



Zaltrap® (ziv-aflibercept) (Intravenous)

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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:

Colorectal Cancer † ^{1,2,6}

- Patient is at least 18 years of age; **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**
 - Patient 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 advanced or metastatic disease in patients not previously treated with 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 indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Disease response with treatment a defined by 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, uncontrolled hypertension, hypertensive crisis, hypertensive encephalopathy, wound healing complications, arterial thromboembolic events, proteinuria (≥ 2 g/24 hours), nephrotic syndrome, thrombotic microangiopathy (TMA), neutropenic complications, reversible posterior leukoencephalopathy syndrome (RPLS), severe diarrhea/dehydration, etc.

V. Dosage/Administration ^{1,2}

| Indication | Dose |
|-------------------|--|
| Colorectal cancer | 4 mg/kg of actual body weight as an intravenous (IV) infusion every two weeks, until disease progression or unacceptable toxicity. |

VI. Billing Code/Availability Information

HCPCS Code:

- 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; June 2020. Accessed August 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 recent and complete version of the Compendium, go online to NCCN.org. Accessed August 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
5. Bach PB, Conti RM, Muller RJ, et al. Overspending driven by oversized single dose vials of cancer drugs. *BMJ.* 2016 Feb 29;352:i788.
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 Oncology*35, no. 4_suppl(February 01, 2017)592-592. DOI: 10.1200/JCO.2017.35.4_suppl.592
7. 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.
8. Palmetto GBA. Local Coverage Article (LCA) for Billing and Coding of Chemotherapy (A56141). Centers for Medicare & Medicaid Services. Updated on 5/26/2020 with effective date 4/30/2020. Accessed August 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 |
| C18.9 | Malignant neoplasm of colon, unspecified |

| ICD-10 | ICD-10 Description |
|---------|--|
| 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 Local Coverage Articles (LCAs) 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/LCA):

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

| 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 |
| L (12) | DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA) | Novitas Solutions, Inc. |

Medicare Part B Administrative Contractor (MAC) Jurisdictions

| Jurisdiction | Applicable State/US Territory | Contractor |
|--------------|-------------------------------|--|
| K (13 & 14) | NY, CT, MA, RI, VT, ME, NH | National Government Services, Inc. (NGS) |
| 15 | KY, OH | CGS Administrators, LLC |