Clinical Policy: Trifluridine/Tipiracil (Lonsurf)

Reference Number: CP.PHAR.383
Effective Date: 11.16.16
Last Review Date: 08.18
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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 Centene Corporation® 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. Age ≥ 18 years;
4. Documentation of RAS (KRAS or NRAS) wild-type gene status;
5. 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.*
6. 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:
Medicaid – 6 months

Commercial – Length of Benefit

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Colorectal Cancer (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Lonsurf for a covered indication and has received this medication for at least 30 days;
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:
Medicaid – 12 months
Commercial – Length of Benefit

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

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 – CP.CPA.09 for commercial and CP.PMN.53 for Medicaid or evidence of coverage documents.

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
Fluoropyrimidine, oxaliplatin, and irinotecan therapeutic agents and examples of regimens.		
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
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)Stivarga® (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
Converted to new template. Minor changes to verbiage and grammar. References updated.	01.10.17	11.17
3Q 2018 annual review: policies combined for Commercial and Centene Medicaid (new); off-label unresectable CRC added per NCCN; age and specialist requirements added; KRAS changed to RAS mutation per NCCN encompassing KRAS and NRAS; Cyramza and Stivarga added as anti-VEGF therapies per NCCN; dosing changed from 80 mg per dose to 160 mg per day to encompass BID regimen; continuation of care statement added; references reviewed and updated.	05.08.18	08.18

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and

accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

 Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.