

Lonsurf® (trifluridine and tipiracil) (Oral)

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I. Length of Authorization

Coverage will be provided for six months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Lonsurf 15 mg/6.14 mg tablet: 60 tablets per 28 days
- Lonsurf 20 mg/8.19 mg tablets: 80 tablets per 28 days

B. Max Units (per dose and over time) [HCPCS Unit]:

- 160 mg daily for 10 days per 28-day cycle

III. Initial Approval Criteria ¹

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

Colorectal Cancer † ^{1-4,7}

- Patient has advanced or metastatic disease; **AND**
- Used as a single agent or in combination with bevacizumab; **AND**
- Used as subsequent therapy for disease progression through all available regimens besides regorafenib

Gastric and Gastro-esophageal Junction Adenocarcinoma † Φ ^{1,2,5,6,8}

- Patient has recurrent, metastatic, or unresectable locally advanced disease OR patient is not a surgical candidate; **AND**
- Used as a single agent; **AND**
- Patient has received at least two (2) prior lines of chemotherapy that included: a fluoropyrimidine-, a platinum, and either a taxane or irinotecan; **AND**

- Patient has been previously treated with HER2/neu-targeted therapy (if HER2 positive disease) (e.g., trastuzumab, etc.)

† FDA-labeled indication(s); ‡ Compendia recommended indication(s); Ⓞ Orphan Drug

IV. Renewal Criteria ¹

Coverage can be renewed based upon the following criteria:

- Patient continues to meet indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe myelosuppression, etc.

V. Dosage/Administration ¹

| Indication | Dose |
|-----------------|---|
| All indications | 35 mg/m ² up to a maximum of 80 mg per dose (based on the trifluridine component) orally twice daily on Days 1 through 5 and Days 8 through 12 of each 28-day cycle (round dose to the nearest 5 mg increment) until disease progression or unacceptable toxicity. |

VI. Billing Code/Availability Information

HCPCS Code:

- J8999 – Prescription drug, oral, chemotherapeutic, nos

NDC:

- Lonsurf 15 mg/6.14 mg tablet: 64842-1025-xx
- Lonsurf 20 mg/8.19 mg tablet: 64842-1020-xx

VII. References

1. Lonsurf [package insert]. Princeton, NJ; Taiho Oncology Inc; December 2019. Accessed May 2021.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium[®]) trifluridine/tipiracil. National Comprehensive Cancer Network, 2021. The NCCN Compendium[®] is a derivative work of the NCCN Guidelines[®]. NATIONAL COMPREHENSIVE CANCER NETWORK[®], NCCN[®], and NCCN GUIDELINES[®] are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed May 2021.

3. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Colon Cancer Version 3.2021. National Comprehensive Cancer Network, 2021. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed May 2021.
4. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Rectal Cancer Version 4.2021. National Comprehensive Cancer Network, 2021. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed May 2021.
5. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Esophageal and Esophagogastric Junction Cancers 2.2021. National Comprehensive Cancer Network, 2021. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed May 2021.
6. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Gastric Cancer Version 2.2021. National Comprehensive Cancer Network, 2021. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed May 2021.
7. Mayer RJ, Van Cutsem E, Falcone A, et al. Randomized trial of TAS-102 for refractory metastatic colorectal cancer. N Engl J Med. 2015 May 14;372(20):1909-19. doi: 10.1056/NEJMoa1414325.
8. 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 Nov;19(11):1437-1448. doi: 10.1016/S1470-2045(18)30739-3. Epub 2018 Oct 21. Erratum in: Lancet Oncol. 2018 Dec;19(12):e668.

Appendix 1 – Covered Diagnosis Codes

| ICD-10 | ICD-10 Description |
|--------|--|
| C15.3 | Malignant neoplasm of upper third of esophagus |
| C15.4 | Malignant neoplasm of middle third of esophagus |
| C15.5 | Malignant neoplasm of lower third of esophagus |
| C15.8 | Malignant neoplasm of overlapping sites of esophagus |
| C15.9 | Malignant neoplasm of esophagus, unspecified |

| ICD-10 | ICD-10 Description |
|--------|--|
| C16.0 | Malignant neoplasm of cardia |
| C16.1 | Malignant neoplasm of fundus of stomach |
| C16.2 | Malignant neoplasm of body of stomach |
| C16.3 | Malignant neoplasm of pyloric antrum |
| C16.4 | Malignant neoplasm of pylorus |
| C16.5 | Malignant neoplasm of lesser curvature of stomach, unspecified |
| C16.6 | Malignant neoplasm of greater curvature of stomach, unspecified |
| C16.8 | Malignant neoplasm of overlapping sites of stomach |
| C16.9 | Malignant neoplasm of stomach, unspecified |
| C17.0 | Malignant neoplasm duodenum |
| C17.1 | Malignant neoplasm jejunum |
| C17.2 | Malignant neoplasm ileum |
| C17.8 | Malignant neoplasm of overlapping sites of small intestines |
| C17.9 | Malignant neoplasm of small intestine, unspecified |
| C18.0 | Malignant neoplasm of cecum |
| C18.1 | Malignant neoplasm of appendix |
| C18.2 | Malignant neoplasm of ascending colon |
| C18.3 | Malignant neoplasm of hepatic flexure |
| C18.4 | Malignant neoplasm of transverse colon |
| C18.5 | Malignant neoplasm of splenic flexure |
| C18.6 | Malignant neoplasm of descending colon |
| C18.7 | Malignant neoplasm of sigmoid colon |
| C18.8 | Malignant neoplasm of overlapping sites of large intestines |
| C18.9 | Malignant neoplasm of colon, unspecified |
| C19 | Malignant neoplasm of rectosigmoid junction |
| C20 | Malignant neoplasm of rectum |
| C21.8 | Malignant neoplasm of overlapping sites of rectum, anus and anal canal |
| C78.00 | Secondary malignant neoplasm of unspecified lung |
| C78.01 | Secondary malignant neoplasm of right lung |
| C78.02 | Secondary malignant neoplasm of left lung |
| C78.6 | Secondary malignant neoplasm of retroperitoneum and peritoneum |
| C78.7 | Secondary malignant neoplasm of liver and intrahepatic bile duct |
| D37.1 | Neoplasm of uncertain behavior of stomach |
| D37.8 | Neoplasm of uncertain behavior of other specified digestive organs |

| ICD-10 | ICD-10 Description |
|---------|---|
| D37.9 | Neoplasm of uncertain behavior of digestive organ, unspecified |
| Z85.00 | Personal history of malignant neoplasm of unspecified digestive organ |
| Z85.028 | Personal history of other malignant neoplasm of stomach |
| Z85.038 | Personal history of other malignant neoplasm of large intestine |
| Z85.068 | Personal history of other malignant neoplasm of small intestine |

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: <http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx>. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

| Medicare Part B Administrative Contractor (MAC) Jurisdictions | | |
|---|---|---|
| Jurisdiction | Applicable State/US Territory | Contractor |
| E (1) | CA, HI, NV, AS, GU, CNMI | Noridian Healthcare Solutions, LLC |
| F (2 & 3) | AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ | Noridian Healthcare Solutions, LLC |
| 5 | KS, NE, IA, MO | Wisconsin Physicians Service Insurance Corp (WPS) |
| 6 | MN, WI, IL | National Government Services, Inc. (NGS) |
| H (4 & 7) | LA, AR, MS, TX, OK, CO, NM | Novitas Solutions, Inc. |
| 8 | MI, IN | Wisconsin Physicians Service Insurance Corp (WPS) |
| N (9) | FL, PR, VI | First Coast Service Options, Inc. |
| J (10) | TN, GA, AL | Palmetto GBA, LLC |
| M (11) | NC, SC, WV, VA (excluding below) | Palmetto GBA, LLC |
| L (12) | DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA) | Novitas Solutions, Inc. |
| K (13 & 14) | NY, CT, MA, RI, VT, ME, NH | National Government Services, Inc. (NGS) |
| 15 | KY, OH | CGS Administrators, LLC |