Clinical Policy: Ziv-aflibercept (Zaltrap)

Reference Number: CP.PHAR.325
Effective Date: 03.01.17
Last Review Date: 11.17
Line of Business: Medicaid

Revision Log

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

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 (which may include office chart notes and lab results) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Zaltrap is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of CRC;
2. Age ≥ 18 years;
3. Member meets a or b:
   a. FDA approved use (i and ii):
      i. For metastatic CRC as subsequent therapy in combination with FOLFIRI*;
      ii. Disease is resistant to or has progressed following an oxaliplatin-containing regimen;
   b. Off-label NCCN recommended use (i or ii):
      i. As primary therapy:
         a) For unresectable metastases and previous adjuvant FOLFOX or CapeOX therapy *(see Appendix B for definitions of "adjuvant", FOLFOX and CapeOx)* within the past 12 months (1 or 2):
            1) In combination with irinotecan;
            2) In combination with FOLFIRI *(see Appendix B for definition of FOLFIRI)*;
      ii. As subsequent therapy (a and b):
         a) After first progression of unresectable advanced or metastatic disease;

b) In combination with irinotecan or FOLFIRI *(see Appendix B for definition of FOLFIRI)* for disease not previously treated with irinotecan-based therapy;

4. 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*).

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy (e.g., no disease progression);
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)*.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 – CP.PHAR.57 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: General Information

- Adjuvant therapy is defined as therapy administered after the main treatment to help decrease the risk of cancer recurring.
- FOLFIRI is fluorouracil, leucovorin, irinotecan; FOLFOX is fluorouracil, leucovorin, oxaliplatin; CapeOX is capecitabine and oxaliplatin.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Colorectal cancer	4 mg/kg as an intravenous infusion over 1 hour every two weeks	4 mg/kg

VI. Product Availability

Injection: 100 mg/4 mL, 200 mg/8 mL

VII. References

1. Zaltrap prescribing information. Bridgewater, NJ: Sanofi-Aventis U.S., LLC; June 2016. Available at http://products.sanofi.us/zaltrap/Zaltrap.pdf. Accessed August 24, 2017.
2. Ziv-aflibercept. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at NCCN.org. Accessed August 24, 2017.
3. Colon cancer (Version 2.2017). In: National Comprehensive Cancer Network Guidelines. Available at NCCN.org. Accessed August 24, 2017.
4. Rectal cancer (Version 3.2017). In: National Comprehensive Cancer Network Guidelines. Available at NCCN.org. Accessed August 24, 2017.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy split from CP.PHAR.182 Excellus Oncology. NCCN off-label recommended uses added.	01.17	03.17
- Added age limit and removed safety-related criteria per the PA Policy for Safety Precautions. - Changed 3/6 month approval durations to 6/12 months.	08.29.17	11.17

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. The Health Plan 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. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

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.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.