RXADVANCE
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| Clinical Policy Title: | ziv-aflibercept |
|---|---|
| Policy Number: | RxA.327 |
| Drug(s) Applied: | Zaltrap® |
| Original Policy Date: | 02/07/2020 |
| Last Review Date: | 09/14/2020 |
| Line of Business Policy Applies to: | All lines of business |

## Background

Ziv-aflibercept (Zaltrap®) is a vascular endothelial growth factor (VEGF) inhibitor. Zaltrap®, in combination with 5-fluorouracil, leucovorin, irinotecan (FOLFIRI), is indicated for patients with metastatic colorectal cancer (mCRC) that is resistant to or has progressed following an oxaliplatin-containing regimen.

## Dosing Information

| Drug Name | Indication | Dosing Regimen | Maximum Dose |
|---|---|---|---|
| Ziv-aflibercept (Zaltrap®) | mCRC | 4 mg/kg IV over 1 hour every two weeks | 4 mg/kg |

## Dosage Forms

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

## Clinical Policy

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

**I. Initial Approval Criteria**

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

1. Diagnosis of mCRC;
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**
**Commercial:** 6 months
**Medicaid:** 6 months
**HIM:** 6 months (for Zaltrap 100 mg/4 mL)

**II. Continued Therapy Approval**

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

1. Currently receiving medication that has been authorized by RxAdvance, 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**
**Commercial:** 6 months
**Medicaid:** 12 months
**HIM:** 12 months (for Zaltrap 100 mg/4 mL)

**III. Appendices**

**APPENDIX A: Abbreviation/Acronym Key**
CapeOX: capecitabine and oxaliplatin
mCRC: metastatic 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 100 mg/m2 IV<br>Day 1: Folinic acid 400 mg/$m^2$ IV<br>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.<br>Repeat cycle every 2 weeks. | See dosing regimen |

| | | |
|---|---|---|
| CapeOX | Day 1: Oxaliplatin 130 mg/m$^2$ IV<br>Days 1–14: Capecitabine 1,000 mg/m$^2$ PO BID.<br>Repeat cycle every 3 weeks. | See dosing regimen |
| FOLFIRI | Day 1: Irinotecan 180 mg/m$^2$ IV<br>Day 1: Leucovorin 400 mg/m$^2$ IV<br>Day 1: Flurouracil 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:<br>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.<br><br>Biweekly regimen:<br>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.<br><br>Weekly regimen:<br>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$^2$ continuous IV with leucovorin 500 mg/m$^2$ IV.<br><br>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**

- Contraindication(s):
  - None reported

- Boxed Warning(s):
  - Hemorrhage, gastrointestinal perforation, compromised wound healing

**APPENDIX D: General Information**

- Not applicable

**References**

1. Zaltrap Prescribing Information. Bridgewater, NJ: Sanofi-Aventis U.S., LLC; Revised November 2019. Available at http://www.zaltrap.com/. Accessed June 24, 2020.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed June 24, 2020.
3. National Comprehensive Cancer Network. Colon Cancer Version 2.2019. Available at: https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Accessed June 24, 2020.
4. National Comprehensive Cancer Network. Rectal Cancer Version 2.2019. Available at: https://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf. Accessed June 24, 2020.

| Review/Revision History | Review/Revised Date | P&T Approval Date |
|---|---|---|
| Policy established. | 01/2020 | 02/07/2020 |
| Policy was reviewed:<br>1. Clinical Policy Title was updated<br>2. Drug(s) Applied was updated<br>3. Line of Business Policy Applies to was updated<br>4. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..."<br>5. Commercial approval duration, Medicaid approval duration and HIM approval duration updated.<br>6. References were updated<br>7. Updated APPENDIX B: Therapeutic Alternatives for Modified FOLFOX 6 dosing regimen Day 1: oxaliplatin added 100 mg/m2 IV<br>8. Updated Initial Approval Criteria and Appendix A from CRC to mCRC | 06/24/2020 | 09/14/2020 |