Retevmo®
selpercatinib tablets
40 mg • 80 mg • 120 mg • 160 mg
A Lilly Medicine

Important change for Retevmo® (selpercatinib)

Retevmo is switching from capsules to tablets, including more dose strengths. Retevmo capsules are offered in 40 mg and 80 mg strengths; Retevmo tablets are offered in 40 mg, 80 mg, 120 mg, and 160 mg strengths.[1,2]

What's changing?

Capsule	Tablet
	
Gelatin-coated capsule	Film-coated tablet
Two dose strengths	Smaller than Retevmo capsules
	Four dose strengths
	Potential to require fewer tablets per day at higher doses[a]

[a]While Retevmo dosing recommendation remains twice daily, patients may be able to take a lower pill count at each dose interval.

Please see full Prescribing Information for dosing, including dose modifications for weight, body mass and adverse reactions.

Tablet and capsule renderings shown may vary in size and color compared to actual tablets and capsules. Color, size, and texture may differ slightly due to differences in digital screen settings and/or printer capabilities.

Please note that for a period of time, patients may receive either the original capsule formulation or the reformulated Retevmo tablets, based on Specialty Pharmacy inventory. Prior to approval of the tablet reformulation, a study was conducted to evaluate the equivalence of the new tablet formulation relative to the capsule formulation. No changes to the risks for selpercatinib are expected with the formulation change. Efficacy data from the capsule also applies to the tablet.[2]

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), and 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*.

*This indication is approved under accelerated approval based on overall response rate (ORR) and duration of response (DoR). Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

SELECT IMPORTANT SAFETY INFORMATION

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.

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Retevmo recommended dosing and administration

Patient selection for treatment with Retevmo should be based on the presence of a *RET* gene fusion (NSCLC, thyroid cancer, or solid tumors) or specific *RET* gene mutation (MTC) in tumor specimens. Information on FDA-approved test(s) for the detection of *RET* gene fusions and *RET* gene mutations is available at: http://www.fda.gov/CompanionDiagnostics. An FDA-approved companion diagnostic test for the detection of *RET* gene fusions and *RET* gene mutations in plasma is not currently available.

- Retevmo may be taken with or without food. When administered with a proton pump inhibitor (PPI), take with food.
- Instruct patients to swallow Retevmo whole. Do not break, crush or chew. Do not administer to pediatric patients who are unable to swallow a capsule.
- Do not take a missed dose unless it is more than 6 hours until next scheduled dose.
- If vomiting occurs after Retevmo administration, do not administer an additional dose, and continue to the next scheduled time for the next dose.

Recommended Retevmo Dosage

Population	Retevmo Dosage
Adult and adolescent patients 12 years of age or older based on body weight	
• Less than 50 kg	120 mg twice daily
• 50 kg or greater	160 mg twice daily
Pediatric patients 2 to less than 12 years of age based on body surface area	
• 0.33 to 0.65 m^2	40 mg three times daily
• 0.66 to 1.08 m^2	80 mg twice daily
• 1.09 to 1.52 m^2	120 mg twice daily
• ≥1.53 m^2	160 mg twice daily
Dosing pediatric patients with body surface area less than 0.33 m^2 is not recommended	

Reduce Retevmo dose in patients with severe hepatic impairment. Retevmo also requires dosage modifications for some Adverse Reactions and use with some concomitant medications. See the full Prescribing Information for details.

FAQs ABOUT RETEVMO TABLETS

1. When will my patients begin receiving Retevmo in tablet form?

a. In September 2024, Retevmo switched from a capsule formulation to tablets. Please specify "Retevmo tablets" when prescribing Retevmo so your patients receive the tablet formulation.

2. What are the differences between Retevmo capsules and Retevmo tablets?

a. The formulations of Retevmo are bioequivalent and contain the same active ingredient. Retevmo capsules are available in 40 mg and 80 mg strengths; Retevmo tablets are available in 40 mg, 80 mg, 120 mg, and 160 mg strengths.[1,2]

3. How will this transition affect the dosing for Retevmo?

a. The recommended dosing for Retevmo has not changed. New dosage strengths are available for patients taking higher dosages. Refer to the chart below for how prescribing may change.

Please see Important Safety Information throughout and full Prescribing Information for Retevmo.

Patient Dose	Capsules If you've been prescribing	Tablets Please prescribe:
160-mg dose twice daily	2 x 80-mg capsules twice daily	1 x 160-mg tablet twice daily
120-mg dose twice daily	3 x 40-mg capsules twice daily	1 x 120-mg tablet twice daily
80-mg dose twice daily	1 x 80-mg capsule twice daily	1 x 80-mg tablet twice daily
40-mg dose twice daily	1 x 40-mg capsule twice daily	1 x 40-mg tablet twice daily
40-mg dose once daily	1 x 40-mg capsule once daily	1 x 40-mg tablet once daily

If the tablets are unavailable for selection at your practice, you must specify the dosage and "Retevmo tablets" on all Retevmo prescriptions.

4. Are new prescriptions required for Retevmo tablets?

a. Patients may require a new prescription to receive Retevmo tablets depending on specialty pharmacy requirements and state pharmacy laws. You should be contacted by your patient's specialty pharmacy if a new prescription is needed.

5. How should Retevmo tablets be taken?

The recommended dose instructions for Retevmo has not changed.

a. Retevmo tablets should be swallowed whole. Patients should be advised not to break, crush or chew the tablets.[1]

b. Avoid concomitant use of a PPI, a histamine-2 (H2) receptor antagonist, or a locally-acting antacid with Retevmo. If concomitant use cannot be avoided:[1]

i. Take Retevmo with food when coadministered with a PPI.[1]

ii. Take Retevmo 2 hours before or 10 hours after administration of an H2 receptor antagonist.[1]

iii. Take Retevmo 2 hours before or 2 hours after administration of a locally-acting antacid.[1]

6. What are the NDCs for Retevmo tablets and capsules?

Tablet Strength	Quantity of Tablets per Bottle	NDC
40 mg	60 count	• NDC 0002-5340-60
80 mg	60 count	• NDC 0002-6082-60
120 mg	60 count	• NDC 0002-6120-60
160 mg	60 count	• NDC 0002-5562-60

NDC=National Drug Code.

Capsule Strength	Quantity of Capsules per Bottle	NDC
40 mg	60 count	• 0002-3977-60
80 mg	60 count	• 0002-2980-60
80 mg	120 count	• 0002-2980-26

7. Are there any additional side effects or safety concerns with the Retevmo tablets?

a. Prior to approval of the tablet reformulation, a study was conducted to evaluate the equivalence of the new tablet formulation relative to the capsule formulation. No changes to the risks for selpercatinib are expected with the formulation change. Efficacy data from the capsule can be applied to the tablet.[2]

8. How should Retevmo tablets be stored?

a. Store at 20°C to 25°C (68°F to 77°F); excursions between 15°C and 30°C (59°F to 86°F) are permitted.[1]

9. Is a new prior authorization required to switch between the tablet and capsule formulations of Retevmo?

a. Retevmo may require a new prior authorization depending on individual payer requirements.

10. Will Lilly stop supplying capsules after tablets are in the market?

a. Yes. We anticipate capsules will no longer be available in the market sometime in the second half of 2024.

11. Will patients need a new savings card when switching to the tablet formulation of Retevmo?

a. No, patients will not need a new Savings Card when switching to Retevmo tablets.

12. When will the tablet formulation of Retevmo be available in the United States?

a. Retevmo tablets will be available to order in the second half of 2024. Until then, Retevmo capsules will be available for use for your appropriate patients with *RET*+ solid tumors.

INDICATIONS AND IMPORTANT SAFETY INFORMATION

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*

*This indication is approved under accelerated approval based on overall response rate (ORR) and duration of response (DoR). Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

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IMPORTANT SAFETY INFORMATION FOR RETEVMO® (SELPERCATINIB)

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.

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.

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IMPORTANT SAFETY INFORMATION FOR RETEVMO® (SELPERCATINIB) (CONT'D)

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.

Slipped capital femoral epiphysis/slipped upper femoral epiphysis in pediatric patients (SCFE/SUFE) occurred in 1 adolescent (3.7% of 27 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 (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%).

Severe adverse reactions (Grade 3-4) occurring in ≥15% of patients who received Retevmo in LIBRETTO-121 were vomiting (7%), constipation (7%), increased weight (7%), nausea (3.7%), and hemorrhage (3.7%).

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 44% of patients who received Retevmo in LIBRETTO-001. 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 in LIBRETTO-001**; 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).

Serious adverse reactions occurred in 22% of patients who received Retevmo in LIBRETTO-121. The serious adverse reactions (in 1 patient each) were abdominal infection, abdominal pain, aspiration, constipation, diarrhea, epiphysiolysis, nausea, pneumonia, pneumatosis intestinalis, rhinovirus infection, sepsis, and vomiting.

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 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%).

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IMPORTANT SAFETY INFORMATION FOR RETEVMO® (SELPERCATINIB) (CONT'D)

Common adverse reactions (all grades) occurring in ≥15% of patients who received Retevmo in LIBRETTO-121 were musculoskeletal pain (56%), diarrhea (41%), headache (33%), nausea (30%), vomiting (30%), coronavirus infection (30%), abdominal pain (26%), fatigue (26%), pyrexia (26%), hemorrhage (26%), upper respiratory tract infection (22%), oropharyngeal pain (22%), cough (22%), hypothyroidism (19%), constipation (19%), edema (19%), increased weight (19%), rash (19%), stomatitis (15%), and proteinuria (15%).

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 (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%).

Laboratory abnormalities (all grades ≥15%; Grade 3-4) worsening from baseline in patients who received Retevmo in LIBRETTO-121 were decreased calcium (59%; 7%), increased ALT (56%; 3.7%), increased alkaline phosphatase (52%; 0%), increased AST (48%; 3.7%), decreased albumin (44%; 0%), decreased neutrophils (44%; 7%), increased bilirubin (30%; 0%), decreased lymphocytes (24%; 4.8%), increased creatinine (22%, 0%), decreased potassium (22%; 3.7%), decreased platelets (22%; 0%), decreased hemoglobin (19%; 7%), and decreased magnesium (15%; 3.7%).

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.

IMPORTANT SAFETY INFORMATION FOR RETEVMO® (SELPERCATINIB) (CONT'D)

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 2 years of age. The safety and effectiveness of Retevmo have been established in pediatric patients 2 years of age 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 All_27SEP24

Please see Important Safety Information throughout and full Prescribing Information for Retevmo.

References:

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

2. Data on File. Lilly USA, LLC. DOF-SE-US-0087.

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