trifluridine/tipiracil (Lonsurf®)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO069

Description

Trifluidine is an orally administered nucleoside analog that is incorporated into DNA to interfere with DNA synthesis and proliferation, and tipiracil increases exposure to trifluridine by inhibiting thymidine phosphorylase. Together they make the product Lonsurf.

Length of Authorization

- Initial: Three months
- Renewal: 12 months

Quantity limits

Product Name	Dosage Form	Indication	Quantity Limit	DDID
trifluridine/tipiracil (Lonsurf)	15 mg – 6.14 mg tablets	Stomach or esophagogastric adenocarcinoma – metastatic, previously treated Colorectal cancer – metastatic, previously treated	80 tablets/28 days	189858
	20 mg – 8.19 mg tablets		80 tablets/30 days	189857

Initial Evaluation

I. Trifluridine/tipiracil (Lonsurf) may be considered medically necessary when the following criteria below are met:
   A. The member is 18 years of age or older; **AND**
   B. The medication is prescribed by or in consultation with an oncologist or gastroenterologist; **AND**
   C. Trifluridine/tipiracil is used as monotherapy; **AND**
   D. A diagnosis of one of the following:
      1. **Colorectal cancer**; **AND**
         i. The disease is metastatic (i.e., stage IV); **AND**
         ii. The tumor has been tested and is documented to be KRAS mutant-type; **OR**
         iii. The tumor has been tested and is documented to be KRAS wild-type; **AND**

a. The member has been previously treated with an anti-EGFR therapy (e.g., cetuximab, panitumumab); **AND**

iv. The member has been previously treated with a fluoropyrimidine (e.g., fluorouracil, capecitabine, S-1), oxaliplatin and irinotecan-based chemotherapy; **AND**

v. The member has been previously treated with an anti-VEGF biological therapy (e.g., bevacizumab); **OR**

2. **Gastric or gastroesophageal junction adenocarcinoma**; **AND**

i. The disease is metastatic (i.e., stage IV); **AND**

ii. The member has been tested and has documentation of HER2/neu negative status; **OR**

a. The member has been tested and has documentation of HER2/neu positive status; **AND**

b. Has received prior HER2/neu targeted therapy (e.g., trastuzumab); **AND**

iii. The member has been previously treated with at least two prior lines of chemotherapy; **AND**

iv. Previous treatments included a fluoropyrimidine (e.g., fluorouracil, capecitabine, S-1), a platinum therapy (e.g., cisplatin, carboplatin, oxaliplatin), and one of the following: a taxane (e.g., docetaxel, paclitaxel) or irinotecan

II. Trifluridine/tipiracil (Lonsurf) is considered investigational when used for all other conditions, including but not limited to:

A. Combination therapy with other oncolytic agents.

B. Colorectal cancer prior to the metastatic setting, and/or prior to use of a fluoropyrimidine, oxaliplatin, and irinotecan-based chemotherapy regimen, and/or prior to use of an anti-VEGF biological therapy, and/or if the member is KRAS mutant-type use prior to an anti-EGFR therapy.

C. Colorectal, gastric, or gastroesophageal cancer at a dose <20 mg/m2 orally twice daily.

D. Non adenocarcinoma gastric or gastroesophageal junction (e.g., squamous cell type).

E. Gastric or gastroesophageal junction adenocarcinoma prior to at least two previous lines of chemotherapy and prior to use of all of the following: a fluoropyrimidine, a platinum therapy, and one of the following – taxane or irinotecan.

F. Biliary track cancers.

G. Tumors that are not colorectal, gastric or gastroesophageal in nature.

Renewal Evaluation

I. The medication is prescribed by or in consultation with an oncologist or gastroenterologist; **AND**
II. Trifluridine/tipiracil (Lonsurf) continues to be used as monotherapy; **AND**
III. Body surface area is provided in meters squared; **AND**
IV. Trifluridine/tipiracil (Lonsurf) is being used at or above a dose of 20 mg/m2; **AND**
V. The member is not experiencing unacceptable toxicity from the therapy; **AND**
VI. The patient has not experienced disease progression while on trifluridine/tipiracil (Lonsurf); **OR**
VII. Documentation of compelling clinical evidence of benefit is provided if therapy is to be continued in the setting of progression.

Supporting Evidence

I. There is lack of safety and efficacy data from clinical trials for use in pediatric patients. This medication has not been evaluated outside of the adult population.
II. Pivotal clinical trials for FDA-approved indications evaluated safety and efficacy of trifluridine/tipiracil (Lonsurf) as monotherapy in heavily pretreated patients. The therapies listed in the above criteria had been tried and failed by the majority of patients enrolled in the clinical trials.
III. There is no globally accepted standard for first-line treatment of HER2/neu negative gastric or gastroesophageal adenocarcinoma. When these indications were added to the policy, NCCN guidelines were not updated to provide recommendations for this agent. Clinical trial experience with extensive patient treatment history is the basis for addition into the policy. Overall survival data in the third line treatment setting was show to be 5.7 months for trifluridine/tipiracil (Lonsurf) vs 3.6 months for placebo.

Investigational or Not Medically Necessary Uses

All indications listed below have not been sufficiently studied for safety and efficacy, or have inconclusive evidence regarding safety and efficacy for use of trifluridine/tipiracil (Lonsurf).

I. Combination therapy with other oncolytic agents.
II. Colorectal cancer prior to the metastatic setting, and/or prior to use of a fluoropyrimidine, oxaliplatin, and irinotecan-based chemotherapy regimen, and/or prior to use of an anti-VEGF biological therapy, and/or if the member is KRAS mutant-type use prior to an anti-EGFR therapy.
III. Colorectal, gastric, or gastroesophageal cancer at a dose < 20 mg/m2 orally twice daily.
IV. Non adenocarcinoma gastric or gastroesophageal junction (e.g., squamous cell type).
V. Gastric or gastroesophageal junction adenocarcinoma prior to at least two previous lines of chemotherapy and prior to use of all of the following: a fluoropyrimidine, a platinum therapy, and one of the following – taxane or irinotecan.

VI. Biliary track cancers.
VII. Tumors that are not colorectal, gastric or gastroesophageal in nature.

References

1. Lonsurf [Prescribing Information]. Princeton, NJ. Taiho Oncology, Inc. Moda Health, Inc. February 2019.
2. Shitara K, Doi T, Dvorkin M, 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;19(11):1437-1448.
3. Longo-muñoz F, Argiles G, Tabernero J, et al. Efficacy of trifluridine and tipiracil (TAS-102) versus placebo, with supportive care, in a randomized, controlled trial of patients with metastatic colorectal cancer from Spain: results of a subgroup analysis of the phase 3 RECOURSE trial. *Clin Transl Oncol*. 2017;19(2):227-235.
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5. UpToDate, Inc. Systemic therapy for locally advanced unresectable metastatic esophageal and gastric cancer. UpToDate, database online. Bendell J., Yoon H. Updated March 4, 2019. Accessed March 11, 2019. Available at: https://www.uptodate.com/contents/systemic-therapy-for-locally-advanced-unresectable-and-metastatic-esophageal-and-gastric-cancer?search=metastatic%20gastric%20cancer%20treatment&source=search_result&selectedTitle=1~38&usage_type=default&display_rank=1
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8. National Comprehensive Cancer Network. Colon Cancer guideline Version 4.2018. Available at: https://www.nccn.org/professionals/physician_gls/default.aspx. Accessed March 11, 2019.

Policy Implementation/Update:

Date Created	May 2015
Date Effective	May 2015
Last Updated	September 2019
Last Reviewed	09/05/2019

Action and Summary of Changes	Date
Added new indication of stomach and esophagogastric adenocarcinoma based on clinical trial data that demonstrated overall survival in the third line treatment setting.	03/2019