UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2025 P 1169-11
Program	Prior Authorization/Notification
Medication	Lonsurf® (trifluridine/tipiracil)
P&T Approval Date	11/2015, 9/2016, 9/2017, 9/2018, 4/2019, 4/2020, 4/2021, 4/2022, 4/2023, 4/2024, 4/2025
Effective Date	7/1/2025

1. Background:

Lonsurf (trifluridine/tipiracil) 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 as a single agent or in combination with bevacizumab 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.
- Metastatic gastric or gastroesophageal junction adenocarcinoma previously treated with at least two prior lines of chemotherapy that included a fluoropyrimidine, a platinum, either a taxane or irinotecan, and if appropriate, HER2/neu-targeted therapy.

In addition, the National Cancer Comprehensive Network (NCCN) also recommends the use of Lonsurf as second-line and subsequent therapy as a single agent, or in combination with bevacizumab (preferred), for advanced or metastatic colon, appendiceal, or rectal cancer.

Coverage Information:
Members will be required to meet the criteria below for coverage. For members under the age of 19 years, the prescription will automatically process without a coverage review.

Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances. Some states also mandate usage of other Compendium references. Where such mandates apply, they supersede language in the benefit document or in the notification criteria.

2. Coverage Criteria[a]:

A. <u>Patients less than 19 years of age</u>

1. **Lonsurf** will be approved based on the following criterion:

   a. Patient is less than 19 years of age

   Authorization will be issued for 12 months.

B. <u>Colorectal Cancer</u>

1. **Lonsurf** will be approved based on **<u>all</u>** of the following criteria:

   a. Diagnosis of advanced or metastatic colorectal cancer (mCRC) (i.e., colon,

appendiceal, or rectal cancer).

-AND-

b. History of failure, contraindication, or intolerance to treatment with **all** of the following:

(1) Fluoropyrimidine-based chemotherapy
(2) Oxaliplatin-based chemotherapy
(3) Irinotecan-based chemotherapy
(4) Anti-VEGF biological therapy

-AND-

c. **One** of the following:

(1) Tumor is *RAS* mutant-type

-OR-

(2) **Both** of the following:

(a) Tumor is *RAS* wild-type
(b) History of failure, contraindication, or intolerance to anti-EGFR therapy

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Lonsurf** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Lonsurf therapy.

Authorization will be issued for 12 months.

C. Gastric/Gastroesophageal Junction Adenocarcinoma

1. **Lonsurf** will be approved based on **both** of the following criteria:

a. Diagnosis of **one** of the following:

(1) Unresectable locally advanced, recurrent, or metastatic gastric cancer
(2) Unresectable locally advanced, recurrent, or metastatic gastroesophageal junction adenocarcinoma

-AND-

b. History of failure, contraindication, or intolerance to treatment with at least **two** prior lines of chemotherapy that consisted of the following agents:

(1) Fluoropyrimidine (e.g, fluorouracil)

(2) Platinum (e.g., carboplatin, cisplatin, oxaliplatin)
(3) Taxane (e.g, docetaxel, paclitaxel) or irinotecan
(4) HER2/neu-targeted therapy (e.g., trastuzumab) (if HER2 overexpression)

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Lonsurf** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Lonsurf therapy

Authorization will be issued for 12 months.

D. NCCN Recommended Regimens

The drug has been recognized for treatment of the cancer indication by The National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium with a Category of Evidence and Consensus of 1, 2A, or 2B

Authorization will be issued for 12 months.

[a] State mandates may apply. Any federal regulatory requirements and the member specific benefit plan coverage may also impact coverage criteria. Other policies and utilization management programs may apply.

3. Additional Clinical Rules:

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class
- Supply limits may be in place.

4. References:

1. Lonsurf [package insert]. Cambridge, MA: ARIAD Pharmaceuticals, Inc.; August 2023.
2. The NCCN Drugs and Biologics Compendium (NCCN Compendium™). Available at https://www.nccn.org/professionals/drug_compendium/content/. Accessed March 6, 2025.

Program	Prior Authorization/Notification - Lonsurf® (trifluridine/tipiracil)
Change Control	
11/2015	New program.
9/2016	Annual review. Updated references.
9/2017	Annual review. Updated references.
9/2018	Annual review. Updated references.
4/2019	Added coverage for metastatic gastric cancer. Updated references.
4/2020	Annual review. Added general NCCN recommendations for use criteria. Updated reference.

4/2021	Annual review with no changes to coverage criteria. Updated background and references.
4/2022	Annual review. Updated references.
4/2023	Annual review. Added state mandate and oncology medications footnote. Updated references.
4/2024	Annual review. Removed oncology medications footnote. Updated background for FDA indications and NCCN recommendations. Updated diagnostic criteria for colorectal cancer. Updated gastric/gastroesophageal junction adenocarcinoma diagnostic criteria. Updated references.
4/2025	Annual review. No changes to clinical criteria. Updated references.