy	
		Line of Business	PA Required in Medical Management System (Yes/No)
		BCBS	No
		BCN	No
		MAPPO	No
		BCNA	No

** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or <http://dailymed.nlm.nih.gov/dailymed/index.cfm>.*