Retevmo®
selpercatinib capsules
40 mg • 80 mg

Retevmo Access, Distribution, & Reimbursement Guide

The following information is presented for informational purposes only and is not intended to provide reimbursement or legal advice. Laws, regulations, and policies concerning reimbursement are complex and are updated frequently. Individual coding decisions should be based upon diagnosis and treatment of individual patients. While we have made an effort to be current as of the issue date of this document, the information may not be as current or comprehensive when you view it. Providers are encouraged to contact third-party payers for specific information on their coverage, coding, and payment policies. Please consult with your legal counsel or reimbursement specialist for any reimbursement or billing questions. For more information, please call the Lilly Oncology Support Center at 1-866-472-8663.

Indications[1]

Retevmo is a kinase inhibitor indicated for the treatment of:

- adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with a *rearranged during transfection (RET)* gene fusion, as detected by an FDA-approved test
- adult and pediatric patients 12 years of age and older with advanced or metastatic medullary thyroid cancer (MTC) with a *RET* mutation, as detected by an FDA-approved test, who require systemic therapy*
- adult and pediatric patients 12 years of age and older with advanced or metastatic thyroid cancer with a *RET* gene fusion, as detected by an FDA-approved test, who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate)*
- adult patients with locally advanced or metastatic solid tumors with a *RET* gene fusion that have progressed on or following prior systemic treatment or who have no satisfactory alternative treatment options*

*These indications are approved under accelerated approval based on overall response rate (ORR) and duration of response (DoR). Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trials.

SELECT IMPORTANT SAFETY INFORMATION FOR RETEVMO

Hepatotoxicity: Serious hepatic adverse reactions occurred in 3% of patients treated with Retevmo. Increased aspartate aminotransferase (AST) occurred in 59% of patients, including Grade 3 or 4 events in 11% and increased alanine aminotransferase (ALT) occurred in 55% of patients, including Grade 3 or 4 events in 12%. Monitor ALT and AST prior to initiating Retevmo, every 2 weeks during the first 3 months, then monthly thereafter and as clinically indicated. Withhold, reduce dose, or permanently discontinue Retevmo based on the severity.

FDA=US Food and Drug Administration.

Please see additional Important Safety Information on pages 4-6 and click for full Prescribing Information for Retevmo.

Lilly

Introduction

This guide includes

- Key information on Retevmo
- Prescription, ordering, and patient support services offered through the Lilly Oncology Support Center
- Specialty pharmacy network and specialty distributor network

Retevmo Supply and National Drug Code (NDC)[1]

All coding and documentation requirements for drugs should be confirmed with each payer.

Dosage	NDC
40-mg capsules — 60-count bottle	0002-3977-60
80-mg capsules — 60-count bottle	0002-2980-60
80-mg capsules — 120-count bottle	0002-2980-26

There Are Several Ways to Get Retevmo, Depending on the Patient's Insurance

Retevmo is available through

- **Contracted specialty pharmacies**†
- **Hospital and health system practices**
- **In-office dispensing practices (IODs)**

Retevmo is available through contracted specialty pharmacies.
For a full list of specialty pharmacies, please visit www.Retevmo.com.

Retevmo can be purchased through authorized specialty distributors, which can be found at lillytrade.com.

†Eligible pharmacies can purchase Retevmo through our authorized distribution partners. A list of authorized distributors can be found at lillytrade.com.

SELECT IMPORTANT SAFETY INFORMATION FOR RETEVMO

Severe, life-threatening, and fatal **interstitial lung disease (ILD)/pneumonitis** can occur in patients treated with Retevmo. ILD/pneumonitis occurred in 1.8% of patients who received Retevmo, including 0.3% with Grade 3 or 4 events, and 0.3% with fatal reactions. Monitor for pulmonary symptoms indicative of ILD/pneumonitis. Withhold Retevmo and promptly investigate for ILD in any patient who presents with acute or worsening of respiratory symptoms which may be indicative of ILD (e.g., dyspnea, cough, and fever). Withhold, reduce dose, or permanently discontinue Retevmo based on severity of confirmed ILD.

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Lilly Oncology Support Center

Lilly Oncology Support Center provides easy-to-use resources and reimbursement options for eligible patients whose doctors have prescribed them Retevmo. Lilly Oncology Support Center addresses financial and coverage issues for qualified patients. Offerings include benefits investigations, financial assistance, and appeals information—all providing individualized support for eligible patients.

Savings & Support **Tailored to Your Patient's Retevmo Treatment Journey‡**

Retevmo Savings Card

- Eligible commercially insured covered patients pay as little as $0 a month[§]
- Digital cards can be downloaded online. You and your patients can get a savings card by visiting Retevmo.com

Retevmo Insurance & Coverage Assistance‡

May help eligible patients minimize co-pay or out-of-pocket costs by providing:

- A benefits investigation
- Guidance through the specialty pharmacy process
- Identification of savings opportunities

Retevmo Interim Access Program

The Retevmo Interim Access Program may provide a temporary supply of Retevmo at no cost to insured, eligible patients who have been prescribed Retevmo for the first time and are experiencing a delay in their insurance coverage decision.[‖]

MyRightDose: Dose Exchange Program[¶]

May simplify midcycle dose exchanges for patients—MyRightDose ships the appropriate dose directly to your patient's home in as early as 48 hours and at no cost to the patient.

Retevmo Ongoing Support‡

Sign up for Retevmo Ongoing Support to receive a Welcome Kit, emails, and texts to help you manage your treatment experience.

For more information about Lilly Oncology Support Center, call 1-866-472-8663, Monday–Friday, 8 AM–10 PM ET, or visit Retevmo.com.

‡Retevmo support programs and offerings are not a guarantee of coverage. Terms and conditions apply for all programs. See enrollment form for details.

§Offer good for up to 12 months from patient qualification into the program. Patients must have coverage for Retevmo through their commercial drug insurance coverage to pay as little as $0 for a 30-day supply of Retevmo. Offer subject to a monthly cap and a separate annual cap of $25,000. Participation in the program requires a valid patient HIPAA authorization. Offer void where prohibited by law. Patient is responsible for any applicable taxes, fees, or amounts exceeding monthly or annual caps. **This offer is invalid for patients without commercial drug insurance or whose prescription claims for Retevmo are eligible to be reimbursed, in whole or in part, by any governmental program, including, without limitation, Medicaid, Medicare, Medicare Part D, Medigap, DoD, VA, TRICARE®/CHAMPUS, or any State Patient or Pharmaceutical Assistance Program.** Offer void where prohibited by law and subject to change or discontinue without notice. Card activation is required. Subject to additional terms and conditions, which can be found www.retevmo.com/savings-support#savings.

‖The Retevmo Interim Access Program (or "Program") provides a 15-day supply of Retevmo at no charge for eligible, insured patients who are: 1) prescribed Retevmo for the first time after testing positive for a *RET* alteration, 2) experiencing a minimum 5-business-day delay in insurance coverage determination, 3) prescribed Retevmo for an FDA-approved indication or an indication medically supported by CMS-recognized compendia, 4) enrolled in the Lilly Oncology Support Center, and 5) a resident of the United States or Puerto Rico. May not be combined with any other offer. Not available to patients whose insurers have made a final determination to deny the patient coverage for Retevmo. If a denial is received after the initial 5 business days have passed and appeal rights are being pursued, or if there is a persistent coverage delay, the patient, under appropriate circumstances, may be eligible for up to 3 additional 15-day supplies of Retevmo. Product provided through the Program is only available through the Program non-commercial specialty pharmacy. Product is provided free of charge and may not be sold, bartered, or returned for credit. Reimbursement cannot be sought from any third party for product provided under the program. Patients enrolled in Medicare Part D are prohibited from counting any portion of the cost of the product provided under the Program towards true out-of-pocket ("TrOOP") costs for prescription drug calculations. No purchase contingency or other obligation accompanies program participation. This Program is not health insurance and does not guarantee coverage. Lilly reserves the right to change or end the program at any time. Benefits under the program are not transferable.

¶Additional terms and conditions apply. See the MyRightDose enrollment form for details.

CMS=Centers for Medicare & Medicaid Services; DoD=US Department of Defense; HIPAA=Health Insurance Portability and Accountability Act; VA=US Department of Veterans Affairs.

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IMPORTANT SAFETY INFORMATION FOR RETEVMO

Hepatotoxicity: Serious hepatic adverse reactions occurred in 3% of patients treated with Retevmo. Increased aspartate aminotransferase (AST) occurred in 59% of patients, including Grade 3 or 4 events in 11% and increased alanine aminotransferase (ALT) occurred in 55% of patients, including Grade 3 or 4 events in 12%. Monitor ALT and AST prior to initiating Retevmo, every 2 weeks during the first 3 months, then monthly thereafter and as clinically indicated. Withhold, reduce dose, or permanently discontinue Retevmo based on the severity.

Severe, life-threatening, and fatal **interstitial lung disease (ILD)/pneumonitis** can occur in patients treated with Retevmo. ILD/pneumonitis occurred in 1.8% of patients who received Retevmo, including 0.3% with Grade 3 or 4 events, and 0.3% with fatal reactions. Monitor for pulmonary symptoms indicative of ILD/pneumonitis. Withhold Retevmo and promptly investigate for ILD in any patient who presents with acute or worsening of respiratory symptoms which may be indicative of ILD (e.g., dyspnea, cough, and fever). Withhold, reduce dose, or permanently discontinue Retevmo based on severity of confirmed ILD.

Hypertension occurred in 41% of patients, including Grade 3 hypertension in 20% and Grade 4 in one (0.1%) patient. Overall, 6.3% had their dose interrupted and 1.3% had their dose reduced for hypertension. Treatment-emergent hypertension was most commonly managed with anti-hypertension medications. Do not initiate Retevmo in patients with uncontrolled hypertension. Optimize blood pressure prior to initiating Retevmo. Monitor blood pressure after 1 week, at least monthly thereafter, and as clinically indicated. Initiate or adjust anti-hypertensive therapy as appropriate. Withhold, reduce dose, or permanently discontinue Retevmo based on the severity.

Retevmo can cause concentration-dependent **QT interval prolongation**. An increase in QTcF interval to >500 ms was measured in 7% of patients and an increase in the QTcF interval of at least 60 ms over baseline was measured in 20% of patients. Retevmo has not been studied in patients with clinically significant active cardiovascular disease or recent myocardial infarction. Monitor patients who are at significant risk of developing QTc prolongation, including patients with known long QT syndromes, clinically significant bradyarrhythmias, and severe or uncontrolled heart failure. Assess QT interval, electrolytes, and thyroid-stimulating hormone (TSH) at baseline and periodically during treatment, adjusting frequency based upon risk factors including diarrhea. Correct hypokalemia, hypomagnesemia, and hypocalcemia prior to initiating Retevmo and during treatment. Monitor the QT interval more frequently when Retevmo is concomitantly administered with strong and moderate CYP3A inhibitors or drugs known to prolong QTc interval. Withhold and dose reduce or permanently discontinue Retevmo based on the severity.

Serious, including fatal, **hemorrhagic events** can occur with Retevmo. Grade ≥3 hemorrhagic events occurred in 3.1% of patients treated with Retevmo including 4 (0.5%) patients with fatal hemorrhagic events, including cerebral hemorrhage (n=2), tracheostomy site hemorrhage (n=1), and hemoptysis (n=1). Permanently discontinue Retevmo in patients with severe or life-threatening hemorrhage.

Hypersensitivity occurred in 6% of patients receiving Retevmo, including Grade 3 hypersensitivity in 1.9%. The median time to onset was 1.9 weeks (range: 5 days to 2 years). Signs and symptoms of hypersensitivity included fever, rash and arthralgias or myalgias with concurrent decreased platelets or transaminitis. If hypersensitivity occurs, withhold Retevmo and begin corticosteroids at a dose of 1 mg/kg prednisone (or equivalent). Upon resolution of the event, resume Retevmo at a reduced dose and increase the dose of Retevmo by 1 dose level each week as tolerated until reaching the dose taken prior to onset of hypersensitivity. Continue steroids until patient reaches target dose and then taper. Permanently discontinue Retevmo for recurrent hypersensitivity.

Tumor lysis syndrome (TLS) occurred in 0.6% of patients with medullary thyroid carcinoma receiving Retevmo. Patients may be at risk of TLS if they have rapidly growing tumors, a high tumor burden, renal dysfunction, or dehydration. Closely monitor patients at risk, consider appropriate prophylaxis including hydration, and treat as clinically indicated.

Please see additional Important Safety Information on pages 5 and 6 and click for full Prescribing Information for Retevmo.

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IMPORTANT SAFETY INFORMATION FOR RETEVMO (CONTINUED)

Impaired wound healing can occur in patients who receive drugs that inhibit the vascular endothelial growth factor (VEGF) signaling pathway. Therefore, Retevmo has the potential to adversely affect wound healing. Withhold Retevmo for at least 7 days prior to elective surgery. Do not administer for at least 2 weeks following major surgery and until adequate wound healing. The safety of resumption of Retevmo after resolution of wound healing complications has not been established.

Retevmo can cause **hypothyroidism**. Hypothyroidism occurred in 13% of patients treated with Retevmo; all reactions were Grade 1 or 2. Hypothyroidism occurred in 13% of patients (50/373) with thyroid cancer and 13% of patients (53/423) with other solid tumors including NSCLC. Monitor thyroid function before treatment with Retevmo and periodically during treatment. Treat with thyroid hormone replacement as clinically indicated. Withhold Retevmo until clinically stable or permanently discontinue Retevmo based on severity.

Based on data from animal reproduction studies and its mechanism of action, Retevmo can cause **fetal harm** when administered to a pregnant woman. Administration of selpercatinib to pregnant rats during organogenesis at maternal exposures that were approximately equal to those observed at the recommended human dose of 160 mg twice daily resulted in embryolethality and malformations. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential and males with female partners of reproductive potential to use effective contraception during treatment with Retevmo and for 1 week after the last dose. There are no data on the presence of selpercatinib or its metabolites in human milk or on their effects on the breastfed child or on milk production. Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment with Retevmo and for 1 week after the last dose.

Severe adverse reactions (Grade 3-4) occurring in ≥20% of patients who received Retevmo in LIBRETTO-001, were hypertension (20%), diarrhea (5%), prolonged QT interval (4.8%), dyspnea (3.1%), fatigue (3.1%), hemorrhage (2.6%), abdominal pain (2.5%), vomiting (1.8%), headache (1.4%), nausea (1.1%), constipation (0.8%), edema (0.8%), rash (0.6%), and arthralgia (0.3%).

Serious adverse reactions occurred in 44% of patients who received Retevmo. The most frequently reported serious adverse reactions (in ≥2% of patients) were pneumonia, pleural effusion, abdominal pain, hemorrhage, hypersensitivity, dyspnea, and hyponatremia.

Fatal adverse reactions occurred in 3% of patients; fatal adverse reactions included sepsis (n=6), respiratory failure (n=5), hemorrhage (n=4), pneumonia (n=3), pneumonitis (n=2), cardiac arrest (n=2), sudden death (n=1), and cardiac failure (n=1).

Common adverse reactions (all grades) occurring in ≥20% of patients who received Retevmo in LIBRETTO-001, were edema (49%), diarrhea (47%), fatigue (46%), dry mouth (43%), hypertension (41%), abdominal pain (34%), rash (33%), constipation (33%), nausea (31%), headache (28%), cough (24%), vomiting (22%), dyspnea (22%), hemorrhage (22%), arthralgia (21%), and prolonged QT interval (21%).

Laboratory abnormalities (all grades ≥20%; Grade 3-4) worsening from baseline in patients who received Retevmo in LIBRETTO-001, were increased AST (59%; 11%), decreased calcium (59%; 5.7%), increased ALT (56%; 12%), decreased albumin (56%; 2.3%), increased glucose (53%; 2.8%), decreased lymphocytes (52%; 20%), increased creatinine (47%; 2.4%), decreased sodium (42%; 11%), increased alkaline phosphatase (40%; 3.4%), decreased platelets (37%; 3.2%), increased total cholesterol (35%; 1.7%), increased potassium (34%; 2.7%), decreased glucose (34%; 1.0%), decreased magnesium (33%; 0.6%), increased bilirubin (30%; 2.8%), decreased hemoglobin (28%; 3.5%), and decreased neutrophils (25%; 3.2%).

Concomitant use of **acid-reducing agents** decreases selpercatinib plasma concentrations which may reduce Retevmo anti-tumor activity. Avoid concomitant use of proton-pump inhibitors (PPIs), histamine-2 (H2) receptor antagonists, and locally-acting antacids with Retevmo. If coadministration cannot be avoided, take Retevmo with food (with a PPI) or modify its administration time (with a H2 receptor antagonist or a locally-acting antacid).

Please see additional Important Safety Information on page 6 and click for full Prescribing Information for Retevmo.

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IMPORTANT SAFETY INFORMATION FOR RETEVMO (CONTINUED)

Concomitant use of **strong and moderate CYP3A inhibitors** increases selpercatinib plasma concentrations which may increase the risk of Retevmo adverse reactions including QTc interval prolongation. Avoid concomitant use of strong and moderate CYP3A inhibitors with Retevmo. If concomitant use of a strong or moderate CYP3A inhibitor cannot be avoided, reduce the Retevmo dosage as recommended and monitor the QT interval with ECGs more frequently.

Concomitant use of **strong and moderate CYP3A inducers** decreases selpercatinib plasma concentrations which may reduce Retevmo anti-tumor activity. Avoid coadministration of Retevmo with strong and moderate CYP3A inducers.

Concomitant use of Retevmo with **CYP2C8 and CYP3A substrates** increases their plasma concentrations which may increase the risk of adverse reactions related to these substrates. Avoid coadministration of Retevmo with CYP2C8 and CYP3A substrates where minimal concentration changes may lead to increased adverse reactions. If coadministration cannot be avoided, follow recommendations for CYP2C8 and CYP3A substrates provided in their approved product labeling.

Retevmo is a P-glycoprotein (P-gp) inhibitor. Concomitant use of Retevmo with **P-gp substrates** increases their plasma concentrations, which may increase the risk of adverse reactions related to these substrates. Avoid coadministration of Retevmo with P-gp substrates where minimal concentration changes may lead to increased adverse reactions. If coadministration cannot be avoided, follow recommendations for P-gp substrates provided in their approved product labeling.

The safety and effectiveness of Retevmo have not been established in **pediatric patients less than 12 years of age**. The safety and effectiveness of Retevmo have been established in pediatric patients aged 12 years and older for medullary thyroid cancer (MTC) who require systemic therapy and for advanced *RET* fusion-positive thyroid cancer who require systemic therapy and are radioactive iodine-refractory (if radioactive iodine is appropriate). Use of Retevmo for these indications is supported by evidence from adequate and well-controlled studies in adults with additional pharmacokinetic and safety data in pediatric patients aged 12 years and older. Monitor open growth plates in **adolescent patients**. Consider interrupting or discontinuing Retevmo if abnormalities occur.

No dosage modification is recommended for patients with **mild to severe renal impairment** (estimated Glomerular Filtration Rate [eGFR] ≥15 to 89 mL/min, estimated by Modification of Diet in Renal Disease [MDRD] equation). A recommended dosage has not been established for patients with end-stage renal disease.

Reduce the dose when administering Retevmo to patients with **severe hepatic impairment** (total bilirubin greater than 3 to 10 times upper limit of normal [ULN] and any AST). No dosage modification is recommended for patients with mild or moderate hepatic impairment. Monitor for Retevmo-related adverse reactions in patients with hepatic impairment.

Please click for full Prescribing Information for Retevmo.

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Indications[1]

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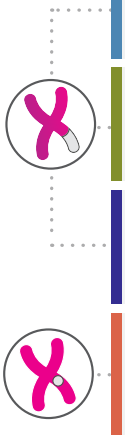
Retevmo is a kinase inhibitor indicated for the treatment of:



- **Adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with a *rearranged during transfection (RET)* gene fusion, as detected by an FDA-approved test**
- **Adult and pediatric patients 12 years of age and older with advanced or metastatic thyroid cancer with a *RET* gene fusion, as detected by an FDA-approved test, who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate)***
- **Adult patients with locally advanced or metastatic solid tumors with a *RET* gene fusion that have progressed on or following prior systemic treatment or who have no satisfactory alternative treatment options***
- **Adult and pediatric patients 12 years of age and older with advanced or metastatic medullary thyroid cancer (MTC) with a *RET* mutation, as detected by an FDA-approved test, who require systemic therapy***

***These indications are approved under accelerated approval based on overall response rate (ORR) and duration of response (DoR). Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trials.**

SELECT IMPORTANT SAFETY INFORMATION FOR RETEVMO

The labeling for Retevmo contains Warnings and Precautions for **hepatotoxicity, interstitial lung disease (ILD)/pneumonitis, hypertension, QT interval prolongation, hemorrhagic events, hypersensitivity, tumor lysis syndrome (TLS), risk of impaired wound healing, hypothyroidism,** and **embryo-fetal toxicity**. Monitor alanine aminotransferase (ALT) and aspartate aminotransferase (AST) prior to initiating Retevmo, every 2 weeks during the first 3 months of treatment, then monthly thereafter and as clinically indicated. Monitor for new or worsening pulmonary symptoms indicative of ILD/pneumonitis. Optimize blood pressure prior to initiating Retevmo. Monitor blood pressure after 1 week, at least monthly, and as clinically indicated. Monitor patients who are at significant risk of developing QTc prolongation, including patients with known long QT syndromes, clinically significant bradyarrhythmias, and severe or uncontrolled heart failure. Monitor the QT interval more frequently when Retevmo is concomitantly administered with strong and moderate CYP3A inhibitors or drugs known to prolong QTc interval. Permanently discontinue Retevmo in patients with severe or life-threatening hemorrhage. If hypersensitivity occurs, withhold Retevmo and begin corticosteroids at a dose of 1 mg/kg prednisone (or equivalent). See full Prescribing Information for further management instructions and dosage modifications for adverse reactions. Closely monitor patients that may be at risk of TLS (rapidly growing tumors, a high tumor burden, renal dysfunction, or dehydration) and consider appropriate prophylaxis including hydration. Withhold Retevmo for at least 7 days prior to elective surgery. Do not administer for at least 2 weeks following major surgery and until adequate wound healing. Monitor thyroid function before and periodically during treatment with Retevmo. Withhold until clinically stable or permanently discontinue Retevmo based on severity of hypothyroidism. Based on data from animal reproduction studies and its mechanism of action, Retevmo can cause fetal harm when administered to a pregnant woman. Advise females and males with female partners of reproductive potential to use effective contraception during treatment with Retevmo and for at least 1 week after the last dose. **Serious adverse reactions** occurred in 44% of patients who received Retevmo. The most frequent serious adverse reactions (in ≥2% of patients) were pneumonia, pleural effusion, abdominal pain, hemorrhage, hypersensitivity, dyspnea, and hyponatremia. **Fatal adverse reactions** occurred in 3% of patients; fatal adverse reactions included sepsis (n=6), respiratory failure (n=5), hemorrhage (n=4), pneumonia (n=3), pneumonitis (n=2), cardiac arrest (n=2), sudden death (n=1), and cardiac failure (n=1). **Most common adverse reactions** (≥25%) were edema, diarrhea, fatigue, dry mouth, hypertension, abdominal pain, constipation, rash, nausea, and headache. **Most common Grade 3 or 4 laboratory abnormalities** (≥5%) were decreased lymphocytes, increased alanine aminotransferase (ALT), increased aspartate aminotransferase (AST), decreased sodium, and decreased calcium.

Please see Important Safety Information on pages 4-6 and click for full Prescribing Information for additional information including dosing modifications.

REFERENCE: 1. Retevmo (selpercatinib). Prescribing Information. Lilly USA, LLC.

PP-SE-US-1199 11/2022

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