

Clinical Policy: Trifluridine/Tipiracil (Lonsurf)

Reference Number: PA.CP.PHAR.383

Effective Date: 10.17.18

Last Review Date: 07/17/19

[Revision Log](#)

Description

Trifluridine-tipiracil (Lonsurf[®]) is a combination of trifluridine, a nucleoside metabolic inhibitor, and tipiracil, a thymidine phosphorylase inhibitor.

FDA Approved Indication(s)

Lonsurf is indicated for the treatment of patients with metastatic colorectal cancer (CRC) 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.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with PA Health & Wellness[®] that Lonsurf is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Colorectal Cancer (must meet all):

1. Diagnosis of metastatic or unresectable CRC;
2. Prescribed by or in consultation with an oncologist;
3. Documentation of RAS (KRAS or NRAS) wild-type gene status;
4. Failure of the following agents unless contraindicated or clinically significant adverse effects are experienced:*
- a. 5-fluorouracil or capecitabine;
- b. Oxaliplatin and irinotecan;
- c. An anti-VEGF agent: Avastin[®], Cyramza[®], Stivarga[®] or Zaltrap[®];
- d. If tumor expresses the RAS wild-type gene, an anti-EGFR agent: Erbitux[®] or Vectibix[®];

**Prior authorization is (or may be) required.*

5. Request meets one of the following (a or b):
 - a. Dose does not exceed 160 mg/day (based on the trifluridine component; round dose to the nearest 5 mg increment given 15 and 20 mg tablets);
 - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

II. Continued Therapy

A. Colorectal Cancer (must meet all):

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):
 - a. New dose does not exceed 160 mg/day (based on the trifluridine component).
 - b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

III. Diagnoses/Indications for which coverage is NOT authorized:

- A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

5-FU: 5-fluorouracil

CRC: colorectal carcinoma

EGFR: epidermal growth factor receptor

FDA: Food and Drug Administration

VEGF: vascular endothelial growth factor

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
<i>Fluoropyrimidine, oxaliplatin, and irinotecan therapeutic agents and examples of regimens.</i>		
5 FU (fluorouracil)*	400 mg/m ² IV on day 1, 1200 mg/m ² for 2 days	2400 mg/m ²
capecitabine (Xeloda®)*	1,250 mg/m ² PO bid days 1-14. Repeat every 21 days for 8 cycles.	2500 mg/m ² /day
irinotecan (Camptosar®)	125 mg/m ² IV in combination with 5-FU based chemotherapy	350 mg/m ²
oxaliplatin	85 mg/m ² IV in combination with 5-FU based chemotherapy	130 mg/m ²

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
FOLFOX = Infusional 5-FU/leucovorin(LV) /Eloxatin™ (oxaliplatin)	Eloxatin (oxaliplatin) 85 mg/m ² IV over 2 hours day 1; leucovorin 200 mg/m ² IV over 2 hours day 1 & 2, followed by 5-FU 400 mg/m ² IV bolus over 2-4 minutes, followed by 600 mg/m ² IV 5-FU continuous infusion over 22 hours on day 1 & 2. Repeat cycle every 14 days	Varies
FOLFIRI = Infusional 5-FU/leucovorin/ irinotecan (Camptosar®)	Camptosar (irinotecan) 180 mg/m ² IV over 90 minutes day 1; Leucovorin 400 mg/m ² IV over 2 hours day 1 followed by 5-FU 400 mg/m ² IV bolus over 2-4 minutes, followed by 2.4-3 gm/m ² IV 5-FU continuous infusion over 46 hours. Repeat cycle every 14 days	Varies
Anti-VEGF therapy.		
Avastin® (bevacizumab)	5 or 10 mg/kg IV every 14 days in combination with 5-FU based chemotherapy	20 mg/kg
Cyramza® (ramucirumab)Stivar ga® (regorafenib)	8 mg/kg IV every 2 weeks plus FOLFIRI regimen	10 mg/kg per dose
Zaltrap® (ziv-aflibercept)	160 mg PO QD for the first 21 days of each 28-day cycle	160 mg/day
Anti-EGFR therapy.		
Erbitux® (cetuximab)	400 mg/m ² IV for initial dose, then weekly infusions of 250 mg/m ² IV	400 mg/m ²
Vectibix® (panitumumab)	6 mg/kg IV every 2 weeks	9 mg/kg every 3 weeks

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

*5-FU and capecitabine are examples of fluoropyrimidine chemotherapeutic agents.

Appendix C: Contraindications

Not applicable.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Metastatic colorectal cancer	35 mg/m ² /dose PO BID on days 1 through 5 and Days 8 through 12 of each 28-day cycle.	160 mg/day (based on the trifluridine component)

VI. Product Availability

Tablet: 15 mg trifluridine/6.14 mg tipiracil
Tablet: 20 mg trifluridine /8.19 mg tipiracil

VII. References

1. Lonsurf Prescribing Information. Princeton, NJ: Taiho Oncology; March 2017. Available at www.taihooncology.com/us/prescribing-information Accessed April 2018.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed April 2018.
3. National Comprehensive Cancer Network. Colon cancer; Version 2.2018. Available at: <http://www.nccn.com>. Accessed April 2018.
4. National Comprehensive Cancer Network. Rectal cancer; Version 2.2018. Available at: <http://www.nccn.com>. Accessed April 2018.
5. Clinical Pharmacology [database online]. Tampa, FL. Available at <http://www.clinicalpharmacology-ip.com/>. Accessed April 2018.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy Created	10/18	
3Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	07/17/19	