

# 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.

#### Indications1

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 (ORR) and duration of response (DoR). 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.



## Introduction

This guide includes:

- 1 Key information on Retevmo
- Prescription, ordering, and patient support services offered through the Lilly Oncology Support Center
- 3 Specialty pharmacy network and specialty distributor network
- 4 Appropriate testing methodologies for *RET* with associated coding

## Retevmo Supply and NDC<sup>1</sup>

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



Dosage	Code
40-mg capsule — 60ct bottle	NDC: 0002-3977-60
80-mg capsule — 60ct bottle	NDC: 0002-2980-60
80-mg capsule — 120ct bottle	NDC: 0002-2980-26

NDC=National Drug Code

# Diagnosis Codes for NSCLC

ICD-10 Code <sup>2</sup> *	Description
C33	Trachea
C34.00	Unspecified main bronchus
C34.01	Right main bronchus
C34.02	Left main bronchus
C34.10	Upper lobe, unspecified bronchus or lung
C34.11	Upper lobe, right bronchus or lung
C34.12	Upper lobe, left bronchus or lung
C34.2	Middle lobe, bronchus or lung
C34.30	Lower lobe, unspecified bronchus or lung
C34.31	Lower lobe, right bronchus or lung
C34.32	Lower lobe, left bronchus or lung
C34.80	Overlapping sites of unspecified bronchus and lung
C34.81	Overlapping sites of right bronchus and lung
C34.82	Overlapping sites of left bronchus and lung
C34.90	Unspecified part of unspecified bronchus or lung
C34.91	Unspecified part of right bronchus or lung
C34.92	Unspecified part of left bronchus or lung
Z85.118	Personal history of malignant neoplasm of bronchus and lung

# Diagnosis Codes for Thyroid Cancer

ICD-10 Code <sup>2*</sup>	Description	\	
C73	Malignant neoplasm of thyroid gland		

<sup>\*</sup>Please check to ensure that codes are used to the highest level of specificity. Providers should use current ICD-10-CM codes to report a patient's diagnosis on claim submissions. This list of ICD-10-CM diagnosis codes may be reasonably related to a diagnosis within the product's approved label. Other codes may be appropriate.

ICD=International Classification of Diseases; nos=not otherwise specified.



Please see Important Safety Information on pages 8 and 9 and click for full <u>Prescribing Information</u> for Retevmo.

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# 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 www.lillytrade.com

#### SELECT IMPORTANT SAFETY INFORMATION FOR RETEVMO

**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.

Please see Important Safety Information on pages 8 and 9 and click for full <u>Prescribing Information</u> for Retevmo.

## Lilly Oncology Support Center

Lilly Oncology Support Center provides easy-to-use resources and reimbursement options for eligible patients whose doctors have prescribed 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<sup>†</sup>
- Digital cards can be downloaded online. You and your patients can get a savings card by visiting Retevmo.com



#### Retevmo Insurance & Coverage Assistance<sup>†</sup>

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.<sup>§</sup>



#### MyRightDose: Dose Exchange Program<sup>®</sup>

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<sup>†</sup>

Dedicated support staff: patients speak to the same person every time. The Companion in Care™ can help patients by:

• Providing emotional support when patients need it • Reiterating treatment information when taking Retevmo

The Companion in Care™ does not replace a trained healthcare provider; when medical questions arise, your patients will always be directed back to your office.

For more information about Lilly Oncology Support Center, call 1-866-472-8663, Monday-Friday, 8AM-10PM 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

\*Offer good for up to 12 months until 12/31/2021. Patients must have coverage for Retevmo through their commercial drug insurance to pay as little as \$0 for a 30-day supply of Retevmo. Offer subject to a monthly cap of wholesale acquisition cost plus usual and customary pharmacy charges and a separate annual cap of \$25,000. Participation in the program requires a valid patient HIPAA authorization. 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 discontinuation without notice. Card activation is required. Subject to additional terms and conditions, which can be found at Retevmo.com.

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, and 4) enrolled in the Lilly Oncology Support Center, 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.

 ${}^\P\!Additional\ terms\ and\ conditions\ apply.\ See\ the\ \underline{MyRightDose\ enrollment\ for\ details}.$ 

HIPAA=Health Insurance Portability and Accountability Act.



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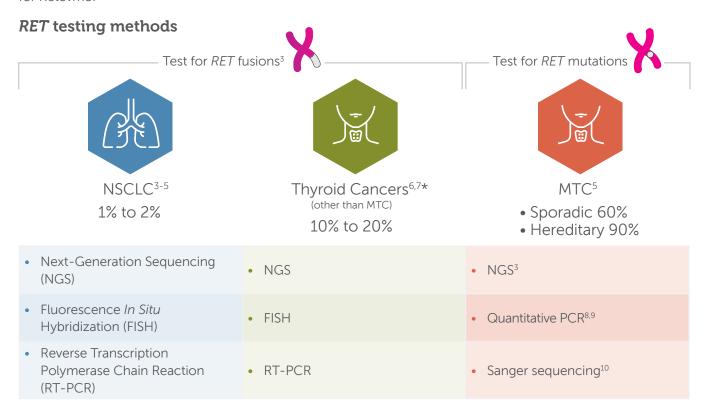
<sup>\*</sup>Eligible pharmacies can purchase Retevmo through our distribution partners. A list of authorized distributors can be found at lillytrade.com.

# RET Alteration Diagnostic Testing: Descriptions and Coding

All coding and documentation requirements for diagnostic tests and testing methods should be confirmed with each payer.

Testing for RET alterations is essential to identify patients who may be eligible for Retevmo.<sup>1</sup>

An FDA-approved test for the detection of *RET* gene fusions and *RET* mutations is not currently available for Reteymo.<sup>1</sup>



Immunohistochemistry (IHC) is not preferred for detecting *RET* alterations due to low sensitivity and variable specificity<sup>11,12</sup>

#### SELECT IMPORTANT SAFETY INFORMATION FOR RETEVMO

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.

Please see Important Safety Information on pages 8 and 9 and click for full <u>Prescribing Information</u> for Retevmo.

#### CPT Codes for RET Alteration Testing Modalities That May Be Used<sup>13†</sup>

Test Modality	CPT Code	Description
	81445	Targeted genomic sequence analysis panel, solid organ neoplasm, DNA analysis, and RNA analysis when performed, 5-50 genes
	81455	Targeted genomic sequence analysis panel, solid organ or hematolymphoid neoplasm, DNA analysis, and RNA analysis when performed, 51 or greater genes
NGS	0022U‡	Oncomine Dx Target Test; Targeted genomic sequence analysis panel, non-small cell lung neoplasia, DNA and RNA analysis, 23 genes
	0037U‡	FoundationOne CDx; Targeted genomic sequence analysis, solid organ neoplasm, DNA analysis of 324 genes including gene rearrangements
	0048U‡	MSK-IMPACT; Oncology (solid organ neoplasia), DNA, targeted sequencing of protein-coding exons of 468 cancer-associated genes
	81404	Molecular pathology procedure, Level 5 (eg, analysis of 2-5 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 6-10 exons)
		• <i>RET (ret proto-oncogene)</i> (eg, multiple endocrine neoplasia, type 2B and familial medullary thyroid carcinoma), common variants (eg, M918T, 2647_2648delinsTT, A883F)
PCR; Sanger Sequencing	81405	Molecular pathology procedure, Level 6 (eg, analysis of 6-10 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 11-25 exons)
Sequencing		• <i>RET</i> (ret proto-oncogene) (eg, multiple endocrine neoplasia, type 2A and familial medullary thyroid carcinoma), targeted sequence analysis (eg, exons 10, 11, 13-16)
	81406	Molecular pathology procedure, Level 7 (eg, analysis of 11-25 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 26-50 exons)
		• RET (ret proto-oncogene) (eg, Hirschsprung disease), full gene sequence RPE65
	88364	In situ hybridization (eg, FISH), per specimen; each additional single probe stain procedure
FISH <sup>§</sup>	88365	In situ hybridization (eg, FISH), per specimen; initial single probe stain procedure
	88366	In situ hybridization (eg, FISH), per specimen; each multiplex probe stain procedure
Unlisted	81479	Unlisted molecular pathology procedure

Note that this is not an all-inclusive list of available diagnostic tests and testing methods to identify *RET* gene fusions or somatic *RET* mutations. The laboratory is responsible for selecting the appropriate billing code for the test that is performed.

<sup>†</sup>PLA (Proprietary Laboratory Assay) code. PLA codes are alpha-numeric CPT codes with a corresponding descriptor, for labs or manufacturers to specifically identify proprietary tests. Tests with PLA codes may not be described using otherwise-applicable CPT codes. CPT is a registered trademark of the American Medical Association.

§For FISH testing, note that there are parallel sets of codes describing manual or computer-assisted morphometric analysis of specimens stained with single and multiplex probes.



<sup>\*</sup>Includes papillary, poorly differentiated, Hürthle, and anaplastic thyroid cancer.<sup>6,7</sup>

### 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 embryolethality 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.

Severe adverse reactions (Grade 3-4) occurring in  $\geq$ 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  $\geq$  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)  $\geq$ 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]  $\geq$ 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 <u>Prescribing Information</u> for Retevmo.

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### Indications<sup>1</sup>

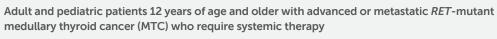
Reteymo is a kinase inhibitor indicated for the treatment of:



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 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 (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, hypertension, QT interval prolongation, hemorrhagic events, hypersensitivity, tumor lysis syndrome (TLS), risk of impaired wound healing, 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. 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 hydration) 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. 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 Reteymo and for at least 1 week after the final dose. Serious adverse reactions occurred in 33% of patients who received Retevmo. The most frequent serious adverse reaction (>2%) 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). Most common adverse reactions, including laboratory abnormalities, (>25%) were increased aspartate aminotransferase (AST), increased alanine aminotransferase (ALT), increased glucose, decreased leukocytes, decreased albumin, decreased calcium, dry mouth, diarrhea, increased creatinine, increased alkaline phosphatase, hypertension, fatigue, edema, decreased platelets, increased total cholesterol, rash, decreased sodium, and constipation.

Please see Important Safety Information on pages 8 and 9 and click for full <u>Prescribing Information</u> for Retevmo.

REFERENCES: 1. Retevmo (selpercatinib) [package insert]. Indianapolis, IN: Eli Lilly and Company; 2021. 2. 2020 ICD-10-CDM Codes. https://www.icd10data.com/ICD10CM/Codes/C00-D49. Accessed January 31, 2020. 3. Drilon A, Hu ZI, Lai GGY, Tan DSW. Targeting RET-driven cancers: lessons from evolving preclinical and clinical landscapes. Nat Rev Clin Oncol. 2018;15(3):151-167. 4. Kato S, Subbiah V, Marchlik E, et al. RET Aberrations in diverse cancers: Next-generation sequencing of 4,871 patients. Clin Cancer Res. 2017; 23(8):1988-1997. 5. Drilon A, Subbiah V, Oxnard GR, et al. LIBRETTO-001: a phase 1 study of LOXO-292, a potent and highly selective RET inhibitor, in patients with RET-altered cancers. J Clin Oncol. 2018;36. Presented at ASCO 2018. 6. Lee M-Y, Ku BM, Kim HS, et al. Genetic alterations and their clinical implications in high-recurrence risk papillary thyroid cancer. Cancer Res Treat. 2017;49(4):906-914. 7. Prescott JD, Zeiger MA. The RET oncogene in papillary thyroid carcinoma. Cancer. 2015;121(13):2137-2146. 8. Oczko-Wojciechowska M, Swierniak M, Krajewska J, et al. Differences in the transcriptome of medullary thyroid cancer regarding the status and type of RET gene mutations. Sci Rep. 2017;7:42074. 9. Matsuda K. PCR-based detection methods for single-nucleotide polymorphism or mutation: real-time PCR and its substantial contribution toward technological refinement. Adv Clin Chem. 2017;80:45-72. 10. Agrawal N, Jiao Y, Sausen M, et al. Exomic sequencing of medullary thyroid cancer reveals dominant and mutually exclusive oncogenic mutations in RET and RAS. J Clin Endocrinol Metab. 2013;98(2): £364-E369. 11. Ferrara R, Auger N, Auclin E, et al. Clinical and translational implications of RET rearrangements in non-small cell lung cancer. J Thorac Oncol. 2018;13(1):27-45. 12. Naidoo J, Drilon A. Molecular diagnostic testing in non-small cell lung cancer. Am J Hematol Oncol. 2014;10(4):4-11. 13. National Center for Biomedical Ontology. Current Procedural Terminology. https://bioportal.bioontology.org/ontologies/CPT?p=classes. Updated November 18, 2019. Accessed January 31, 2020.

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