Answers That Matter.

יוני 2024

רופא/ה נכבד/ה
רוקח/ת נכבד/ה

Retevmo 40mg
Retevmo 80mg
Capsules

חברת לילי מבקשת להודיעכם כי העלונים לרופא ולצרכן של התכשיר שבנידון עודכנו.
בהודעה זו מצוינים רק הסעיפים בהם נעשה שינוי המהווה החמרה. קיימים עדכונים נוספים.
טקסט שהתווסף מודגש בקו תחתון, טקסט שנמחק מסומן בקו חוצה.
העלונים המעודכנים לרופא ולצרכן מפורסמים במאגר התרופות שבאתר משרד הבריאות וניתן לקבלם מודפסים על ידי פנייה לבעל הרישום :
אלי לילי ישראל בע"מ, השיזף 4, רעננה , טל': 09-9606234

בברכה,
אלי לילי ישראל

החומר הפעיל:

Selpercatinib 40 & 80mg

ההתוויה המאושרת לתכשירים:

Metastatic RET Fusion-Positive Non-Small Cell Lung Cancer
RETEVMO is indicated for the treatment of adult patients with metastatic RET fusion-positive non-small cell lung cancer (NSCLC) .

RET-Mutant Medullary Thyroid Cancer
RETEVMO is indicated for the treatment of adult and pediatric patients 12 years of age and older with advanced or metastatic RET-mutant medullary thyroid cancer (MTC) who require systemic therapy .

RET Fusion-Positive Thyroid Cancer
RETEVMO is indicated for the treatment of 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).

העדכונים העיקריים בעלון לרופא הינם:

- **WARNINGS AND PRECAUTIONS**

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Slipped Capital Femoral Epiphysis/Slipped Upper Femoral Epiphysis in Pediatric Patients

Slipped capital femoral epiphysis/slipped upper femoral epiphysis (SCFE/SUFE) occurred in 1 adolescent (3.7% of 27 patients) receiving RETEVMO in LIBRETTO-121 *[see Adverse Reactions (6.1)]*. Monitor patients for symptoms indicative of SCFE/SUFE and treat as medically and surgically appropriate *[see Adverse Reactions (6.1)]*.

- **ADVERSE REACTIONS**

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- Slipped Capital Femoral Epiphysis/Slipped Upper Femoral Epiphysis in Adolescent Patients *[see Warnings and Precautions (5.11)]*.

- **Clinical Trials Experience**

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Clinically relevant adverse reactions in ≤15% of patients who received RETEVMO include hypothyroidism (13%); pneumonia (11%), hypersensitivity (6%); interstitial lung disease/pneumonitis, chylothorax, chylous ascites or tumor lysis syndrome (all < 2%).

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LIBRETTO-121

The safety population described below reflects exposure to RETEVMO as a single agent at 92 mg/m^2 orally twice daily evaluated in 27 patients with advanced solid tumors harboring an activating RET alteration in LIBRETTO-121 [see Clinical Studies (14)]. Among the 27 pediatric and adolescent patients who received RETEVMO, 81% were exposed for 6 months or longer and 59% were exposed for greater than one year.

The median age was 13 years (range: 2 to 20 years); 22% were pediatric patients 2 to 12 years of age; 59% were male; and 52% were White, 26% were Asian, and 11% were Black or African American; and 19% were Hispanic/Latino. The most common cancers were MTC (52%), and papillary thyroid cancer (37%).

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

Dosage interruptions due to an adverse reaction occurred in 22% of patients who received RETEVMO. Adverse reactions requiring dosage interruption in ≥5% of patients included decreased neutrophils.

Dose reductions due to an adverse reaction occurred in 15% of patients who received RETEVMO. Adverse reactions requiring dosage reductions in ≥2% of patients included decreased neutrophils, increased ALT, and increased weight.

The most common adverse reactions (≥25%) were musculoskeletal pain, diarrhea, headache, nausea, vomiting, coronavirus infection, abdominal pain, fatigue, pyrexia, and hemorrhage.

The most common Grade 3 or 4 laboratory abnormalities (≥5%) were decreased calcium, decreased hemoglobin, and decreased neutrophils.

Table 7 summarizes the adverse reactions in LIBRETTO-121.

Table 7: Adverse Reactions (≥15%) in Patients Who Received RETEVMO in LIBRETTO-121

Adverse Reactions	**RETEVMO N= 27**	
	Grades 1-4# %	**Grades 3-4 %**
Musculoskeletal and Connective Tissue Disorders		
Musculoskeletal pain[1]	56	0
Gastrointestinal disorders		
Diarrhea[2]	41	0
Nausea	30	3.7*

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Adverse Reactions	RETEVMO N= 27	
	Grades 1-4# %	Grades 3-4 %
Vomiting	30	7*
Abdominal pain[3]	26	0
Constipation	19	7*
Stomatitis[4]	15	0
Nervous System Disorders		
Headache	33	0
Infections and Infestations		
Coronavirus infection	30	0
Upper respiratory tract infection	22	0
General Disorders and Administration Site Conditions		
Fatigue[5]	26	0
Pyrexia	26	0
Edema[6]	19	0
Increased weight	19	7*
Blood and Lymphatic System Disorders		
Hemorrhage[7]	26	3.7*
Respiratory, Thoracic and Mediastinal Disorders		
Oropharyngeal pain	22	0
Cough	22	0
Endocrine Disorders		
Hypothyroidism[8]	19	0
Skin and Subcutaneous Tissue Disorders		
Rash [9]	19	0
Renal and Urinary Disorders		
Proteinuria	15	0

[1] Musculoskeletal pain includes arthralgia, back pain, bone pain, musculoskeletal chest pain, noncardiac chest pain, neck pain, pain in extremity

[2] Diarrhea includes, anal incontinence

[3] Abdominal pain includes abdominal pain upper

[4] Stomatitis includes angular cheilitis

[5] Fatigue includes asthenia and malaise

[6] Edema includes edema peripheral, face edema, localized edema, generalized edema, swelling

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[7] Hemorrhage includes mouth hemorrhage, epistaxis

[8] Hypothyroidism includes blood thyroid stimulating hormone increased, thyroglobulin increased

[9] Rash includes rash maculopapular

[*] No Grade 4 events were reported.
[#] Graded according to National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) version 5.0.

Clinically relevant adverse reactions in <15% of patients who received RETEVMO include dizziness (11%), urinary tract infection (11%), decreased appetite (7%), electrocardiogram QT prolonged (7%), hypersensitivity (7%), hypertension (7%), and pneumonia (3.7%).

Table 8 summarizes the laboratory abnormalities in LIBRETTO-121.

Table 8: Select Laboratory Abnormalities (≥15%) Worsening from Baseline in Patients Who Received RETEVMO in LIBRETTO-121

Laboratory Abnormality	**RETEVMO[1]**	
	Grades 1-4# (%)	Grades 3-4 (%)
Chemistry		
Decreased calcium	59	7
Increased ALT	56	3.7*
Increased alkaline phosphatase	52	0
Increased AST	48	3.7*
Decreased albumin	44	0
Increased bilirubin	30	0
Increased creatinine	22	0
Decreased potassium	22	3.7
Decreased magnesium	15	3.7
Hematology		
Decreased neutrophils	44	7*
Decreased lymphocytes	24	4.8
Decreased platelets	22	0
Decreased hemoglobin	19	7*

[1] Denominator for each laboratory parameter is based on the number of patients with a baseline and post-treatment laboratory value available, which ranged from 21 to 27 patients.
[*] No Grade 4 abnormalities were reported.
[#] Graded according to National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) version 5.

העדכונים העיקריים בעלון לצרכן הינם:

4. תופעות לוואי

רטבמו עלולה לגרום לתופעות לוואי חמורות, כולל:

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- **בעיות במפרק הירך (החלקה של הקצה המוארך של עצם הירך או של הירך העליון) בילדים.** פנה מיד אל הרופא אם אתה מפתח סימנים ותסמינים של בעיות בירך, כולל כאב בירך או בברך או צליעה ללא כאבים.

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