Zaltrap® (ziv-aflibercept)
(Intravenous)

Document Number: IC-0161

Last Review Date: 03/03/2020
Date of Origin: 02/07/2013
Dates Reviewed: 12/2013, 03/2014, 06/2014, 09/2014, 12/2014, 03/2015, 05/2015, 08/2015, 11/2015, 02/2016, 05/2016, 08/2016, 11/2016, 02/2017, 05/2017, 08/2017, 11/2017, 2/2018, 5/2018, 09/2018, 12/2018, 03/2019, 06/2019, 9/2019, 12/2019, 03/2020

I. Length of Authorization

Coverage will be provided for six months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Zaltrap 100 mg injection: 2 vials per 28 days
- Zaltrap 200 mg injection: 4 vials per 28 days

B. Max Units (per dose and over time) [HCPCS Unit]:

- 500 billable units every 14 days

III. Initial Approval Criteria[1,2,6]

Coverage is provided in the following conditions:

Universal Criteria [1,6]

- Patient must have no recent history of hemorrhage or hemoptysis (the presence of blood in sputum); AND
- Patient must not have had a surgical procedure within the preceding 28 days or have a surgical wound that has not fully healed; AND

Colorectal Cancer[1,2,6] †

- Patient is at least 18 years old; AND
- Must be used in combination with irinotecan or FOLFIRI (fluorouracil, leucovorin, and irinotecan) regimen; AND
  - Patient has metastatic disease that is resistant to or has progressed following an oxaliplatin-containing regimen (e.g., FOLFOX, CapeOX) †; OR
  - Used as primary treatment for patients with unresectable metachronous metastases; AND

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- Patient has received previous adjuvant FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin) within the past 12 months; **OR**

- Used as subsequent therapy for progression of unresectable advanced or metastatic disease in a patient who has not previously received irinotecan-based therapy

† FDA-labeled indication(s), ‡ Compendia Recommended Indication(s)

IV. Renewal Criteria[1,2]

Coverage can be renewed based upon the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Tumor response with stabilization of disease or decrease in size or spread of tumor; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: hemorrhage, gastrointestinal perforation, fistula formation, hypertension, wound healing complications, arterial thromboembolic events, proteinuria, neutropenic complications, reversible posterior leukoencephalopathy syndrome (RPLS), severe diarrhea/dehydration, etc.

V. Dosage/Administration[1,2]

Indication	Dose
Colorectal cancer	4 mg/kg as an intravenous (IV) infusion over 1 hour every two weeks, until disease progression or unacceptable toxicity.

VI. Billing Code/Availability Information

HCPCS:

- J9400 – Injection, ziv-aflibercept, 1 mg; 1 billable unit = 1 mg

NDC:

- Zaltrap 100 mg/4 mL solution, single-use vial: 00024-5840 -xx
- Zaltrap 200 mg/8 mL solution, single-use vial: 00024-5841 -xx

VII. References

1. Zaltrap [package insert]. Bridgewater, NJ; Sanofi-Aventis U.S. LLC; December 2019. Accessed January 2020.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) ziv-aflibercept. National Comprehensive Cancer Network, 2020. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most

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recent and complete version of the Compendium, go online to NCCN.org. Accessed January 2020.
3. Fahrenbruch R, Kintzel P, Bott AM, et al. Dose Rounding of Biologic and Cytotoxic Anticancer Agents: A Position Statement of the Hematology/Oncology Pharmacy Association. J Oncol Pract. 2018 Mar;14(3):e130-e136.
4. Hematology/Oncology Pharmacy Association (2019). *Intravenous Cancer Drug Waste Issue Brief*. Retrieved from http://www.hoparx.org/images/hopa/advocacy/Issue-Briefs/Drug_Waste_2019.pdf
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6. Tabernero J, Paccard C, Chiron M, et al. Placental growth factor and the angiogenic environment based on analysis of baseline plasma biomarkers from the VELOUR trial. Journal of Clinical Oncology35, no. 4_suppl(February 01, 2017)592-592. DOI: 10.1200/JCO.2017.35.4_suppl.592
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8. Sanofi. A Multinational, Randomized, Double-blind Study, Comparing the Efficacy of Aflibercept Once Every 2 Weeks Versus Placebo in Patients With Metastatic Colorectal Cancer (MCRC) Treated With Irinotecan / 5-FU Combination (FOLFIRI) After Failure of an Oxaliplatin Based Regimen. Available from: https://clinicaltrials.gov/ct2/show/NCT00561470?term=NCT00561470&draw=2&rank=1. ClinicalTrials.gov Identifier: NCT00561470. Accessed January 2020.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C17.0	Malignant neoplasm duodenum
C17.1	Malignant neoplasm jejunum
C17.2	Malignant neoplasm ileum
C17.8	Malignant neoplasm of overlapping sites of small intestines
C17.9	Malignant neoplasm of small intestine, unspecified
C18.0	Malignant neoplasm of cecum
C18.1	Malignant neoplasm of appendix
C18.2	Malignant neoplasm of ascending colon
C18.3	Malignant neoplasm of hepatic flexure
C18.4	Malignant neoplasm of transverse colon
C18.5	Malignant neoplasm of splenic flexure
C18.6	Malignant neoplasm of descending colon
C18.7	Malignant neoplasm of sigmoid colon
C18.8	Malignant neoplasm of overlapping sites of large intestines

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ICD-10	ICD-10 Description
C18.9	Malignant neoplasm of colon, unspecified
C19	Malignant neoplasm of rectosigmoid junction
C20	Malignant neoplasm of rectum
C21.8	Malignant neoplasm of overlapping sites of rectum, anus and anal canal
C78.00	Secondary malignant neoplasm of unspecified lung
C78.01	Secondary malignant neoplasm of right lung
C78.02	Secondary malignant neoplasm of left lung
C78.6	Secondary malignant neoplasm of retroperitoneum and peritoneum
C78.7	Secondary malignant neoplasm of liver and intrahepatic bile duct
Z85.038	Personal history of other malignant neoplasm of large intestine
Z85.068	Personal history of other malignant neoplasm of small intestine

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Articles may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/Article):

Jurisdiction(s): J-M	**NCD/LCD/Article Document (s):** A56141
https://www.cms.gov/medicare-coverage-database/search/article-date-search.aspx?DocID=A56141&bc=gAAAAAAAAAAA	

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC

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Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

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