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5.21.064

Section:	Prescription Drugs	**Effective Date:**	January 1, 2025
Subsection:	Antineoplastic Agents	**Original Policy Date:**	October 16, 2015
Subject:	Lonsurf	**Page:**	1 of 5

Last Review Date: December 13, 2024

Lonsurf

Description

Lonsurf (trifluridine/tipiracil)

Background

Lonsurf is a medication used to treat patients with metastatic colorectal cancer and metastatic gastric or gastroesophageal junction adenocarcinoma who are no longer responding to other therapies such as chemotherapy and biological therapy. Lonsurf is a combination of two drugs, trifluridine and tipiracil. Trifluridine works by imitating a component of DNA (genetic material in every cell) called thymidine, and permanently inhibiting an essential enzyme for DNA to work called thymidylate synthetase. By inhibiting this important enzyme, as well as incorporating itself into the DNA, trifluridine stops the DNA from working properly and the cell dies. Tipiracil, the second drug, works by stopping an enzyme called thymidine phosphorylase from breaking down the first drug, trifluridine, so that it can work better (1).

Regulatory Status

FDA-approved indications: Lonsurf is a combination of trifluridine, a nucleoside metabolic inhibitor, and tipiracil, a thymidine phosphorylase inhibitor, indicated for the treatment of adult patients with: (1)

1. 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.

2. 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.

Off-label use: (2)

1. Metastatic colorectal cancer in combination with bevacizumab who have been previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, and an anti-EGFR therapy if RAS wild type left-sided tumor.

Lonsurf can cause severe and life-threatening myelosuppression. High rates of anemia, neutropenia, thrombocytopenia, and febrile neutropenia were observed. Due to this risk, complete blood counts need to be obtained prior to and on Day 15 of each cycle of Lonsurf. They may be done more frequently if clinically indicated. In the case of febrile neutropenia, absolute neutrophil count (ANC) less than 500/mm^3, or platelets less than 50,000/mm^3, withhold Lonsurf. When the patient recovers, Lonsurf may be resumed at a lower dose (1).

The safety and effectiveness of Lonsurf in pediatric patients have not been established (1).

Related policies

Policy

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

Lonsurf may be considered **medically necessary** if the conditions indicated below are met.

Lonsurf may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Metastatic colorectal cancer

a. Previously treated with fluoropyrimidine-based, oxaliplatin-based, and irinotecan-based chemotherapy
b. Using in combination with bevacizumab **OR** patient was previously treated with an anti-VEGF biological therapy
c. For left-sided tumors **only**: If RAS wild-type, previously treated with an anti-EGFR therapy

2. Metastatic gastric or gastroesophageal junction adenocarcinoma
    a. Previously treated with **ALL** of the following:
        i. A fluoropyrimidine
        ii. A platinum
        iii. A taxane or irinotecan
    b. If patient has a HER2-positive tumor, the patient has received prior anti-HER2 therapy

AND the following for **ALL** indications:
1. Complete blood counts monitored prior to each cycle and on Day 15 of each cycle

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** the following:

1. Metastatic colorectal cancer
2. Metastatic gastric or gastroesophageal junction adenocarcinoma

AND ALL of the following for **ALL** indications:
1. Complete blood counts monitored prior to each cycle and on Day 15 of each cycle
2. **NO** disease progression or unacceptable toxicity

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Lonsurf is a combination medication used to treat patients with metastatic colorectal cancer and metastatic gastric or gastroesophageal junction adenocarcinoma that are no longer responding to other chemotherapy and biological therapy. Lonsurf works by interfering with DNA synthesis through various mechanisms. There are no adequate and well-controlled studies to document the safety and efficacy of Lonsurf in pediatric patients (1).

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

References

1. Lonsurf [package insert]. Princeton, NJ: Taiho Oncology, Inc.; August 2023.
2. NCCN Drugs & Biologics Compendium® Trifluridine/Tipiracil 2024. National Comprehensive Cancer Network, Inc. Accessed on October 3, 2024.

Policy History

Date	Action
October 2015	Addition to PA
December 2015	Annual review
June 2016	Annual editorial review Policy code changed from 5.04.64 to 5.21.64
June 2017	Annual editorial review and reference update Addition of age limit to renewal criteria
June 2018	Annual editorial review and reference update
March 2019	Addition of indication of metastatic gastric or gastroesophageal junction adenocarcinoma
June 2019	Annual review
June 2020	Annual review and reference update

June 2021	Annual review and reference update
June 2022	Annual review and reference update
June 2023	Annual review and reference update. Changed policy number to 5.21.064
September 2023	Per reconsideration review, revised requirement for previous anti-VEGF treatment only for patients not using in combination with bevacizumab and revised requirement of previous anti-EGFR therapy to only apply to left-sided tumors.
December 2023	Annual review and reference update
March 2024	Annual review and reference update
December 2024	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 13, 2024 and is effective on January 1, 2025.