Clinical Policy: Ziv-aflibercept (Zaltrap)

Reference Number: LA.PHAR.325
Effective Date: 11.04.23
Last Review Date: 04.09.24 ~~06.16.23~~ Coding Implications
Line of Business: Medicaid Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

****Please note: This policy is for medical benefit****

Description
Ziv-aflibercept (Zaltrap®) is a vascular endothelial growth factor (VEGF) inhibitor.

FDA Approved Indication(s)
Zaltrap, in combination with 5-fluorouracil, leucovorin, irinotecan (FOLFIRI), is indicated for patients with metastatic colorectal cancer (CRC) that is resistant to or has progressed following an oxaliplatin-containing regimen.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of Louisiana Healthcare Connections that Zaltrap is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Colorectal Cancer (must meet all)**:**

1. Diagnosis of advanced, unresectable, or metastatic CRC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Previous treatment with one of the following (a, b, or c):
   a. An oxaliplatin-containing regimen (e.g., FOLFOX, CapeOX);
   b. A 5-fluorouracil and leucovorin-containing regimen (off-label);
   c. A capecitabine-containing regimen (off-label);
5. Prescribed in combination with irinotecan or FOLFIRI;
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 4 mg/kg every 2 weeks;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

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B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: LA.PMN.53 for Medicaid.

II. Continued Therapy

A. Colorectal Cancer (must meet all)**:**
1. Currently receiving medication via Louisiana Healthcare Connections benefit, or documentation supports that member is currently receiving Zaltrap for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed 4 mg/kg every 2 weeks;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence)*.

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

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B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: LA.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – LA.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CapeOX: capecitabine and oxaliplatin
CRC: colorectal cancer
FDA: Food and Drug Administration
FOLFIRI: fluorouracil, leucovorin, irinotecan
FOLFOX: fluorouracil, leucovorin, oxaliplatin
VEGF: vascular endothelial growth factor

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Modified FOLFOX 6	Day 1: oxaliplatin 85 mg/m^2 IV Day 1: Folinic acid 400 mg/m^2 IV Days 1–3: 5-FU 400 mg/m^2 IV bolus on day 1, then 1,200 mg/m^2/day × 2 days (total 2,400 mg/m^2 over 46–48 hours) IV continuous infusion. Repeat cycle every 2 weeks.	See dosing regimen
CapeOX	Day 1: Oxaliplatin 130 mg/m^2 IV Days 1–14: Capecitabine 1,000 mg/m^2 PO BID. Repeat cycle every 3 weeks.	See dosing regimen
FOLFIRI	Day 1: Irinotecan 180 mg/m^2 IV Day 1: Leucovorin 400 mg/m^2 IV Day 1: ~~Flurouracil~~Fluorouracil 400 mg/m^2 IV followed by 2400 mg/m^2 continuous IV over 46 hours Repeat cycle every 14 days.	See dosing regimen
5-fluorouracil and leucovorin	Roswell Park regimen: Leucovorin 500 mg/m^2 IV followed by 5-FU 500 mg/m^2 IV bolus one hour after start of leucovorin on days 1, 8, 15, 22, 29, 36. Repeat every 8 weeks. Biweekly regimen: Leucovorin 400 mg/m^2 IV on day one followed by 5-FU 400 mg/m^2 IV bolus then 1,200 mg/m^2 continuous IV. Repeat every 2 weeks. Weekly regimen: Leucovorin 20 mg/m^2 IV on day one followed 5-FU 500 mg/m^2 IV bolus one hour after start of leucovorin. Alternatively 5-FU 2,600 mg/m^2 ~~continous~~continuous IV with leucovorin 500 mg/m^2 IV. Repeat weekly.	See dosing regimen
capecitabine	850 – 1,250 mg/m^2 PO BID on days 1-14. Repeat every 3 weeks.	2,500 mg/m^2/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
None reported

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V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CRC	4 mg/kg IV over 1 hour every two weeks	4 mg/kg

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VI. Product Availability

Single-use vials for injection: 100 mg/4 mL, 200 mg/8 mL

VII. References

1. Zaltrap Prescribing Information. Bridgewater, NJ: Sanofi-Aventis U.S., LLC; December 2020. Available at~~:~~ http://www.zaltrap.com/. Accessed ~~August 5, 2022~~July 7, 2023.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed August ~~5, 2022~~15, 2023.
3. National Comprehensive Cancer Network. Colon Cancer Version ~~1.2022~~2.2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Accessed August ~~5, 2022~~15, 2023.
4. National Comprehensive Cancer Network. Rectal Cancer Version ~~1.2022~~4.2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf. Accessed August ~~5, 2022~~15, 2023.

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Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9400	Injection, ziv-aflibercept, 1 mg

Reviews, Revisions, and Approvals	Date	LDH Approval Date
Converted corporate to local policy.	06.16.23	10.05.23
Annual review: no significant changes; references reviewed and updated.	04.09.24	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

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This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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