PRIOR AUTHORIZATION POLICY

POLICY: Oncology (Injectable) – Zaltrap Prior Authorization Policy
- Zaltrap® (ziv-aflibercept intravenous infusion – Regeneron/Sanofi-Aventis)

REVIEW DATE: 10/16/2024; selected revision 10/30/2024

OVERVIEW

Zaltrap, a vascular endothelial growth factor inhibitor, is indicated in combination with FOLFIRI (5-fluorouracil [5-FU], leucovorin, and irinotecan), for **metastatic colorectal cancer** in patients with disease that is resistant to or has progressed following an oxaliplatin-containing regimen.[1]

Guidelines

The National Comprehensive Cancer Network (NCCN) **colon cancer** guidelines (version 5.2024 – August 22, 2024) and **rectal cancer** guidelines (version 4.2024 – August 22, 2024) recommend Zaltrap as: [2-4]

- Initial treatment for patients with unresectable metachronous metastases and previous FOLFOX (5-FU, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin) regimens within the past 12 months in combination with irinotecan OR with FOLFIRI, or
- Subsequent therapy after first progression of advanced or metastatic disease (proficient mismatch repair/microsatellite-stable or ineligible for or progressed on checkpoint inhibitor immunotherapy for deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] or polymerase epsilon/delta [POLE/POLD1] mutation positive disease) in combination with irinotecan or with FOLFIRI for disease not previously treated with an irinotecan-based regimen.

Both of these uses have a category 2A recommendation. Zaltrap has a category 2B recommendation for use as adjuvant therapy, in combination with FOLFIRI or irinotecan, for unresectable metachronous metastases (proficient mismatch repair/microsatellite-stable or ineligible for or progressed on checkpoint inhibitor immunotherapy for deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] or polymerase epsilon/delta [POLE/POLD1] mutation positive disease) that convert to resectable disease after primary treatment.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Zaltrap. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Zaltrap as well as the monitoring required for adverse events and long-term efficacy, approval requires Zaltrap to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Zaltrap is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Colon and Rectal Cancer, Appendiceal Adenocarcinoma.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):

A) Patient is ≥ 18 years of age; AND
B) Patient meets ONE of the following (i or ii):
- **i.** Patient meets ALL of the following (a, b, c, and d):
  - **a)** Patient has unresectable metachronous metastases; AND
  - **b)** Disease is proficient mismatch repair/microsatellite-stable (pMMR/MSS); AND
  - **c)** Patient has been previously treated with FOLFOX or CapeOX; AND
    Note: FOLFOX includes 5-fluorouracil (5-FU), leucovorin, and oxaliplatin and CapeOX includes capecitabine and oxaliplatin.
  - **d)** Medication is used for initial therapy; OR
- **ii.** Patient meets ALL of the following (a, b, c, and d):
  - **a)** Patient has advanced or metastatic disease; AND
  - **b)** Patient meets ONE of the following [(1) or (2)]:
    - **(1)** Disease is proficient mismatch repair/microsatellite-stable (pMMR/MSS); OR
    - **(2)** Patient is ineligible for or progressed on checkpoint inhibitor therapy for deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) or polymerase epsilon/delta (POLE/POLD1) mutation positive; AND
      Note: Examples of checkpoint inhibitors include Keytruda (pembrolizumab intravenous infusion) and Opdivo (nivolumab intravenous infusion).
  - **c)** Patient has not previously been treated with irinotecan or FOLFIRI; AND
    Note: FOLFIRI includes 5-fluorouracil (5-FU), leucovorin, and irinotecan.
  - **d)** Medication is used for subsequent therapy; AND

C) Zaltrap will be used in combination with 5-fluorouracil (5-FU) and/or irinotecan; AND
D) The medication is prescribed by or in consultation with an oncologist.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Zaltrap is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Zaltrap® intravenous infusion [prescribing information]. Bridgewater, NJ: Regeneron/Sanofi-Aventis; December 2023.
2. The NCCN Colon Cancer Clinical Practice Guidelines in Oncology (version 5.2024 – August 22, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on October 8, 2024.
3. The NCCN Rectal Cancer Clinical Practice Guidelines in Oncology (version 4.2024 – August 22, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on October 8, 2024.
4. The NCCN Drugs and Biologics Compendium. © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on October 8, 2024. Search term: ziv-aflibercept.