

# Evolent Clinical Guideline 3176 for Lonsurf<sup>TM</sup> (trifluridine and tipiracil)

<b>Guideline Number:</b> Evolent_CG_3176	<b>Applicable Codes</b>	
<p><b><i>"Evolent" refers to Evolent Health LLC and Evolent Specialty Services, Inc.</i></b></p> <p><b><i>© 2017 - 2025 Evolent. All rights Reserved.</i></b></p>		
<b>Original Date:</b> April 2017	<b>Last Revised Date:</b> September 2025	<b>Implementation Date:</b> September 2025

## TABLE OF CONTENTS

<b>STATEMENT .....</b>	<b>2</b>
PURPOSE .....	2
<b>INDICATIONS.....</b>	<b>2</b>
COLORECTAL CANCER .....	2
GASTRIC OR GASTROESOPHAGEAL JUNCTION (GEJ) ADENOCARCINOMA .....	2
<b>CONTRAINDICATIONS/WARNINGS .....</b>	<b>2</b>
<b>EXCLUSION CRITERIA .....</b>	<b>3</b>
<b>CODING AND STANDARDS .....</b>	<b>3</b>
CODES.....	3
APPLICABLE LINES OF BUSINESS .....	4
<b>POLICY HISTORY.....</b>	<b>4</b>
<b>LEGAL AND COMPLIANCE .....</b>	<b>4</b>
GUIDELINE APPROVAL .....	4
Committee .....	4
DISCLAIMER .....	4
<b>REFERENCES.....</b>	<b>5</b>

# STATEMENT

## Purpose

To define and describe the accepted indications for Lonsurf (trifluridine and tipiracil) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

## INDICATIONS

**Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided**

- The member has not experienced disease progression on the requested medication AND
- The requested medication was used within the last year without a lapse of more than 30 days of having an active authorization AND
- Additional medication(s) are not being added to the continuation request.

### Colorectal Cancer

- The member has unresectable/advanced/metastatic colorectal cancer and Lonsurf (trifluridine and tipiracil) is being used as a single agent or in combination with bevacizumab/bevacizumab biosimilar in members who have been previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-VEGF biological therapy, and if RAS wild-type, an anti-EGFR therapy.

### Gastric or Gastroesophageal Junction (GEJ)

#### Adenocarcinoma

- The member is not a surgical candidate or has unresectable/locally advanced/recurrent/metastatic gastric or gastroesophageal junction (GEJ) adenocarcinoma, and Lonsurf (trifluridine and tipiracil) is being used as monotherapy as third-line or subsequent therapy following 2 prior lines of therapy.

## CONTRAINDICATIONS/WARNINGS

- None

## EXCLUSION CRITERIA

- Lonsurf (trifluridine and tipiracil) is being used after disease progression with the same regimen.
- Dosing exceeds single dose limit of Lonsurf (trifluridine and tipiracil) 80 mg (based on the trifluridine component).
- Treatment exceeds the maximum limit of 80 (20 mg) or 60 (15 mg) tablets/month.
- Investigational use of Lonsurf (trifluridine and tipiracil) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:
  - Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
  - Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
  - Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definitions of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
  - Whether the experimental design, considering the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
  - That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
  - That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
  - That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

## CODING AND STANDARDS

### Codes

- J8999 - trifluridine and tipiracil

## Applicable Lines of Business

<input type="checkbox"/>	CHIP (Children's Health Insurance Program)
<input checked="" type="checkbox"/>	Commercial
<input checked="" type="checkbox"/>	Exchange/Marketplace
<input checked="" type="checkbox"/>	Medicaid
<input type="checkbox"/>	Medicare Advantage

## POLICY HISTORY

Date	Summary
September 2025	<ul style="list-style-type: none"> <li>Converted to new Evolent guideline template</li> <li>This guideline replaces UM ONC_1311 Lonsurf (trifluridine and tipiracil)</li> <li>Updated indication section</li> <li>Updated maximum dosage form quantities in exclusion criteria</li> <li>Updated references</li> </ul>
September 2024	<ul style="list-style-type: none"> <li>Updated NCH verbiage to Evolent</li> </ul>

## LEGAL AND COMPLIANCE

### Guideline Approval

#### Committee

Reviewed / Approved by Evolent Specialty Clinical Guideline Review Committee

### Disclaimer

*Evolent Clinical Guidelines do not constitute medical advice. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Evolent uses Clinical Guidelines in accordance with its contractual obligations to provide utilization management. Coverage for services varies for individual members according to the terms of their health care coverage or government program. Individual members' health care coverage may not utilize some Evolent Clinical Guidelines. Evolent clinical guidelines contain guidance that requires prior authorization and service limitations. A list of procedure codes, services or drugs may not be all inclusive and does not imply that a service or drug is a covered or non-covered service or drug. Evolent reserves the right to review and update*

*this Clinical Guideline in its sole discretion. Notice of any changes shall be provided as required by applicable provider agreements and laws or regulations. Members should contact their Plan customer service representative for specific coverage information.*

## REFERENCES

1. Van Cutsem E, et al; RECOURSE Study Group. The subgroups of the phase III RECOURSE trial of trifluridine/tipiracil (TAS-102) versus placebo with best supportive care in patients with metastatic colorectal cancer. *Eur J Cancer*. 2018 Feb;90:63-72. doi: 10.1016/j.ejca.2017.10.009.
2. Mayer RJ, et al; RECOURSE Study Group. Randomized trial of TAS-102 for refractory metastatic colorectal cancer. *N Engl J Med*. 2015 May 14;372(20):1909-19. doi: 10.1056/NEJMoa1414325.
3. Prager GW, et al; SUNLIGHT Investigators. Trifluridine-Tipiracil and Bevacizumab in Refractory Metastatic Colorectal Cancer. *N Engl J Med*. 2023 May 4;388(18):1657-1667. doi: 10.1056/NEJMoa2214963.
4. Shitara K, et al. Trifluridine/tipiracil versus placebo in patients with heavily pretreated metastatic gastric cancer (TAGS): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Oncol*. 2018 Nov;19(11):1437-1448. doi: 10.1016/S1470-2045(18)30739-3.
5. Bando H, et al. A multicenter phase II study of TAS-102 monotherapy in patients with pre-treated advanced gastric cancer (EPOC1201). *Eur J Cancer*. 2016 Jul;62:46-53. doi: 10.1016/j.ejca.2016.04.009.
6. Lonsurf prescribing information. Taiho Oncology, Inc., Princeton, NJ 2023.
7. Clinical Pharmacology Elsevier Gold Standard 2025.
8. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2025.
9. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2025.
10. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2025.
11. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. *J Clin Oncol*. 2014 Apr 20;32(12):1277-80.
12. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: <https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf>.
13. Current and Resolved Drug Shortages and Discontinuations Reported to the FDA: <http://www.accessdata.fda.gov/scripts/drugshortages/default.cfm>.