Lonsurf®
(trifluridine and tipiracil) tablets

VETERANS ADMINISTRATION AND TRICARE STATUS

VA: Approved on formulary with Criteria for Use[a]

For LONSURF + bevacizumab combination treatment in mCRC, prescription is permitted in the VA utilizing the established CFU

TRICARE: Approved on the TRICARE Uniform Formulary

For LONSURF + bevacizumab combination treatment in mCRC, prescription is permitted in the TRICARE network utilizing the PA process for bevacizumab

10.8 months median overall survival (OS) with LONSURF used in combination with bevacizumab in 3L mCRC[1,b]

Scan this QR code to calculate the recommended starting dosage of LONSURF

2 tablet strengths for personalized dosing[1]

15-mg trifluridine/ 6.14-mg tipiracil tablet

20-mg trifluridine/ 8.19-mg tipiracil tablet

Tablets shown are not actual size.

4-week dosage cycle (28 days)[1]			
	LONSURF		IN COMBINATION WITH BEVACIZUMAB
Week 1	Twice daily for 5 days with food	2 days rest	IV dose (Day 1)
Week 2	Twice daily for 5 days with food	2 days rest	–
Week 3	Rest		IV dose (Day 15)
Week 4	Rest		–

Obtain complete blood cell counts prior to and on Day 15 of each cycle.

The efficacy of LONSURF in combination with bevacizumab was evaluated in an international, randomized, open-label study in patients with previously treated mCRC.[1] Patients were required to have received no more than 2 prior treatments for advanced disease, including a fluoropyrimidine, irinotecan, oxaliplatin, an anti-VEGF monoclonal antibody (optional) and an anti-EGFR monoclonal antibody for patients with RAS wild-type.[1] Patients were randomized to receive LONSURF 35 mg/m^2 administered orally twice daily on Days 1 to 5 and 8 to 12 of each 28-day cycle with or without bevacizumab 5 mg/kg administered intravenously every 2 weeks (on Day 1 and Day 15) of each 4-week cycle until disease progression or unacceptable toxicity.[1] The major efficacy outcome was OS.[1,b] A total of 492 patients were randomized to receive LONSURF in combination with bevacizumab (N=246) or LONSURF as a single agent (N=246).[1] Median OS with LONSURF used in combination with bevacizumab was 10.8 months (95% CI: 9.4, 11.8) compared to 7.5 months (95% CI: 6.3, 8.6) with LONSURF monotherapy (HR=0.61 [95% CI: 0.49, 0.77], and *P*-value=<0.001).[1,c-e]

3L, third-line; CFU, Criteria for Use; CI, confidence interval; HR, hazard ratio; IV, intravenous; mCRC, metastatic colorectal cancer; PA, prior authorization; VA, Veterans Affairs.

[a]The VA National PBM-MAP-VPE Monograph on LONSURF can be viewed at https://www.pbm.va.gov/PBM/clinicalguidance/drugmonographs.asp
[b]Compared to 7.5 months with LONSURF monotherapy.[1]
[c]OS was defined as the number of months from randomization until death and are Kaplan-Meier estimates.[1,2]
[d]HR and *P* values refer to the entire Kaplan-Meier OS curve, and not any individual timepoint.[2]
[e]The widths of the CIs have not been adjusted for multiplicity.[2]

INDICATIONS

LONSURF is indicated as a single agent or in combination with bevacizumab for the treatment of adult patients with metastatic colorectal cancer previously treated with fluoropyrimidine- , oxaliplatin- and irinotecan-based chemotherapy, an anti-VEGF biological therapy, and if *RAS* wild-type, an anti-EGFR therapy.

LONSURF is indicated for the 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, HER2/neu-targeted therapy.

TAIHO ONCOLOGY

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Severe Myelosuppression: In the 1114 patients who received LONSURF as a single agent, LONSURF caused severe or life-threatening myelosuppression (Grade 3-4) consisting of neutropenia (38%), anemia (17%), thrombocytopenia (4%) and febrile neutropenia (3%). Three patients (0.3%)

Please see additional Important Safety Information on back and full Prescribing Information at LONSURF.com/PI.

FEDERAL PRODUCT PORTFOLIO RESOURCES

Looking for more information?

Email FederalAccounts@taihooncology.com

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Severe Myelosuppression (cont'd): died due to neutropenic infection/sepsis; four other patients (0.5%) died due to septic shock. A total of 14% of patients received granulocyte-colony stimulating factors. In the 246 patients who received LONSURF in combination with bevacizumab, LONSURF caused severe or life-threatening myelosuppression (Grade 3-4) consisting of neutropenia (52%), anemia (5%), thrombocytopenia (4%) and febrile neutropenia (0.4%). One patient (0.4%) died due to abdominal sepsis and two other patients (0.8%) died due to septic shock. A total of 29% of patients received granulocyte-colony stimulating factors. Obtain complete blood counts prior to and on Day 15 of each cycle of LONSURF and more frequently as clinically indicated. Withhold LONSURF for severe myelosuppression and resume at the next lower dosage.

Embryo-Fetal Toxicity: LONSURF can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to the fetus. Advise females of reproductive potential to use effective contraception during treatment and for at least 6 months after the final dose.

USE IN SPECIFIC POPULATIONS

Lactation: It is not known whether LONSURF or its metabolites are present in human milk. There are no data to assess the effects of LONSURF or its metabolites on the breastfed child or the effects on milk production. Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment with LONSURF and for 1 day following the final dose.

Male Contraception: Because of the potential for genotoxicity, advise males with female partners of reproductive potential to use condoms during treatment with LONSURF and for at least 3 months after the final dose.

Geriatric Use: Patients 65 years of age or older who received LONSURF as a single agent had a higher incidence of the following hematologic laboratory abnormalities compared to patients younger than 65 years: Grade 3 or 4 neutropenia (46% vs 32%), Grade 3 anemia (20% vs 14%), and Grade 3 or 4 thrombocytopenia (6% vs 3%). Patients 65 years of age or older who received LONSURF in combination with bevacizumab had a higher incidence of the following hematologic laboratory abnormalities compared to patients younger than 65 years: Grade 3 or 4 neutropenia (60% vs 46%) and Grade 3 or 4 thrombocytopenia (5% vs 4%).

Renal Impairment: No adjustment to the starting dosage of LONSURF is recommended in patients with mild or moderate renal impairment (CLcr of 30 to 89 mL/min). Reduce the starting dose of LONSURF for patients with severe renal impairment (CLcr of 15 to 29 mL/min) to a recommended dosage of 20 mg/m^2.

Hepatic Impairment: Do not initiate LONSURF in patients with baseline moderate or severe (total bilirubin > 1.5 times ULN and any AST) hepatic impairment. Patients with severe hepatic impairment (total bilirubin > 3 times ULN and any AST) were not studied. No adjustment to the starting dosage of LONSURF is recommended for patients with mild hepatic impairment.

ADVERSE REACTIONS

Serious adverse reactions occurred in 25% of patients. The most frequent serious adverse reactions (≥2%) were intestinal obstruction (2.8%), and COVID-19 (2%). Fatal adverse reactions occurred in 1.2% of patients who received LONSURF in combination with bevacizumab, including rectal fistula (0.4%), bowel perforation (0.4%) and atrial fibrillation (0.4%).

The most common adverse reactions or laboratory abnormalities (≥10% in incidence) in patients treated with single-agent LONSURF at a rate that exceeds the rate in patients receiving placebo in mCRC: anemia (77% vs 33%), neutropenia (67% vs 0.8%), asthenia/fatigue (52% vs 35%), nausea (48% vs 24%), thrombocytopenia (42% vs 8%), decreased appetite (39% vs 29%), diarrhea (32% vs 12%), vomiting (28% vs 14%), abdominal pain (21% vs 19%), and pyrexia (19% vs 14%). In metastatic gastric cancer or gastroesophageal junction (GEJ): neutropenia (66% vs 4%), anemia (63% vs 38%), nausea (37% vs 32%), thrombocytopenia (34% vs 9%), decreased appetite (34% vs 31%), vomiting (25% vs 20%), infections (23% vs 16%) and diarrhea (23% vs 14%).

Pulmonary emboli occurred more frequently in LONSURF-treated patients compared to placebo: in mCRC (2% vs 0%) and in metastatic gastric cancer and GEJ (3% vs 2%).

Interstitial lung disease (0.2%), including fatalities, has been reported in clinical studies and clinical practice settings in Asia.

The most common adverse reactions or laboratory abnormalities (≥20% in incidence) in patients treated with LONSURF in combination with bevacizumab vs LONSURF alone were neutropenia (80% vs 68%), anemia (68% vs 73%), thrombocytopenia (54% vs 29%), fatigue (45% vs 37%), nausea (37% vs 27%), increased aspartate aminotransferase (34% vs 28%), increased alanine aminotransferase (33% vs 23%), increased alkaline phosphate (31% vs 36%), decreased sodium (25% vs 20%), diarrhea (21% vs 19%), abdominal pain (20% vs 18%), and decreased appetite (20% vs 15%).

Please see full Prescribing Information at LONSURF.com/PI.

References: 1. LONSURF. Prescribing Information. Taiho Oncology, Inc; 2023.
2. Prager GW, Taieb J, Fakih M, et al. Trifluridine–tipiracil and bevacizumab in mefractory metastatic colorectal cancer. *N Engl J Med.* 2023;388(18):1657-1667. doi: 10.1056/NEJMoa2214963

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