אוגוסט 2026

הנדון:

RETEVMO 40 MG TABLETS — רטבמו 40 מ''ג טבליות
RETEVMO 80 MG TABLETS — רטבמו 80 מ''ג טבליות
RETEVMO 120 MG TABLETS — רטבמו 120 מ''ג טבליות
RETEVMO 160 MG TABLETS — רטבמו 160 מ''ג טבליות

רופא/ה נכבד/ה
רוקח/ת נכבד/ה,

חברת אלי לילי ישראל בע"מ מבקשת להודיעכם כי העלונים לרופא ולצרכן של התכשירים שבנדון עודכנו.

שם של התכשיר	מס' רישיון	צורת המינון	מרכיב הפעיל וחוזקו
RETEVMO 40 MG TABLETS	99-38203-75-179	Film coated tablets	Selpercatinib 40 mg
RETEVMO 80 MG TABLETS	99-38202-74-179	Film coated tablets	Selpercatinib 80 mg
RETEVMO 120 MG TABLETS	99-38201-73-179	Film coated tablets	Selpercatinib 120 mg
RETEVMO 160 MG TABLETS	99-38200-72-179	Film coated tablets	Selpercatinib 160 mg

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.

מכתב זה מדגים את השינויים המהותיים בלבד. קיימים עדכונים נוספים. למידע נוסף יש לעיין בעלון לרופא ובעלון לצרכן המעודכנים.

מקרא לעדכונים המסומנים:
שינויים המהווים החמרה מסומנים בכתב צהוב, מידע שהתווסף מסומן בכתב כחול ומידע שהוסר מסומן בכתב ~~אדום~~.

העדכונים העיקריים בעלון לרופא הינם:

6 WARNINGS AND PRECAUTIONS

6.1 Hepatotoxicity

Serious hepatic adverse reactions occurred in ~~3~~4.6% of patients treated with RETEVMO. Increased AST occurred in ~~59~~62% of patients, including Grade 3 or 4 events in 11% and increased ALT occurred in ~~55~~58% of patients, including Grade 3 or 4 events in ~~12~~13% *[see Adverse Reactions (7.1)]*. The median time to first onset for increased AST was ~~6~~ 5 weeks (range: ~~1~~ 4.9 days to ~~3.4~~6 years) and increased ALT was ~~5.8~~4.9 weeks (range: ~~1~~ 6 days to ~~2.~~5 years).

[…]

6.2 Interstitial Lung Disease/ Pneumonitis

Severe, life-threatening, and fatal interstitial lung disease (ILD)/pneumonitis can occur in patients treated with RETEVMO. ILD/pneumonitis occurred in ~~1.8~~3% of patients who received RETEVMO, including 0.3% with Grade 3 or 4 events, and 0.~~3~~2% with fatal reactions.

[…]

6.3 Hypertension

Hypertension occurred in ~~11~~43% of patients, including Grade 3 hypertension in 20% and Grade 4 in one (0.1%) patient *[see Adverse Reactions (7.1)]*. Overall, 6.43% had their dose interrupted, ~~and~~ 1.5~~3~~% had their dose reduced, and 0.2% discontinued RETEVMO for hypertension. Treatment-emergent hypertension was most commonly managed with anti-hypertension medications.

[…]

6.4 QT Interval Prolongation

RETEVMO can cause concentration-dependent QT interval prolongation *[see Clinical Pharmacology (11.2)]*. An increase in QTcF interval to >500 ms was measured in 8~~7~~% of patients and an increase in the QTcF interval of at least 60 ms over baseline was measured in ~~20~~22% of patients *[see Adverse Reactions (7.1)]*. RETEVMO has not been studied in patients with clinically significant active cardiovascular disease or recent myocardial infarction.

[…]

6.5 Hemorrhagic Events

Serious including fatal hemorrhagic events can occur with RETEVMO. Grade ≥3 hemorrhagic events occurred in 4.3~~.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 each).

Permanently discontinue RETEVMO in patients with severe or life-threatening hemorrhage *[see Dosage and Administration (3.5)]*.

6.6 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 in 2~~1.9~~%. The median time to onset was 1.9 weeks (range: 5 days to 6.5~~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 (7.2)]*. Discontinue RETEVMO in patients with Stevens Johnson Syndrome.

[…]

6.7 Tumor Lysis Syndrome

Tumor lysis syndrome (TLS) occurred in 0.9~~6~~% of patients with medullary thyroid carcinoma and 0.3% of patients with non-small cell lung cancer receiving RETEVMO *[see Adverse Reactions (7.1)]*.

[…]

6.9 Hypothyroidism

RETEVMO can cause hypothyroidism. Hypothyroidism occurred in ~~13~~15% of patients treated with RETEVMO; all reactions were Grade 1 or 2. Hypothyroidism occurred in ~~13~~15% of patients (59/390~~50/373~~) with thyroid cancer and ~~13~~14% of patients (65/467~~53/423~~) with other solid tumors including NSCLC *[see Adverse Reactions (7.1)]*.

7 ADVERSE REACTIONS

[…]

7.1 Clinical Trials Experience

[…]

RET Gene Fusion or Gene Mutation Positive Solid Tumors

LIBRETTO-001

Among the ~~796~~ 857 patients who received RETEVMO, ~~84~~74% were exposed for ~~6~~ 12 months or longer and ~~73~~57% were exposed for 24 months or longer~~greater than one year~~. Among these patients, ~~96~~97% received at least one dose of RETEVMO at the recommended dosage of 160 mg orally twice daily.

The median age was 59 years (range: 15 to 92 years); 0.2~~3~~% were pediatric patients 12 to 16 years of age; 51% were male; and ~~69~~68% were White, ~~23~~24% were Asian, and 3% were Black or African American; and 5% were Hispanic/Latino. The most common tumors were NSCLC (~~45~~43%), MTC (~~40~~39%), and non-medullary thyroid carcinoma (~~7~~8%).

Serious adverse reactions occurred in ~~44~~58% of patients who received RETEVMO. The most frequent serious adverse reactions (≥2% of patients) were pneumonia, hemorrhage~~pleural effusion~~, abdominal pain, ~~hemorrhage, hypersensitivity,~~ dyspnea, pleural effusion, sepsis, musculoskeletal pain, ~~and~~ hyponatremia,

vomiting, diarrhea, and increased blood creatinine. Fatal adverse reactions occurred in 3% of patients; fatal adverse reactions included sepsis (n = 6), respiratory failure (n = 5), hemorrhage (n = 4), pneumonia (n = 43), pneumonitis (n = 2), cardiac arrest (n=3), pneumonitis, cardiac failure (n=2 each), sudden death, cerebral infarction and dyspnea (n = 1 each), and cardiac failure (n = 1).

Permanent discontinuation due to an adverse reaction occurred in 810% of patients who received RETEVMO. Adverse reactions resulting in permanent discontinuation in ≥0.5% of patients included increased ALT (0.76%), fatigue (0.6%), sepsis (0.5%), pneumonia (0.5%), and increased AST (0.5%).

Dosage interruptions due to an adverse reaction occurred in 6472% of patients who received RETEVMO. Adverse reactions requiring dosage interruption in ≥5% of patients included increased ALT, increased AST, diarrhea, and hypertension, and QT prolongation.

Dose reductions due to an adverse reaction occurred in 4145% of patients who received RETEVMO. Adverse reactions requiring dosage reductions in ≥2% of patients included increased ALT, increased AST, fatigue, QT prolongation, fatigue, diarrhea, drug hypersensitivity, and ascitesedema.

The most common adverse reactions (≥25%) were musculoskeletal pain, edema, diarrhea, fatigue, dry mouth, hypertension, abdominal pain, constipation, rash, nausea, constipation, and headache, vomiting, cough, dyspnea, and hemorrhage.

The most common Grade 3 or 4 laboratory abnormalities (≥5%) were decreased lymphocytes, increased alanine aminotransferase (ALT), decreased sodium, increased aspartate aminotransferase (AST), decreased calciumsodium, and decreased phosphatecalcium.

Table 6 summarizes the adverse reactions in LIBRETTO-001.

Table 6: Adverse Reactions (≥20%) in Patients Who Received RETEVMO in LIBRETTO-001

Adverse Reaction	RETEVMO (n = 857796)	
	Grades 1-4# (%)	Grades 3-4 (%)
Musculoskeletal and Connective Tissue Disorders		
Musculoskeletal pain[1]	59	4.1*
General Disorders and Administration Site Conditions		
Edema[1]	49	0.8*
Fatigue[2]	46	3.1*
Edema[2] Arthralgia	5321	01.3*
Fatigue[3]	49	4.7*
Gastrointestinal Disorders		
Diarrhea[34]	5247	56.2*
Dry Mmouth[5]	4443	0
Abdominal pain[46]	3934	23.5*
Nausea Constipation	3633	0.81.9*
Nausea Constipation	3531	1.10.8*
Vomiting[7]	2922	1.82.9*
Vascular Disorders		
Hypertension[8]	4341	20
Skin and Subcutaneous Tissue Disorders		
Rash[59]	3833	0.86*
Nervous System Disorders		
Headache[6]	28	1.4*
Respiratory, Thoracic and Mediastinal Disorders		
Cough[710]	3024	0
Dyspnea[811]	2822	34.1
Nervous System Disorders		
Headache[12]	30	1.8*
Dizziness[13]	22	0.5*
Blood and Lymphatic System Disorders		
Hemorrhage[914]	2622	3.92.6
Metabolism and Nutrition Disorders		
Decreased appetite	23	0.9*
Investigations		

Prolonged QT interval[15]	21	54.8*
Infections and Infestations		
Urinary tract infection	20	2.2*

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

[12] Edema includes edema peripheral, face edema, periorbital edema, eye edema, eyelid edema, orbital edema, localized edema, lymphedema, scrotal edema, peripheral swelling, scrotal swelling, swelling, swelling face, eye swelling, generalized edema, genital edema, angioedema, penile edema, skin edema, testicular swelling, vulvovaginal swelling.

[23] Fatigue includes asthenia, and malaise.

[34] Diarrhea includes defecation urgency, frequent bowel movements, gastrointestinal hypermotility, anal incontinence.

[5] Dry mouth includes mucosal dryness

[46] Abdominal pain includes abdominal pain upper, abdominal pain lower, abdominal discomfort, abdominal tenderness, epigastric discomfort, gastrointestinal pain.

[7] Vomiting includes regurgitation, retching.

[8] Hypertension includes blood pressure increased

[59] Rash includes skin exfoliation, rash erythematous, rash macular, rash maculopapular, rash morbilliform, rash papular, rash pruritic, butterfly rash, exfoliative rash, rash follicular, rash generalized, rash vesicular, dermatitis, urticaria, dermatitis allergic, rash pustular.

[6] Headache includes sinus headache, tension headache.

[710] Cough includes productive cough, upper airway cough syndrome.

[811] Dyspnea includes dyspnea exertional, dyspnea at rest.

[12] Headache includes sinus headache, tension headache.

[13] Dizziness includes vertigo, presyncope, dizziness postural.

[914] Hemorrhage includes epistaxis, hematuria, hemoptysis, contusion, rectal hemorrhage, vaginal hemorrhage, ecchymosis, hematochezia, international normalized ratio increased, petechiae, traumatic hematoma, anal hemorrhage, blood blister, blood urine present, cerebral hemorrhage, hematocrit decreased, gastric hemorrhage, hemorrhage intracranial, hemorrhage subcutaneous, spontaneous hematoma, abdominal wall hematoma, angina bullosa hemorrhagica, arterial hemorrhage, coagulopathy, conjunctival hemorrhage, disseminated intravascular coagulation, diverticulum intestinal hemorrhagic, eye contusion, eye hematoma, eye hemorrhage, gastrointestinal hemorrhage, gingival bleeding, hematemesis, hemorrhagic stroke, hemothorax, hemorrhoidal hemorrhage, hepatic hemorrhage, menorrhagia, hepatic hematoma, intraabdominal hemorrhage, laryngeal hemorrhage, lower gastrointestinal hemorrhage, melena, mouth hemorrhage, occult blood positive, esophageal hemorrhage, post procedural hemorrhage, postmenopausal hemorrhage, pulmonary hemorrhage, pelvic hematoma, periorbital hematoma, periorbital hemorrhage, pharyngeal hemorrhage, pulmonary contusion, purpura, activated partial thromboplastin time prolonged, retinal hemorrhage, retroperitoneal hematoma, scleral hemorrhage, skin hemorrhage, subarachnoid hemorrhage, subdural hemorrhage, subdural hematoma, testicular hemorrhage, tracheal hemorrhage, traumatic hemothorax, tumor hemorrhage, upper gastrointestinal hemorrhage, uterine hemorrhage, vessel puncture site hematoma.

[15] Prolonged QT interval includes electrocardiogram QT prolonged, electrocardiogram QT interval abnormal.

* Only includes a grade 3 adverse reaction.

\# Graded according to National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) version 4.03

Clinically relevant adverse reactions in ≤15% of patients who received RETEVMO include hypothyroidism (1315%); pneumonia (1114%), hypersensitivity (6%); interstitial lung disease/pneumonitis, chylothorax, chylous ascites or tumor lysis syndrome (all < 23%).

Table 7 summarizes the laboratory abnormalities in LIBRETTO-001.

Table 7: Select Laboratory Abnormalities (≥20%) Worsening from Baseline in Patients Who Received RETEVMO in LIBRETTO-001

	RETEVMO[1]	
Laboratory Abnormality	**Grades 1-4[#] (%)**	**Grades 3-4 (%)**
Chemistry		
Increased AST	5962	11
Decreased calcium	5961	5.7

~~Increased ALT~~	~~56~~	~~12~~
Decreased albumin	~~56~~61	~~2.~~3.6
Increased ALT	58	13
Increased glucose	~~53~~56	~~2.8~~4.0
Increased creatinine	~~47~~51	~~2.4~~3.6
Decreased sodium	~~42~~49	~~11~~13
Increased alkaline phosphatase	~~40~~43	~~3~~4.4
~~Increased total cholesterol~~	~~35~~	~~1.7~~
Increased potassium	~~34~~39	~~2.7~~3.5
Decreased glucose	~~34~~39	1.5~~0~~
Increased total cholesterol	37	1.7
Decreased magnesium	~~33~~37	0.7~~6~~
Increased bilirubin	~~30~~32	2.9~~8~~
Decreased phosphate	25	5
Hematology		
Decreased lymphocytes	~~52~~56	~~20~~22
Decreased platelets	~~37~~41	~~3.2~~4.0
Decreased hemoglobin	~~28~~36	~~3.5~~4.1
Decreased neutrophils	~~25~~27	3.8~~2~~

[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 ~~765~~ 823 to ~~791~~ 855 patients.

[#] Graded according to National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) version 4.03

העדכונים העיקריים בעלון לצרכן הינם:

2. לפני השימוש בתרופה

[...]

היריון, הנקה ופוריות

היריון

ספרי לרופא אם את בהיריון או שאת מתכננת להכנס להיריון. רטבמו יכולה להזיק לעובר שלך. אין להרות במהלך הטיפול ברטבמו.

נשים שמסוגלות להרות:

- ~~אם את מסוגלת להרות,~~ הרופא יבצע בדיקת היריון לפני ~~שתתחילי~~ תחילת הטיפול ברטבמו.
- ~~נשים שמסוגלות להרות צריכות~~יש להשתמש באמצעי מניעה יעיל במהלך הטיפול ובמשך **שבוע אחד** לאחר המנה האחרונה של רטבמו. ~~התייעצי~~שוחחי עם הרופא בנוגע לאמצעי מניעת ~~ה~~היריון ~~שיכול~~שעשויים להתאים ~~עבורך~~לך.
- ספרי לרופא מייד אם נכנסת להיריון או ~~ש~~אם את חושבת שאת עלולה להיות בהיריון במהלך הטיפול ברטבמו.

גברים שיש להם בנות זוג שמסוגלות להרות:

- ~~צריכים~~יש להשתמש באמצעי מניעה יעיל במהלך הטיפול ברטבמו ובמשך **שבוע אחד** לאחר המנה האחרונה של רטבמו.
- ספר לרופא מייד אם בת זוגך נכנסה להיריון במהלך הטיפול שלך ברטבמו.

[...]

4. תופעות לוואי

[...]

רטבמו ~~עלולה~~ יכולה לגרום לתופעות לוואי חמורות, הכוללות:

[...]

- **תגובות אלרגיות.** רטבמו יכולה לגרום לתגובות אלרגיות, לרבות תגובות עור חמורות, במיוחד במהלך החודש הראשון של הטיפול. ספר לרופא מייד אם מופיעים אצלך חום, פריחה, כאבי שרירים או כאבי מפרקים בכל עת במהלך הטיפול ברטבמו, ~~במיוחד במהלך החודש הראשון של הטיפול. פנה אל הרופא אם אתה סובל מאחד מבין תסמינים אלו.~~

[…]

תופעות לוואי נוספות

תופעות הלוואי השכיחות ביותר (תופעות שמופיעות ביותר ממשתמש אחד מעשרה) של רטבמו במבוגרים עם גידולים סולידיים כוללות:

- כאבי שרירים ועצמות
- נפיחות בזרועות, ברגליים, בכפות הידיים ובכפות הרגליים (בצקת)
- שלשול
- עייפות
- יובש בפה
- לחץ דם גבוה
- כאב באיזור הבטן
- פריחה
- בחילה
- ~~כאב באיזור הקיבה (כאב בטן)~~
- עצירות
- ~~פריחה~~שיעול
- ~~בחילה~~כאב ראש
- ~~כאב ראש~~הקאה
- קוצר נשימה
- דימום

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

- כאבי שרירים ועצמות
- שלשול
- בחילה ~~כאב ראש~~
- דימום ~~בחילה~~
- חום ~~הקאה~~
- כאב באיזור הבטן ~~שיעול~~
- כאב ראש ~~זיהום בדרכי הנשימה העליונות~~
- הקאה ~~הדבקות בנגיף הקורונה~~
- עייפות ~~כאב באיזור הקיבה (כאב בטן)~~
- שיעול ~~עייפות~~
- פריחה ~~חום~~
- זיהום בנגיף הקורונה ~~דימומים~~
- זיהום בדרכי הנשימה העליונות ~~פריחה~~
- נפיחות בזרועות, ברגליים, בכפות הידיים ובכפות הרגליים (בצקת)

תוצאות בדיקות המעבדה החריגות החמורות השכיחות ביותר עם רטבמו במבוגרים עם גידולים סולידיים כוללות ירידה בספירת תאי הדם הלבנים, עלייה באנזימי כבד, ירידה ברמות הנתרן בדם, ~~ו~~ירידה ברמות הסידן בדם וירידה ברמות הפוספאט (זרחן) בדם.

[…]

העלונים המעודכנים לרופא ולצרכן מפורסמים במאגר התרופות שבאתר משרד הבריאות:

https://israeldrugs.health.gov.il/#!/byDrug

וניתן לקבלם מודפסים על ידי פנייה לבעל הרישום:
אלי לילי ישראל בע"מ, רח' השיזף 4, רעננה , טל': 09-960623

בברכה,

ארינה שייקביץ
רוקחת ממונה
אלי לילי ישראל בע"מ