OVERVIEW
Lonsurf is a combination of trifluridine, a nucleoside metabolic inhibitor, and tipiracil, a thymidine phosphorylase inhibitor, indicated for the treatment of adult patients with metastatic colorectal cancer (mCRC) who have been previously treated with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy, an anti-vascular endothelial growth factor (VEGF) biological therapy, and if RAS wild-type, an anti-epidermal growth factor receptor (EGFR) therapy. Fluoropyrimidines include 5-fluorouracil (5-FU) intravenous (IV) injection and capecitabine tablets. Anti-VEGF therapies for mCRC include Avastin® (bevacizumab solution for IV injection) and Cyramza® (ramucirumab injection for IV use). Anti-EGFR therapies for mCRC include Erbitux® (cetuximab injection for IV infusion) and Vectibix® (panitumumab injection for IV infusion).

Lonsurf is indicated for the treatment of adult patients with metastatic gastric or gastroesophageal junction adenocarcinoma previously treated with at least two lines of chemotherapy that included a fluoropyrimidine, a platinum, either a taxane or irinotecan, and if appropriate, human epidermal growth factor receptor 2 (HER2)/neu-targeted therapy.

Guidelines
Colon and/or Rectal Cancer
The National Comprehensive Cancer Network (NCCN) colon cancer (version 4.2018 – October, 19, 2018) and rectal cancer (version 3.2018 – August 7, 2018) guidelines recommend Lonsurf as subsequent therapy as a single agent for unresectable advanced or metastatic disease not previously treated with Lonsurf for the following uses: for first progression (KRAS/NRAS mutant only) or second progression for disease previously treated with FOLFOXIRI (5-FU/leucovorin, irinotecan, oxaliplatin) with or without Avastin, for second progression for disease previously treated with irinotecan- and oxaliplatin-based regimens, or for progression for disease that progressed through all available regimens, including Stivarga® (regorafenib tablets). Lonsurf may be given before or after Stivarga.

POLICY STATEMENT
Prior authorization is recommended for prescription benefit coverage of Lonsurf. All approvals are provided for 3 years in duration unless otherwise noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA
Coverage of Lonsurf is recommended in those who meet the following criteria:

FDA-Approved Indications
1. **Colorectal Cancer, Metastatic (mCRC).** Approve for 3 years if the patient meets the following criteria (A, B, C, and D):¹
   A) The patient has been previously treated with a fluoropyrimidine (e.g., capecitabine, 5-fluorouracil [5-FU]); AND
   B) The patient has been previously treated with oxaliplatin; AND
   C) The patient has been previously treated with irinotecan; AND
   D) If the patient’s tumor or metastases are wild-type RAS (KRAS wild-type and/or NRAS wild-type) [that is, the tumors or metastases are KRAS and/or NRAS mutation negative], Erbitux (cetuximab injection for intravenous infusion) or Vectibix (panitumumab injection for intravenous infusion) has been tried.

2. **Gastric or Gastroesophageal Junction Adenocarcinoma, Metastatic.** Approve for 3 years if the patient meets the following criteria:
   A) The patient has been previously treated with at least two chemotherapy regimens for gastric or gastroesophageal junction adenocarcinoma (e.g., regimens containing one or more of the following agents: capecitabine, 5-fluorouracil [5-FU], oxaliplatin, paclitaxel, docetaxel, and irinotecan).

**CONDITIONS NOT RECOMMENDED FOR APPROVAL**

Lonsurf has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions.

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**


**OTHER REFERENCES UTILIZED**

### HISTORY

<table>
<thead>
<tr>
<th>Type of Revision</th>
<th>Summary of Changes*</th>
<th>TAC Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>New Policy</td>
<td>--</td>
<td>10/14/2015</td>
</tr>
<tr>
<td>Annual</td>
<td>No criteria changes.</td>
<td>10/05/2016</td>
</tr>
<tr>
<td>Annual</td>
<td>Colorectal Cancer criteria revised to add wild-type RAS. Previously criteria stated KRAS and/or NRAS that are the components of RAS. Wild-type refers to both KRAS and NRAS.</td>
<td>10/25/2017</td>
</tr>
<tr>
<td>Annual</td>
<td>Removed criteria for patient already started on Lonsurf</td>
<td>10/17/2018</td>
</tr>
<tr>
<td>Early annual revision</td>
<td>Added gastric and gastroesophageal junction adenocarcinoma, metastatic as a new condition of approval.</td>
<td>03/06/2019</td>
</tr>
</tbody>
</table>

*TAC – Therapeutic Assessment Committee; * For a further summary of criteria changes, refer to respective TAC minutes available at: [http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx](http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx)*