

Drug Policy:

Lonsurf™ (trifluridine/tipiracil)

POLICY NUMBER UM ONC_1311	SUBJECT Lonsurf™ (trifluridine/tipiracil)		DEPT/PROGRAM UM Dept	PAGE 1 of 3
DATES COMMITTEE REVIEWED 04/05/17, 04/11/18, 04/10/19, 12/11/19, 04/08/20, 04/14/21, 11/15/21, 03/09/22, 05/11/22, 07/13/22, 06/14/23, 09/13/23, 09/18/24	APPROVAL DATE September 18, 2024	EFFECTIVE DATE September 27, 2024	COMMITTEE APPROVAL DATES 04/05/17, 04/11/18, 04/10/19, 12/11/19, 04/08/20, 04/14/21, 11/15/21, 03/09/22, 05/11/22, 07/13/22, 06/14/23, 09/13/23, 09/18/24	
PRIMARY BUSINESS OWNER: UM		COMMITTEE/BOARD APPROVAL Utilization Management Committee		
NCQA STANDARDS UM 2		ADDITIONAL AREAS OF IMPACT		
CMS REQUIREMENTS	STATE/FEDERAL REQUIREMENTS		APPLICABLE LINES OF BUSINESS Commercial, Exchange, Medicaid	

I. PURPOSE

To define and describe the accepted indications for Lonsurf (trifluridine/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.

II. INDICATIONS FOR USE/INCLUSION CRITERIA

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

1. The requested medication was used within the last year, **AND**
2. The member has not experienced disease progression and/or no intolerance to the requested medication, **AND**
3. Additional medication(s) are not being added to the continuation request.

B. Colorectal Cancer

1. The member has unresectable/advanced/metastatic colorectal cancer and Lonsurf (trifluridine/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.

C. Gastric or Gastroesophageal Junction (GEJ) Adenocarcinoma

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

III. EXCLUSION CRITERIA

- A. Lonsurf (trifluridine/tipiracil) is being used after disease progression with the same regimen.
- B. Dosing exceeds single dose limit of Lonsurf (trifluridine/tipiracil) 80 mg (based on the trifluridine component).
- C. Treatment exceeds the maximum limit of 80 (20 mg) or 120 (15 mg) tablets/month.
- D. Investigational use of Lonsurf (trifluridine/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:
 1. Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
 2. Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
 3. 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.
 4. 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).
 5. 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.
 6. That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
 7. 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.

IV. MEDICATION MANAGEMENT

- A. Please refer to the FDA label/package insert for details regarding these topics.

V. APPROVAL AUTHORITY

- A. Review – Utilization Management Department
- B. Final Approval – Utilization Management Committee

VI. ATTACHMENTS

- A. None

VII. REFERENCES

- A. Van Cutsem E, et al. RECURSE Clinical Trial. The subgroups of the phase III RECURSE 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. Epub 2017 Dec 21.
- B. Mayer RJ, et al. RECURSE Clinical Trial. 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. PMID: 25970050.
- C. 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.
- D. 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
- E. Lonsurf prescribing information. Taiho Oncology. Princeton, NJ 2023.
- F. Clinical Pharmacology Elsevier Gold Standard 2024.
- G. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2024.
- H. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2024.
- I. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2024.
- J. 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.
- K. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: <https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf>.