Pharmacy Policy Bulletin: J-0639 Lonsurf (trifluridine-tipiracil) – Commercial and Healthcare Reform	
Number: J-0639	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Miscellaneous Specialty Drugs Oral= Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0639-012	**Original Date:** 12/02/2015
Effective Date: 10/28/2024	**Review Date:** 10/02/2024

Drugs Product(s):	• Lonsurf (trifluridine/tipiracil)
FDA-Approved Indication(s):	• 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. • Treatment of adult patients with 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, a HER2/neu targeted therapy.

Background:	• Trifluridine is a nucleoside metabolic inhibitor, which interferes with DNA synthesis and inhibits cellular proliferation. The inhibition of cellular proliferation reduces uncontrolled cell growth and division, which are features of cancer development.
	• Tipiracil is a thymidine phosphorylase inhibitor, which increases exposure to trifluridine by inhibiting its metabolism.
	• NCCN Colon Cancer guidelines state that cetuximab or panitumumab should be used only in left-sided tumors when used as initial therapy. Left-sided tumors are defined as splenic flexure to rectum. Evidence suggests that patients with tumors originating on the right side of the colon (hepatic flexure through cecum) are unlikely to respond to cetuximab and panitumumab.
	• Prescribing Considerations
	  ○ Complete blood counts should be obtained prior to and on day 15 of each cycle due to risk of severe myelosuppression.
	  ○ The dose of Lonsurf should be reduced in patients with severe renal impairment.
	  ○ Lonsurf should not be used in patients with baseline moderate or severe hepatic impairment.
	  ○ The safety and effectiveness of Lonsurf have not been established in pediatric patients.

Chemotherapy Class	Examples of Medications
Fluoropyrimidine	capecitabine, floxuridine, fluorouracil
Platinum	oxaliplatin, carboplatin, cisplatin
Anti-VEGF	bevacizumab, ramucirumab, ziv-aflibercept
Anti-EGFR	cetuximab, panitumumab
Taxane	paclitaxel, docetaxel
HER2/neu receptor inhibitor	trastuzumab

Approval Criteria

I. Initial Authorization

A. Colorectal Cancer

When a benefit, coverage of Lonsurf may be approved when all of the following criteria are met **(1. through 4.)**:

1. The member is 18 years of age or older.

2. The member has a diagnosis of metastatic colorectal cancer (ICD-10: C19).

3. The member will be using Lonsurf as a single agent or in combination with bevacizumab.

4. The member has been previously treated with all of the following **(a., b., and c.)**:

a. Fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy

b. An anti-VEGF therapy

c. If the member's genetic status is *RAS* wild type and disease is left-sided, an anti-EGFR therapy

B. Gastric Cancer

When a benefit, coverage of Lonsurf may be approved when all of the following criteria are met **(1., 2., and 3.)**:

1. The member is 18 years of age or older.

2. The member has a diagnosis of one (1) of the following **(a. or b.)**:

a. Metastatic gastric cancer (ICD-10: C16)

b. Metastatic gastroesophageal junction adenocarcinoma (ICD-10: C15.5)

3. The member has been previously treated with at least two (2) of the following **(a. through d.)**:

a. Fluoropyrimidine-containing chemotherapy

b. Platinum-containing chemotherapy

c. Taxane-containing chemotherapy or irinotecan containing chemotherapy

d. HER2/neu-targeted therapy

II. Reauthorization

When a benefit, reauthorization of Lonsurf may be approved when the following criterion is met **(A.)**:

A. The prescriber attests that the member is tolerating therapy and has experienced a therapeutic response defined as one (1) of the following **(1. or 2.)**:

1. Disease improvement

2. Delayed disease progression

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

IV. Coverage of oncology medications listed in this policy may be approved on a case-by-case basis per indications supported in the most current NCCN guidelines.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of their FDA-approved indication(s) should be denied based on the lack of clinical data to support their effectiveness and safety in other conditions unless otherwise noted in the approval criteria.

II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None

References:

1. Lonsurf [package insert]. Princeton, NJ: Taiho Pharmaceutical Co., Ltd.; August 2023.
2. NCCN Guidelines. Colon Cancer v.4.2024. National Comprehensive Cancer Network. August 20, 2024.
3. NCCN Guidelines. Gastric Cancer v.4.2024. National Comprehensive Cancer Network. Available at: https://www.nccn.org/professionals/physician_gls/pdf/gastric.pdf. Accessed August 20, 2024.