

Composing a Letter of Medical Necessity

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. Eli Lilly and Company does not guarantee success in obtaining insurance payments. 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 policies. For more information, please call the Lilly Oncology Support Center[®] at 1-866-472-8663.

Many health plans require that a Letter of Medical Necessity accompanies a Coverage Authorization Appeals Letter.* The purpose of a Letter of Medical Necessity is to explain the prescribing healthcare provider's (HCP's) rationale and clinical decision making when choosing a treatment.

This resource, **Composing a Letter of Medical Necessity**, provides information on the process of drafting a Letter of Medical Necessity. Included on the following page is a list of considerations, which can be followed when creating a Letter of Medical Necessity. In addition, two sample letters are attached to this document and include information that plans often require. Note that some plans have specific Coverage Authorization Forms that must be used to document a Letter of Medical Necessity. Also see **Preparing a Coverage Authorization Appeals Letter** for more information.

Follow the patient's plan requirements when requesting Retevmo[®], otherwise treatment may be delayed.

*For Medicare beneficiaries, specific requirements must be met for the HCP to be considered a legal representative of the patient in an appeal. For additional information, please visit <https://www.cms.gov/Medicare/CMS-Forms/CMS-Forms/downloads/cms1696.pdf>.

INDICATIONS

Retevmo is a kinase inhibitor indicated for the treatment of:

- adult patients with metastatic *RET* fusion-positive non-small cell lung cancer (NSCLC)
- adult and pediatric patients 12 years of age and older with advanced or metastatic *RET*-mutant medullary thyroid cancer (MTC) who require systemic therapy
- adult and pediatric patients 12 years of age and older with advanced or metastatic *RET* fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate)

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

RET=rearranged during transfection.

SELECT IMPORTANT SAFETY INFORMATION FOR RETEVMO

Hepatotoxicity: Serious hepatic adverse reactions occurred in 2.6% of patients treated with Retevmo. Increased aspartate aminotransferase (AST) occurred in 51% of patients, including Grade 3 or 4 events in 8% and increased alanine aminotransferase (ALT) occurred in 45% of patients, including Grade 3 or 4 events in 9%. The median time to first onset for increased AST was 4.1 weeks (range: 5 days to 2 years) and increased ALT was 4.1 weeks (range: 6 days to 1.5 years). 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.

Composing a Letter of Medical Necessity

Letter of Medical Necessity Considerations

1. Include the patient's full name, date of birth, plan identification number, and case identification number if a decision has already been rendered.
2. Provide a copy of the patient's records with the following details: patient's history (including relevant clinical and progress notes), diagnosis with specific International Classification of Diseases (ICD) code, and condition.
3. Supply diagnostic testing results to confirm *RET*-fusion or *RET*-mutation positivity that identifies the patient as a candidate for Retevmo.
4. Note the severity of the patient's condition.
5. Document prior treatments, the duration of each, and the rationale for discontinuation. It may be beneficial to include common procedural terminology (CPT)-4 and/or J-codes to define prior services/treatments, so that the health plan can conduct research and make a timely determination.
6. Attach clinical documentation that supports your recommendation; this information may be found in the Retevmo prescribing information and/or clinical peer-reviewed literature.

Sample Letter of Medical Necessity

HCPs can follow this format for patients who are **NOT** currently receiving treatment with Retevmo (selpercatinib).

[Date]
[Medical Director]
[Name of Health Plan]
[Mailing Address]

Re: [Patient's Name]
[Plan Identification Number]
[Date of Birth]
[Case Identification]

To whom it may concern:

I am writing to provide additional information to support my claim for [patient's name]'s treatment of [metastatic **RET** fusion-positive NSCLC OR advanced or metastatic **RET**-mutant MTC in patients who require systemic therapy OR advanced **RET** fusion-positive thyroid cancer in patients who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate)] with Retevmo® (selpercatinib). In brief, treatment with Retevmo [dose, frequency] is medically appropriate and necessary for this patient. This letter outlines the patient's medical history and previous treatments to support my recommendation for treatment with Retevmo.

Patient's history, diagnosis, condition, and symptoms*:

Patient must have a diagnosis for an indication of Retevmo. Retevmo is a kinase inhibitor indicated for the treatment of:

- adult patients with metastatic **RET** fusion-positive non-small cell lung cancer (NSCLC)
- adult and pediatric patients 12 years of age and older with advanced or metastatic **RET**-mutant medullary thyroid cancer (MTC) who require systemic therapy
- adult and pediatric patients 12 years of age and older with advanced or metastatic **RET** fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate)

Patient must also have one of the following:

- For Retevmo use in adult patients with **RET** fusion-positive NSCLC, patient must have metastatic disease
- For Retevmo use in adult and pediatric patients 12 years of age and older with **RET**-mutant MTC, patient must have advanced or metastatic disease
- For Retevmo use in adult and pediatric patients 12 years of age and older with **RET** fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate), patient must have advanced or metastatic disease

Past Treatments†

Start/Stop Dates

Reason(s) for Discontinuing

[Provide clinical rationale for this treatment; this information may be found in the Retevmo prescribing information and/or clinical peer-reviewed literature.]

[Insert your recommendation summary here, including your professional opinion of the patient's likely prognosis or disease progression without treatment with Retevmo.]

Please feel free to contact me, [HCP's name], at [office phone number] for any additional information you may require. I look forward to receiving your timely response and approval of this claim.

Sincerely,

[Physician's name and signature]
[Physician's medical specialty]
[Physician's NPI]
[Physician's practice name]
[Phone #]
[Fax #]

[Patient's name and signature]

Encl: Medical records
Clinical trial information

[Please detail all that apply and add additional lines as needed.]

*Include patient's medical records and supporting documentation.

†Identify drug name, strength, dosage form, and therapeutic outcome.

Sample Letter of Medical Necessity

HCPs can follow this format for patients who **HAVE** been treated with Retevmo (selpercatinib) and have had treatment interruptions.

[Date]

[Medical Director]

[Name of Health Plan]

[Mailing Address]

Re: [Patient's Name]

[Plan Identification Number]

[Date of Birth]

[Case Identification]

To whom it may concern:

I am writing to provide additional information to support my claim for [patient's name]'s treatment of **[metastatic *RET* fusion-positive NSCLC OR advanced or metastatic *RET*-mutant MTC in patients who require systemic therapy OR advanced *RET* fusion-positive thyroid cancer in patients who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate)]** with Retevmo® (selpercatinib). In brief, treatment with Retevmo [dose, frequency] is medically appropriate and necessary for this patient. This letter outlines the patient's medical history and previous treatments to support my recommendation for treatment with Retevmo.

[In this section, describe the severity of advanced cancer at the time when the patient was first prescribed Retevmo. In addition, include a summary of the patient's clinical response to Retevmo and list improvements (if any) in clinical presentation since treatment began.]

Patient's history, diagnosis, condition, and symptoms*:

Patient must have a diagnosis for an indication of Retevmo. Retevmo is a kinase inhibitor indicated for the treatment of:

- adult patients with metastatic *RET* fusion-positive non-small cell lung cancer (NSCLC)
- adult and pediatric patients 12 years of age and older with advanced or metastatic *RET*-mutant medullary thyroid cancer (MTC) who require systemic therapy
- adult and pediatric patients 12 years of age and older with advanced or metastatic *RET* fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate)

Patient must also have one of the following:

- For Retevmo use in adult patients with *RET* fusion-positive NSCLC, patient must have metastatic disease
- For Retevmo use in adult and pediatric patients 12 years of age and older with *RET*-mutant MTC, patient must have advanced or metastatic disease
- For Retevmo use in adult and pediatric patients 12 years of age and older with *RET* fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate), patient must have advanced or metastatic disease

Past Treatments†

Start/Stop Dates

Reason(s) for Discontinuing

[Provide clinical rationale for this treatment; this information may be found in the Retevmo prescribing information and/or clinical peer-reviewed literature.]

[Insert your recommendation summary here, including your professional opinion of the patient's likely prognosis or disease progression without treatment with Retevmo.]

Please feel free to contact me, [HCP's name], at [office phone number] for any additional information you may require. I look forward to receiving your timely response and approval of this claim.

Sincerely,

[Physician's name and signature]

[Physician's medical specialty]

[Physician's NPI]

[Physician's practice name]

[Phone #]

[Fax #]

[Patient's name and signature]

Encl: Medical records

Clinical trial information

[Please detail all that apply and add additional lines as needed.]

*Include patient's medical records and supporting documentation.

†Identify drug name, strength, dosage form, and therapeutic outcome.

Please see Important Safety Information on pages 5 and 6 and click for full [Prescribing Information for Retevmo](#).

IMPORTANT SAFETY INFORMATION FOR RETEVMO

Hepatotoxicity: Serious hepatic adverse reactions occurred in 2.6% of patients treated with Retevmo. Increased aspartate aminotransferase (AST) occurred in 51% of patients, including Grade 3 or 4 events in 8% and increased alanine aminotransferase (ALT) occurred in 45% of patients, including Grade 3 or 4 events in 9%. The median time to first onset for increased AST was 4.1 weeks (range: 5 days to 2 years) and increased ALT was 4.1 weeks (range: 6 days to 1.5 years). 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.

Hypertension occurred in 35% of patients, including Grade 3 hypertension in 17% and Grade 4 in one (0.1%) patient. Overall, 4.6% 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 6% of patients and an increase in the QTcF interval of at least 60 ms over baseline was measured in 15% 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 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 2.3% of patients treated with Retevmo including 3 (0.4%) patients with fatal hemorrhagic events, including one case each of cerebral hemorrhage, tracheostomy site hemorrhage, and hemoptysis. Permanently discontinue Retevmo in patients with severe or life-threatening hemorrhage.

Hypersensitivity occurred in 4.3% of patients receiving Retevmo, including Grade 3 hypersensitivity in 1.6%. The median time to onset was 1.7 weeks (range 6 days to 1.5 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 1% 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.

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.

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 embryoletality and malformations. Advise pregnant women 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 at least 1 week after the final 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 final dose.

Please see Important Safety Information continued on page 6 and click for full [Prescribing Information for Retevmo](#).



IMPORTANT SAFETY INFORMATION FOR RETEVMO (CONTINUED)

Severe adverse reactions (Grade 3-4) occurring in ≥15% of patients who received Retevmo in LIBRETTO-001, were hypertension (18%), prolonged QT interval (4%), diarrhea (3.4%), dyspnea (2.3%), fatigue (2%), abdominal pain (1.9%), hemorrhage (1.9%), headache (1.4%), rash (0.7%), constipation (0.6%), nausea (0.6%), vomiting (0.3%), and edema (0.3%).

Serious adverse reactions occurred in 33% of patients who received Retevmo. The most frequently reported serious adverse reaction (in ≥ 2% of patients) was pneumonia.

Fatal adverse reactions occurred in 3% of patients; fatal adverse reactions which occurred in >1 patient included sepsis (n=3), cardiac arrest (n=3) and respiratory failure (n=3).

Common adverse reactions (all grades) occurring in ≥15% of patients who received Retevmo in LIBRETTO-001, were dry mouth (39%), diarrhea (37%), hypertension (35%), fatigue (35%), edema (35%), rash (27%), constipation (25%), nausea (23%), abdominal pain (23%), headache (23%), cough (18%), prolonged QT interval (17%), dyspnea (16%), vomiting (15%), and hemorrhage (15%).

Laboratory abnormalities (all grades; Grade 3-4) ≥20% worsening from baseline in patients who received Retevmo in LIBRETTO-001, were AST increased (51%; 8%), ALT increased (45%; 9%), increased glucose (44%; 2.2%), decreased leukocytes (43%; 1.6%), decreased albumin (42%; 0.7%), decreased calcium (41%; 3.8%), increased creatinine (37%; 1.0%), increased alkaline phosphatase (36%; 2.3%), decreased platelets (33%; 2.7%), increased total cholesterol (31%; 0.1%), decreased sodium (27%; 7%), decreased magnesium (24%; 0.6%), increased potassium (24%; 1.2%), increased bilirubin (23%; 2.0%), and decreased glucose (22%; 0.7%).

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).

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.

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](#).

SE HCP ISI AIL_25MAR2021

Retevmo® is a registered trademark owned or licensed by Eli Lilly and Company, its subsidiaries or affiliates.

PP-SE-US-0555 04/2021 ©Lilly USA, LLC 2021. All rights reserved.



Retevmo®
selpercatinib capsules
40 mg • 80 mg