דצמבר 2025

רופא/ה נכבד/ה
רוקח/ת נכבד/ה,

חברת אלי לילי ישראל בע"מ מבקשת להודיעכם כי עודכנו העלונים לרופא ולצרכן של התכשירים RETEVMO 40 mg ו-RETEVMO 80 mg.

בהודעה זו נכללים השינויים המהותיים בלבד. שינויים המהווים החמרה מסומנים בצהוב, מידע שהתווסף מסומן בכחול ומידע שהוסר מסומן באדום. ישנם עדכונים נוספים.

העלונים המעודכנים לרופא ולצרכן מפורסמים במאגר התרופות שבאתר משרד הבריאות וניתן לקבלם מודפסים על ידי פנייה לבעל הרישום:

אלי לילי ישראל בע"מ, רח' השיזף 4, רעננה , טל': 09-9606234

בברכה,
ליאת אטיאס
רוקחת ממונה

שם התכשיר	RETEVMO 80 MG ,RETEVMO 40 MG
החומר הפעיל	SELPERCATINIB
צורת מינון	CAPSULES
ההתוויה המאושרת לתכשיר	•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). •Other RET Fusion-Positive Solid Tumors RETEVMO as monotherapy is indicated for the treatment of adults with advanced RET fusion-positive solid tumors, when treatment options not targeting RET provide limited clinical benefit, or have been exhausted.

העדכונים העיקריים בעלון לרופא הינם:

5 WARNINGS AND PRECAUTIONS

[…]

5.6 Hypersensitivity

~~Hypersensitivity~~ 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 ~~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. Stevens Johnsons Syndrome has been observed in the post-marketing setting [see Adverse Reactions (6.2)]. 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 *[see Dosage and Administration (2.5)]*. Continue steroids until patient reaches target dose and then taper. Permanently discontinue RETEVMO for recurrent hypersensitivity.

6 ADVERSE REACTIONS

[…]

6.1 Clinical Trials Experience

[…]

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~~36 patients with advanced solid tumors harboring an activating RET alteration in LIBRETTO-121 *[see Clinical Studies (14)]*. Among the ~~27~~ 36 pediatric and adolescent patients who received RETEVMO, ~~81~~86% were exposed for 6 months or longer and ~~59~~72% were exposed for greater than one year.

The median age was 13 years (range: 2 to 20 years); ~~22~~31% were pediatric patients 2 to 12 years of age; ~~59~~53% were male; and ~~52~~47% were White, ~~26~~28% were Asian, and ~~11~~8% were Black or African American; and 19% were Hispanic/Latino. The most common cancers were MTC (~~52~~42%), and papillary thyroid cancer (~~37~~42%).

Serious adverse reactions occurred in ~~22~~42% of patients who received RETEVMO. ~~The s~~Serious adverse reactions occurring ~~(~~in more than 1 patient ~~each)~~ were ~~abdominal infection, abdominal pain, aspiration, constipation, diarrhea, epiphysiolysis, nausea, pneumonia, pneumatosis intestinalis, rhinovirus infection, sepsis,~~ vomiting and fracture (2 patients each).

Dosage interruptions due to an adverse reaction occurred in ~~22~~42% of patients who received RETEVMO. Adverse reactions requiring dosage interruption in ≥5% of patients included increased ALT, increased AST, ascites, increased bilirubin, decreased neutrophils, and pyrexia.

Dose reductions due to an adverse reaction occurred in ~~15~~22% of patients who received RETEVMO. Adverse reactions requiring dosage reductions in ≥2% of patients included increased ALT, decreased neutrophils, increased weight, and increased bilirubin.

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

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

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~~36	
	Grades 1-4[#] %	Grades 3-4 %
Musculoskeletal and Connective Tissue Disorders		
Musculoskeletal pain[1]	~~56~~58	0
Gastrointestinal Disorders		
Diarrhea[2]	~~41~~47	~~0~~2.8*
Nausea	~~30~~42	2.8*
Abdominal pain[3]	~~26~~36	0
Vomiting	~~30~~31	~~7~~8*
Constipation	~~19~~22	6*
~~Stomatitis~~	~~15~~	~~0~~
Blood and Lymphatic System Disorders		
Hemorrhage[4]	~~26~~39	0
General Disorders and Administration Site Conditions		
Pyrexia	~~26~~39	0
Fatigue[5]	~~26~~31	0
Edema[6]	~~19~~25	0
Nervous System Disorders		
Headache	33	0
Respiratory, Thoracic and Mediastinal Disorders		
Cough	~~22~~31	0
Oropharyngeal pain	22	0
Skin and Subcutaneous Tissue Disorders		
Rash[7]	~~19~~28	0
Infections and Infestations		
Coronavirus infection	28	0
Upper respiratory tract infection	~~22~~28	~~0~~2.8*
Urinary tract infection[8]	19	2.8*
Endocrine Disorders		
Hypothyroidism[9]	~~19~~22	0
Investigations		
Increased weight	19	~~7~~11*

[1] Musculoskeletal pain includes arthralgia, back pain, bone pain, musculoskeletal chest pain, non-cardiac chest pain, neck pain, pain in extremity

[2] Diarrhea includes anal incontinence

[3] Abdominal pain includes abdominal pain upper, abdominal discomfort

[4] ~~Stomatitis includes angular cheilitis~~

[4] Hemorrhage includes epistaxis, hematuria, anal hemorrhage, blood urine present, hemoptysis, menorrhagia, mouth hemorrhage

[5] Fatigue includes asthenia, malaise

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

[7] Rash includes rash maculopapular, rash erythematous, urticaria

[8] Urinary tract infection includes cystitis

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

[*] 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~~14%), electrocardiogram QT prolonged (~~7~~14%), hypersensitivity (~~7~~11%), stomatitis (14%), proteinuria (11%), hypertension (~~7~~8%), decreased appetite (8%), erectile dysfunction (6%), chylous ascites (2.8%), dry mouth (2.8%), epiphysiolysis (2.8%), and pneumonia (~~3.7~~2.8%).

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~~61	~~7~~11
Increased ALT	~~56~~58	~~3.7~~8*
Decreased albumin	~~44~~53	0
Increased alkaline phosphatase	50	0
Increased AST	~~48~~50	2.8*
Increased bilirubin	~~30~~31	~~0~~2.8*
Increased cholesterol	28	0
Decreased magnesium	~~15~~28	~~3.7~~6
Increased potassium	28	2.8
Increased creatinine	19	~~0~~2.8
Decreased potassium	19	~~3.7~~6
Decreased sodium	17	0
Hematology		
Decreased neutrophils	40	~~7*~~8
Decreased hemoglobin	~~19~~36	~~7~~11*

Increased hemoglobin	33	2.8*
Decreased platelets	~~22~~28	~~0~~2.8*
Decreased lymphocytes	~~24~~28	~~4.8~~14

[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~~18 to ~~27~~36 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

[...]

תופעות הלוואי השכיחות ביותר~~(≥25%)~~ (תופעות שמופיעות ביותר ממשתמש אחד מעשרה) של רטבמו בילדים מגיל 12 ומעלה עם גידולים סולידיים כוללות:

- כאבי שרירים ועצמות
- שלשול
- כאב ראש
- בחילה
- הקאה
- שיעול
- זיהום בדרכי נשימה עליונות
- הדבקות בנגיף הקורונה
- כאב באיזור הקיבה (כאב בטן)
- עייפות
- חום
- דימומים
- פריחה
- נפיחות

[...]

תוצאות בדיקות המעבדה החמורות השכיחות ביותר עם רטבמו בילדים מגיל 12 ומעלה עם גידולים סולידיים כוללות
ירידה בספירת תאי דם לבנים, ירידה ברמות הסידן בדם, ירידה בספירת תאי דם אדומים, עלייה באנזימי כבד, ירידה ברמות המגנזיום בדם וירידה ברמות האשלגן בדם.