Zaltrap

Description

Zaltrap (ziv-aflibercept)

Background
Zaltrap (ziv-aflibercept) is a recombinant fusion protein consisting of Vascular Endothelial Growth Factor (VEGF)-binding portions from the extracellular domains of human VEGF receptor 1 and 2 fused to the Fc portion of the human IgG1. VEGF is responsible for creating new blood vessels to assure adequate perfusion of blood or oxygen. Inhibition of VEGF is one of the methods used in cancer treatment by cutting blood supply to cancer cells. Zaltrap works by binding to human VEGF-A to VEGF-B, and to human PIGF. By binding to these endogenous ligands, it inhibits the blood supply to tumors (1).

Regulatory Status
FDA-approved indication: 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 (1).

Zaltrap carries a boxed warning for hemorrhage, gastrointestinal perforation, and compromised wound healing. Severe and sometimes fatal hemorrhage, including gastrointestinal hemorrhage has been reported in patients who have received Zaltrap in combination with Folfiri. Patients must be monitored for signs and symptoms of bleeding. Do not initiate Zaltrap in patients with severe hemorrhage and discontinue in patients who develop severe hemorrhage during treatment. Gastrointestinal (GI) perforation including fatal GI perforation can occur in patients receiving Zaltrap. Patients must be monitored for signs and symptoms and discontinuation of therapy is required if patients experience gastrointestinal perforation (1).
Severe proteinuria, nephrotic syndrome, and thrombotic microangiopathy (TMA) occurred more frequently in patients treated with Zaltrap. Zaltrap administration should be suspended for proteinuria 2 grams per 24 hours or more, and resumed when proteinuria is less than 2 grams per 24 hours. Discontinue Zaltrap in patients who develop nephrotic syndrome or TMA (1).

Zaltrap impairs wound healing and severe compromised wound healing can occur in patients receiving Zaltrap and therapy must be discontinued. Zaltrap therapy must be suspended for at least 4 weeks prior to elective surgery, and not to be resumed for at least 4 weeks following major surgery and until the surgical wound is fully healed. For minor surgery such as central venous access port placement, biopsy, and tooth extraction, Zaltrap may be initiated/resumed once the surgical wound is fully healed (1).

The safety and effectiveness of Zaltrap have not been established in pediatric patients (1). There are no adequate and well-controlled studies with Zaltrap in pregnant women (1).

**Related policies**
Avastin, Cyramza

**Policy**
This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Zaltrap may be considered medically necessary in patients that are 18 years of age or older with a confirmed diagnosis of metastatic colorectal cancer (mCRC) and if the conditions indicated below are met.

Zaltrap is considered investigational in patients who are less than 18 years of age and for all other indications.

**Prior-Approval Requirements**

**Age**  
18 years of age or older

**Diagnosis**  
The patient must have the following:

Metastatic colorectal cancer (mCRC)
AND ALL of the following:
1. Concurrent use with 5-fluorouracil, leucovorin, and irinotecan
2. History of resistance to or has progressed following an oxaliplatin-containing regimen.
3. NO signs or symptoms of severe hemorrhage
4. NO signs or symptoms of gastrointestinal perforation
5. NO major surgery within the last 4 weeks and any wounds are fully healed

Prior – Approval **Renewal** Requirements

**Age**  18 years of age or older

**Diagnosis**

The patient must have the following:

Metastatic colorectal cancer (mCRC)

AND ALL of the following:
1. Concurrent use with 5-fluorouracil, leucovorin, and irinotecan
2. NO signs or symptoms of severe hemorrhage
3. NO signs or symptoms of gastrointestinal perforation or fistula formation
4. Any wounds from major or minor surgery are fully healed

**Policy Guidelines**

**Pre - PA Allowance**

None

**Prior - Approval Limits**

**Duration**  12 months

**Prior – Approval **Renewal** Limits**

Same as above

**Rationale**
Summary
Zaltrap is a recombinant Vascular Endothelial Growth Factor inhibitor approved for treatment of colorectal cancer that has spread to other parts of the body (metastatic) and that is resistant to or has progressed after an oxaliplatin containing chemotherapy regimen. Zaltrap (ziv-aflibercept), combined with 5-fluorouracil, leucovorin, and irinotecan is approved for treatment of metastatic colorectal cancer that is resistant to or has progressed following an oxaliplatin-containing regimen (1).

Prior approval is required to ensure the safe, clinically appropriate and cost effective use of Zaltrap while maintaining optimal therapeutic outcomes.

References

Policy History
<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>October 2012</td>
<td>New policy</td>
</tr>
<tr>
<td>December 2012</td>
<td>Annual editorial review and update</td>
</tr>
<tr>
<td>March 2014</td>
<td>Annual editorial review and reference update</td>
</tr>
<tr>
<td></td>
<td>Addition of NO fistula formation in criteria</td>
</tr>
<tr>
<td>September 2014</td>
<td>Annual editorial review and reference update</td>
</tr>
<tr>
<td>March 2015</td>
<td>Annual editorial review and reference update</td>
</tr>
<tr>
<td>March 2016</td>
<td>Annual editorial review</td>
</tr>
<tr>
<td></td>
<td>Policy number change from 5.04.25</td>
</tr>
<tr>
<td>June 2017</td>
<td>Annual editorial review and reference update</td>
</tr>
<tr>
<td></td>
<td>Addition of age limits to renewal criteria</td>
</tr>
<tr>
<td>June 2018</td>
<td>Annual editorial review</td>
</tr>
<tr>
<td>June 2019</td>
<td>Annual review</td>
</tr>
<tr>
<td>December 2019</td>
<td>Annual review</td>
</tr>
</tbody>
</table>

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 6, 2019 and is effective on January 1, 2020.