

Composing a Letter of Medical Necessity

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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 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 2 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 2 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 and pediatric patients 2 years of age and older with locally advanced or metastatic solid tumors with a *RET* gene fusion, as detected by an FDA-approved test, that have progressed on or following prior systemic treatment or who have no satisfactory alternative treatment options

SELECT IMPORTANT SAFETY INFORMATION FOR RETEVMO

Hepatotoxicity: Serious hepatic adverse reactions occurred in 4.6% of patients treated with Retevmo. Increased aspartate aminotransferase (AST) occurred in 62% of patients, including Grade 3 or 4 events in 11% and increased alanine aminotransferase (ALT) occurred in 58% of patients, including Grade 3 or 4 events in 13%. 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 severity.

FDA=US Food and Drug Administration.

Please see Important Safety Information on pages 5-8 and click for full [Prescribing Information](#) for Retevmo.

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* gene 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 [locally advanced or metastatic NSCLC with a *RET* gene fusion, as detected by an FDA-approved test OR advanced or metastatic MTC with a *RET* mutation, as detected by an FDA-approved test, in patients who require systemic therapy OR advanced or metastatic thyroid cancer with a *RET* gene fusion, as detected by an FDA-approved test, in patients who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate) OR 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] 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 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 2 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 2 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 and pediatric patients 2 years of age and older with locally advanced or metastatic solid tumors with a *RET* gene fusion, as detected by an FDA-approved test, that have progressed on or following prior systemic treatment or who have no satisfactory alternative treatment options

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 [locally advanced or metastatic NSCLC with a *RET* gene fusion, as detected by an FDA-approved test, OR advanced or metastatic MTC with a *RET* mutation, as detected by an FDA-approved test, in patients who require systemic therapy OR advanced or metastatic thyroid cancer with a *RET* gene fusion, as detected by an FDA-approved test, in patients who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate) OR 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] 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 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 2 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 2 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 and pediatric patients 2 years of age and older with locally advanced or metastatic solid tumors with a *RET* gene fusion, as detected by an FDA-approved test, that have progressed on or following prior systemic treatment or who have no satisfactory alternative treatment options

Past Treatments†

Start/Stop Dates

Reason(s) for Discontinuing

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

[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

*Include patient's medical records and supporting documentation.

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

IMPORTANT SAFETY INFORMATION FOR RETEVMO® (selpercatinib)

Hepatotoxicity: Serious hepatic adverse reactions occurred in 4.6% of patients treated with Retevmo. Increased aspartate aminotransferase (AST) occurred in 62% of patients, including Grade 3 or 4 events in 11% and increased alanine aminotransferase (ALT) occurred in 58% of patients, including Grade 3 or 4 events in 13%. 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 severity.

Severe, life-threatening, and fatal **interstitial lung disease (ILD)/pneumonitis** can occur in patients treated with Retevmo. ILD/pneumonitis occurred in 3% of patients who received Retevmo, including 0.3% with Grade 3 or 4 events, and 0.2% 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 43% of patients, including Grade 3 hypertension in 20% and Grade 4 in one (0.1%) patient. Overall, 6.4% had their dose interrupted, 1.5% had their dose reduced, and 0.2% discontinued Retevmo 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 severity.

Retevmo can cause concentration-dependent **QT interval prolongation**. An increase in QTcF interval to >500 ms was measured in 8% of patients and an increase in the QTcF interval of at least 60 ms over baseline was measured in 22% 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 4.3% of patients treated with Retevmo including 4 (0.5%) patients with fatal hemorrhagic events, including cerebral hemorrhage (n=2), tracheostomy site hemorrhage and hemoptysis (1 each). Permanently discontinue Retevmo in patients with severe or life-threatening hemorrhage.

Retevmo can cause **hypersensitivity**, including severe skin reactions such as Stevens-Johnson Syndrome. All grade hypersensitivity occurred in 6% of patients receiving Retevmo, including Grade 3 in 2%. The median time to onset was 1.9 weeks (range: 5 days to 6.5 years). Signs and symptoms of hypersensitivity included fever, rash and arthralgias or myalgias with concurrent decreased platelets or transaminitis. Stevens-Johnson Syndrome has been observed in the post-marketing setting. Discontinue Retevmo in patients with Stevens-Johnson Syndrome. 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 0.9% of patients with medullary thyroid carcinoma and 0.3% of patients with non-small cell lung cancer 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.

Retevmo can cause **hypothyroidism**. Hypothyroidism occurred in 15% of patients treated with Retevmo; all reactions were Grade 1 or 2. Hypothyroidism occurred in 15% of patients (59/390) with thyroid cancer and 14% of patients (65/467) 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

Please see Important Safety Information continued on pages 6-8 and click for full [Prescribing Information](#) for Retevmo.



IMPORTANT SAFETY INFORMATION FOR RETEVMO® (selpercatinib) (CONTINUED)

human dose of 160 mg twice daily resulted in embryoletality 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.

Slipped capital femoral epiphysis/slipped upper femoral epiphysis in pediatric patients (SCFE/SUFE) occurred in 1 adolescent (2.8% of 36 patients) receiving Retevmo in LIBRETTO-121 and 1 adolescent patient (0.5% of 193 patients) receiving Retevmo in LIBRETTO-531. Monitor patients for symptoms indicative of SCFE/SUFE and treat as medically and surgically appropriate.

Severe adverse reactions (Grade 3-4) occurring in ≥20% of patients who received Retevmo in LIBRETTO-001 were hypertension (20%), diarrhea (6.2%), prolonged QT interval (5%), fatigue (4.7%), musculoskeletal pain (4.1%), dyspnea (4.1%), hemorrhage (3.9%), abdominal pain (3.5%), vomiting (2.9%), urinary tract infection (2.2%), nausea (1.9%), headache (1.8%), edema (1.3%), decreased appetite (0.9%), constipation (0.8%), rash (0.8%), and dizziness (0.5%).

Severe adverse reactions (Grade 3-4) occurring in ≥15% of patients who received Retevmo in LIBRETTO-121 were increased weight (11%), vomiting (8%), constipation (6%), diarrhea (2.8%), nausea (2.8%), upper respiratory tract infection (2.8%), and urinary tract infection (2.8%).

Severe adverse reactions (Grade 3-4) occurring in ≥15% of patients who received Retevmo or chemotherapy with or without pembrolizumab in LIBRETTO-431 were hypertension (20% vs 3.1%), electrocardiogram QT prolonged (9% vs 0%), fatigue (3.2% vs 5%), edema (2.5% vs 0%), rash (1.9% vs 1.0%), diarrhea (1.3% vs 2.0%), abdominal pain (0.6% vs 2.0%), pyrexia (0.6% vs 0%), COVID19 infection (0.6% vs 0%), constipation (0% vs 1.0%), nausea (0% vs 1.0%), vomiting (0% vs 1.0%), and decreased appetite (0% vs 2.0%).

Severe adverse reactions (Grade 3-4) occurring in ≥10% of patients who received Retevmo in LIBRETTO-531 were (Retevmo vs cabozantinib / vandetanib) hypertension (19% vs 18%), electrocardiogram QT prolonged (4.7% vs 2.1%), fatigue (4.1% vs 9%), diarrhea (3.1% vs 8%), rash (1.6% vs 4.1%), pyrexia (1.0% vs 0%), nausea (1.0% vs 5%), dry mouth (0.5% vs 1.0%), abdominal pain (0.5% vs 2.1%), stomatitis (0.5% vs 13%), headache (0.5% vs 0%), and decreased appetite (0.5% vs 5%).

Serious adverse reactions occurred in 58% of patients who received Retevmo in LIBRETTO-001. The most frequently reported serious adverse reactions (in ≥2% of patients) were pneumonia, hemorrhage, abdominal pain, dyspnea, pleural effusion, sepsis, musculoskeletal pain, hyponatremia, vomiting, diarrhea, and increased blood creatinine. **Fatal adverse reactions occurred in 3% of patients in LIBRETTO-001;** fatal adverse reactions included sepsis (n=6), respiratory failure (n=5), hemorrhage (n=4), pneumonia (n=4), cardiac arrest (n=3), pneumonitis (n=2), cardiac failure (n=2), sudden death (n=1), cerebral infarction (n=1), and dyspnea (n=1).

Serious adverse reactions occurred in 42% of patients who received Retevmo in LIBRETTO-121. Serious adverse reactions occurring in more than 1 patient were vomiting and fracture (2 patients each).

Serious adverse reactions occurred in 35% of patients who received Retevmo in LIBRETTO-431. The most frequently reported serious adverse reactions (≥2% of patients) were pleural effusion and abnormal hepatic function. **Fatal adverse reactions occurred in 4.4% of patients who received Retevmo in LIBRETTO-431;** fatal adverse reactions included myocardial infarction (n=2), respiratory failure (n=2), cardiac arrest, malnutrition, and sudden death (n=1 each).

Serious adverse reactions occurred in 22% of patients who received Retevmo in LIBRETTO-531. The most frequent serious adverse reactions were pneumonia and pyrexia (n=3 each), and hypertension and urinary tract infection (n=2 each). **Fatal adverse reactions occurred in 2.1% of patients who received Retevmo in LIBRETTO-531;** fatal adverse reactions included COVID19, diabetic ketoacidosis, multiple organ dysfunction syndrome, and sudden death (n=1 each).

Common adverse reactions (all grades) occurring in ≥20% of patients who received Retevmo in LIBRETTO-001, were musculoskeletal pain (59%), edema (53%), diarrhea (52%), fatigue (49%), dry mouth (44%), hypertension (43%), abdominal pain (39%), rash (38%), nausea (36%), constipation (35%), cough (30%), headache (30%), vomiting (29%), dyspnea (28%), hemorrhage (26%), decreased appetite (23%), dizziness (22%), prolonged QT interval (21%), and urinary tract infection (20%).

Common adverse reactions (all grades) occurring in ≥15% of patients who received Retevmo in LIBRETTO-121 were musculoskeletal pain (58%), diarrhea (47%), nausea (42%), hemorrhage (39%), pyrexia (39%), abdominal pain (36%), headache (33%), vomiting (31%), fatigue (31%), cough (31%), rash (28%), coronavirus infection (28%), upper respiratory tract infection (28%), edema (25%), constipation (22%), oropharyngeal pain (22%), hypothyroidism (22%), urinary tract infection (19%), and increased weight (19%).

Please see Important Safety Information continued on pages 7 and 8 and click for full [Prescribing Information](#) for Retevmo.



IMPORTANT SAFETY INFORMATION FOR RETEVMO® (selpercatinib) (CONTINUED)

Common adverse reactions (all grades) occurring in ≥15% of patients who received Retevmo or chemotherapy with or without pembrolizumab in LIBRETTO-431 were hypertension (48% vs 7%), diarrhea (44% vs 24%), edema (41% vs 28%), dry mouth (39% vs 6%), rash (33% vs 30%), fatigue (32% vs 50%), abdominal pain (25% vs 19%), musculoskeletal pain (25% vs 28%), constipation (22% vs 40%), electrocardiogram QT prolonged (20% vs 1.0%), COVID19 infection (19% vs 18%), stomatitis (18% vs 16%), decreased appetite (17% vs 34%), nausea (13% vs 44%), vomiting (13% vs 23%), and pyrexia (13% vs 23%).

Common adverse reactions (all grades) occurring in ≥10% of patients who received Retevmo in LIBRETTO-531 (Retevmo vs cabozantinib / vandetanib) were hypertension (43% vs 41%), edema (33% vs 5%), dry mouth (32% vs 10%), fatigue (28% vs 47%), diarrhea (26% vs 61%), headache (23% vs 21%), rash (19% vs 27%), abdominal pain (18% vs 21%), constipation (16% vs 12%), erectile dysfunction (16% vs 0%), stomatitis (14% vs 42%), electrocardiogram QT prolonged (14% vs 13%), pyrexia (12% vs 2.1%), decreased appetite (12% vs 28%), hypothyroidism (11% vs 21%), and nausea (10% vs 32%).

Laboratory abnormalities (all grades ≥20%; Grade 3-4) worsening from baseline in patients who received Retevmo in LIBRETTO-001, were increased AST (62%; 11%), decreased calcium (61%; 7%), decreased albumin (61%; 3.6%), increased ALT (58%; 13%), increased glucose (56%; 4.0%), decreased lymphocytes (56%; 22%), increased creatinine (51%; 3.6%), decreased sodium (49%; 13%), increased alkaline phosphatase (43%; 4.4%), decreased platelets (41%; 4.0%), increased potassium (39%; 3.5%), decreased glucose (39%; 1.5%), increased total cholesterol (37%; 1.7%), decreased magnesium (37%; 0.7%), decreased hemoglobin (36%; 4.1%), increased bilirubin (32%; 2.9%), decreased neutrophils (27%; 3.8%), and decreased phosphate (25%; 5%).

Laboratory abnormalities (all grades ≥15%; Grade 3-4) worsening from baseline in patients who received Retevmo in LIBRETTO-121 were decreased calcium (61%; 11%), increased ALT (58%; 8%), decreased albumin (53%; 0%), increased alkaline phosphatase (50%; 0%), increased AST (50%; 2.8%), increased bilirubin (31%; 2.8%), increased cholesterol (28%; 0%), decreased magnesium (28%; 6%), increased potassium (28%; 2.8%), increased creatinine (19%; 2.8%), decreased potassium (19%; 6%), decreased sodium (17%; 0%), decreased neutrophils (40%; 8%), decreased hemoglobin (36%; 11%), increased hemoglobin (33%; 2.8%), decreased platelets (28%; 2.8%), and decreased lymphocytes (28%; 14%).

Laboratory abnormalities (all grades ≥20%; Grade 3-4) worsening from baseline in patients who received Retevmo or chemotherapy with or without pembrolizumab in LIBRETTO-431 were increased ALT (81%; 21% vs 63%; 4.1%), increased AST (77%; 10% vs 46%; 0%), decreased calcium (53%; 1.9% vs 24%; 1.0%), decreased platelets (53%; 3.2% vs 39%; 5%), decreased lymphocytes (53%; 8% vs 64%; 15%), decreased neutrophils (53%; 2.0% vs 58%; 11%), increased bilirubin (52%; 1.3% vs 9%; 0%), increased alkaline phosphatase (35%; 1.3% vs 22%; 0%), decreased sodium (31%; 3.2% vs 41%; 2.1%), decreased albumin (25%; 0% vs 5%; 0%), increased blood creatinine (23%; 0% vs 21%; 0%), decreased hemoglobin (21%; 0% vs 91%; 5%), decreased potassium (17%; 1.3% vs 15%; 1.0%), and decreased magnesium (16%; 0.6% vs 8%; 0%).

Laboratory abnormalities (all grades ≥5%; Grade 3-4) worsening from baseline in patients who received Retevmo in LIBRETTO-531 (Retevmo vs cabozantinib / vandetanib) were decreased calcium (55%; 5% vs 62%; 11%), increased ALT (53%; 16% vs 72%; 7%), increased AST (47%; 5% vs 68%; 3.2%), decreased lymphocytes (41%; 18% vs 36%; 13%), increased alkaline phosphatase (37%; 6% vs 28%; 5%), increased bilirubin (32%; 1.1% vs 30%; 3.2%), decreased neutrophils (33%; 14% vs 42%; 19%), decreased platelets (28%; 1.1% vs 34%; 1.1%), increased creatinine (27%; 6% vs 16%; 8%), decreased sodium (20%; 3.2% vs 16%; 0%), decreased hemoglobin (18%; 2.1% vs 23%; 2.1%), decreased albumin (11%; 1.1% vs 7%; 0), magnesium decreased (9%; 3.3% vs 26%; 9%), and decreased potassium (8%; 0% vs 22%; 4.4%).

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.

Please see Important Safety Information continued on page 8 and click for full [Prescribing Information](#) for Retevmo.



IMPORTANT SAFETY INFORMATION FOR RETEVMO® (selpercatinib) (CONTINUED)

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

The safety and effectiveness of Retevmo have not been established in pediatric patients less than 2 years of age. The safety and effectiveness of Retevmo have been established in pediatric patients aged 2 years and older for the treatment of advanced or metastatic medullary thyroid cancer (MTC) with a *RET* mutation who require systemic therapy, advanced or metastatic thyroid cancer with a *RET* gene fusion who require systemic therapy and are radioactive iodine-refractory (if radioactive iodine is appropriate), and 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.

Monitor open growth plates in **pediatric 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.

Retevmo (selpercatinib) is available as 40 mg and 80 mg capsules, and 40 mg, 80 mg, 120 mg, and 160 mg tablets.

SE HCP ISI AIL_JUL2026

Please click for full [Prescribing Information and Instructions for Use](#), for Retevmo.

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