DOSING GUIDE FOR NURSES

The importance of treatment management

for your patients on LONSURF® (trifluridine/tipiracil) tablets

LONSURF is indicated 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.

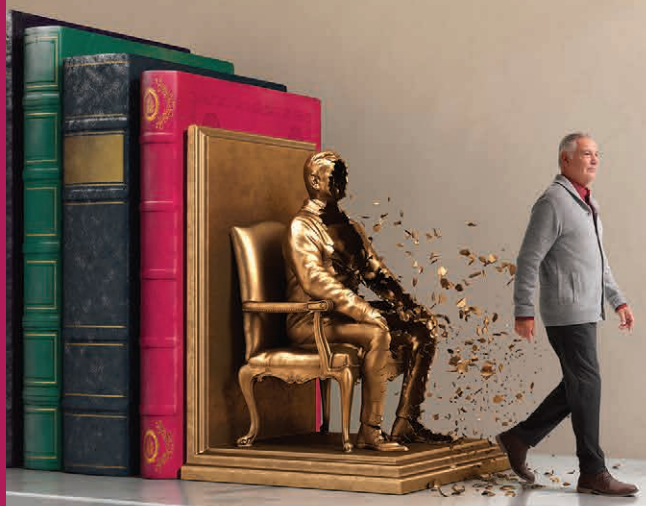
Selected Important Safety Information

WARNINGS AND PRECAUTIONS

Severe Myelosuppression:

LONSURF caused severe and life-threatening myelosuppression (Grade 3-4) consisting of neutropenia (38%), anemia (18%), thrombocytopenia (5%), and febrile neutropenia (3%). Two patients (0.2%) died due to neutropenic infection. A total of 12% of LONSURF-treated 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 febrile neutropenia, absolute neutrophil count less than 500/mm^3, or platelets less than 50,000/mm^3. Upon recovery, resume LONSURF at a reduced dose as clinically indicated.

Please see additional Important Safety Information throughout and full Prescribing Information in pocket.



Lonsurf®
(trifluridine and tipiracil) tablets

Actor portrayal.

Proper dosing is important for treatment results

Oral treatment starts with indicated dosing

- Calculate by body surface area (BSA)—35 mg/m^2*†
- Dose oral treatment twice daily, with food
- Provide the proper number of 15-mg and 20-mg tablets to make up the calculated dose
- Never exceed 80 mg for a single dose,* or 160 mg total daily dose*
- In patients with severe renal impairment, the recommended dosage is 20 mg/m^2 twice daily. For patients who are unable to tolerate this dose, reduce the dose to 15 mg/m^2 twice daily. Permanently discontinue LONSURF® tablets–FTD/TPI in patients who are unable to tolerate a dose of 15 mg/m^2 twice daily

If needed

- Round BSA-based calculation up to the nearest 5-mg increment

Important for proper dosing

- Instruct patients to swallow tablets whole
- Instruct patients not to retake any doses that are missed or vomited and to continue with the next scheduled dose
- LONSURF is a cytotoxic drug. Follow applicable special handling and disposal procedures. Store at 20°C to 25°C (68°F to 77°F); excursions are permitted from 15°C to 30°C (59°F to 86°F). If stored outside original bottle, discard after 30 days

For more information on dosing modifications including severe renal impairment, hematologic ARs, or other ARs, visit **LONSURFHCP.com/dosing/dosage-modifications**

AR=adverse reaction; FTD/TPI=trifluridine/tipiracil.
*Based on the trifluridine component.
†In patients with severe renal impairment (CLcr of 15 to 29 mL/min), the recommended dosage is 20 mg/m^2.

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Dosed over a 4-week cycle (28 days)

- Active treatment days include days 1 to 5 and days 8 to 12 of each cycle
- Obtain complete blood cell counts prior to and on day 15 of each cycle

Week 1	Twice daily for 5 days with food	2 days rest
Week 2	Twice daily for 5 days with food	2 days rest
Week 3	Rest	
Week 4	Rest	

2 tablet strengths

15 mg trifluridine/
6.14 mg tipiracil tablet

20 mg trifluridine/
8.19 mg tipiracil tablet

Tablets shown at actual size.

In the RECOURSE trial:

- **86%** of patients taking LONSURF did not require a dose reduction‡
  - The most common adverse event or lab abnormalities leading to dose reduction were neutropenia, anemia, febrile neutropenia, fatigue, and diarrhea
- 3.6% of patients taking LONSURF discontinued treatment due to an AR

In the TAGS trial:

- **89%** of patients taking LONSURF did not require a dose reduction§
  - The most common ARs or lab abnormalities leading to dose reduction were neutropenia, anemia, febrile neutropenia, and diarrhea
- 13% of patients taking LONSURF discontinued treatment due to an AR vs 17% of patients taking placebo

Calculate the proper dose for your patients by scanning this QR Code

AR=adverse reaction; RECOURSE=**Re**fractory **Co**l**o**r**e**ctal Cancer **S**tudy; TAGS=**TA**S-102 **G**astric **S**tudy.
‡In the RECOURSE trial, 14% of patients required a dose reduction.
§In the TAGS trial, 11% of patients required a dose reduction.

Selected Important Safety Information

WARNINGS AND PRECAUTIONS

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.

Lonsurf® (trifluridine and tipiracil) tablets

AR management at cycle start

DELAY FIRST for ARs already present at cycle start, and then reinitiate as recommended[1,2]

Neutropenia

(ANC 500/mm³ to <1500/mm³) → Delay treatment until recovery: ANC is ≥1500/mm³ → Start cycle at previous dose

(ANC <500/mm³) → Delay treatment until recovery: ANC is ≥1500/mm³
- Recovery ≤1 week → Start cycle at previous dose
- Recovery >1 week → Resume at 5 mg/m²/dose lower than previous dose

Febrile neutropenia

(ANC <1000/mm³ with 101.0°F temperature or 100.4°F >1 hour) → Delay treatment until ANC is ≥1500/mm³ and fever is resolved → After recovery, resume at 5 mg/m²/dose lower than previous dose

Thrombocytopenia

(Platelet count 25,000 to <75,000/mm³) → Delay treatment until platelet count is ≥75,000/mm³ → After recovery, start cycle at previous dose

(Platelet count <25,000 mm³) → Delay treatment until platelet count is ≥75,000/mm³
- Recovery ≤1 week → Start cycle at previous dose
- Recovery >1 week → Resume at 5 mg/m²/dose lower than previous dose

Nonhematologic ARs[a]

(Grades 3-4) → Delay treatment until resolved to Grade 0 or 1 → Resume at 5 mg/m²/dose lower than previous dose

[a]For all Grade 3 or 4 ARs except for Grade 3 nausea and/or vomiting controlled by antiemetic therapy or Grade 3 diarrhea responsive to antidiarrheal medication.

Selected Important Safety Information

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 breast-fed infant or the effects on milk production. Because of the potential for serious adverse reactions in breast-fed infants, advise women not to breastfeed during treatment with LONSURF and for 1 day following the final dose.

Please see additional Important Safety Information throughout and full Prescribing Information in pocket.

AR management during a treatment cycle

WITHHOLD for ARs occurring during active treatment, and then reinitiate as recommended[1,2*]

Neutropenia

(ANC <500/mm³) → Withhold treatment until recovery: ANC is ≥1500/mm³
- Recovery ≤1 week → Start cycle at previous dose
- Recovery >1 week → Resume at 5 mg/m²/dose lower than previous dose

Febrile neutropenia

(ANC <1000/mm³ with 101.0°F temperature or 100.4°F >1 hour) → Withhold treatment until ANC is ≥1500/mm³ and fever is resolved → After recovery, resume at 5 mg/m²/dose lower than previous dose

Thrombocytopenia

(Platelet count 25,000 to <50,000/mm³) → Withhold treatment until platelet count is ≥75,000/mm³ → After recovery, start cycle at previous dose

(Platelet count <25,000 mm³) → Withhold treatment until platelet count is ≥75,000/mm³
- Recovery ≤1 week → Start cycle at previous dose
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[a]For all Grade 3 or 4 ARs except for Grade 3 nausea and/or vomiting controlled by antiemetic therapy or Grade 3 diarrhea responsive to antidiarrheal medication.

A maximum of 3 dose reductions are permitted. Permanently discontinue LONSURF® tablets–FTD/TPI in patients unable to tolerate a dose of 20 mg/m² orally twice daily. Do not escalate LONSURF dosage after it has been reduced.

In patients with **severe renal impairment** who are unable to tolerate a dose of 20 mg/m² twice daily, reduce dose to 15 mg/m² twice daily

ANC=absolute neutrophil count.

*Active treatment occurs on days 1 through 5 and days 8 through 12 of each 28-day cycle.

Lonsurf® (trifluridine and tipiracil) tablets

Managing common ARs

Here are some tips to share with your patients to help them manage common ARs at home.

For fatigue/weakness, remind your patients to[3]:

- Rest often and limit activities
- Make a bedtime routine
- Ask family for help when needed
- Stay active with simple exercises
- Talk to their healthcare provider about medication options

For diarrhea, remind your patients to[3]:

- Eat smaller meals throughout the day, including foods high in sodium and potassium and low in fiber*
- Stay hydrated with clear, room-temperature liquids
- Discuss medication options with their healthcare provider

For fever, remind your patients to[6,7]:

- Rest, stay hydrated, and keep cool
- Alert their healthcare provider immediately

For nausea and vomiting, remind your patients to[3,4]:

- Eat smaller meals throughout the day, avoiding greasy, fried, sweet, and spicy foods*
- Try small bites of an ice pop or ice cube, unless the temperature bothers them
- Talk to their healthcare provider about possible medications

For abdominal pain, remind your patients to[3,5]:

- Exercise regularly
- Eat foods high in fiber
- Let their caregiver know about the pain
- Relax with yoga or deep breathing

*Smaller, more frequent meals will not affect the patient's dosing cycle.

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Selected Important Safety Information

USE IN SPECIFIC POPULATIONS (cont'd)

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 over who received LONSURF had a higher incidence of the following compared to patients younger than 65 years: Grade 3 or 4 neutropenia (46% vs 32%), Grade 3 anemia (22% vs 16%), and Grade 3 or 4 thrombocytopenia (7% vs 4%).

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

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.

ADVERSE REACTIONS

Most Common Adverse Drug Reactions in Patients Treated With LONSURF (≥5%): The most common adverse drug reactions in LONSURF-treated patients vs placebo-treated patients with mCRC, respectively, were asthenia/fatigue (52% vs 35%), nausea (48% vs 24%), decreased appetite (39% vs 29%), diarrhea (32% vs 12%), vomiting (28% vs 14%), infections (27% vs 16%), abdominal pain (21% vs 18%), pyrexia (19% vs 14%), stomatitis (8% vs 6%), dysgeusia (7% vs 2%), and alopecia (7% vs 1%). In metastatic gastric cancer or gastroesophageal junction (GEJ), the most common adverse drug reactions, respectively were, nausea (37% vs 32%), 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.

Laboratory Test Abnormalities in Patients Treated With LONSURF: The most common laboratory test abnormalities in LONSURF-treated patients vs placebo-treated patients with mCRC, respectively, were anemia (77% vs 33%), neutropenia (67% vs 1%), and thrombocytopenia (42% vs 8%). In metastatic gastric cancer or GEJ, the test abnormalities, respectively, were neutropenia (66% vs 4%), anemia (63% vs 38%), and thrombocytopenia (34% vs 9%).

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TAIHO ONCOLOGY PATIENT SUPPORT

Supporting your treatment journey

Taiho Oncology Patient Support™ is here to help you obtain access to your Taiho Oncology medicine. The program offers benefits review to confirm coverage, co-pay assistance* enrollment, specialty pharmacy prescription coordination, and personalized nurse support for patients taking LONSURF® tablets–FTD/TPI.

For more support for your patients taking LONSURF:

- **Call 1-844-TAIHO-4U** (1-844-824-4648) Monday to Friday, 8 AM to 8 PM ET
- **Visit LONSURF.com/resources**
- **See** the Patient Access Brochure available at **TaihoPatientSupport.com**

*For commercially insured eligible patients, visit TaihoPatientSupport.com to see full eligibility criteria.

References: 1. LONSURF [package insert]. Princeton, NJ: Taiho Oncology, Inc.; 2019. **2.** National Cancer Institute. Common terminology criteria for adverse events v4.03 (CTCAE). Bethesda, MD: National Institutes of Health; 2010. NIH publication 09-5410. **3.** National Cancer Institute. Chemotherapy and you. Bethesda, MD: National Institutes of Health; September 2018. NIH publication 18-7157. **4.** Nausea and vomiting in people with cancer. National Cancer Institute website. https://www.cancer.gov/about-cancer/treatment/side-effects/nausea. Updated January 23, 2020. Accessed November 8, 2021. **5.** Abdominal pain. MedlinePlus website. https://medlineplus.gov/ency/article/003120.htm. Updated August 4, 2020. Accessed November 8, 2021. **6.** Fever. American Cancer Society website. https://www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/low-blood-counts/fever.html. Updated February 1, 2020. Accessed November 8, 2021. **7.** LONSURF [patient information leaflet]. Princeton, NJ: Taiho Oncology, Inc.; 2020.

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