J-C Health Care Ltd.

Kibbutz Shefayim 6099000, ISRAEL
tel +972-9-959-1111
fax +972-9-958-3636

08/2023

רופא/ה נכבד/ה
רוקח/ת נכבד/ה

הנדון:

טקוואילי™ 10 מ"ג/מ"ל Tecvayli® 10mg/ml
טקוואילי™ 90 מ"ג/מ"ל Tecvayli® 90mg/ml

חברת J-C Health Care Ltd מבקשת להודיעכם כי העלונים לרופא ולצרכן של התכשיר שבנדון התעדנו **באוגוסט 2023.**

פרטי העדכון העיקריים מופיעים בהמשך (טקסט שנוסף מסומן באדום, טקסט שהושמט מסומן בטקסט ~~בחול עם קו חוצה~~, טקסט המהווה החמרה מודגש ברקע צהוב),אך קיימים עדכונים נוספים.

ההתוויות המאושרות לתכשיר בישראל:

TECVAYLI is indicated as monotherapy for the treatment of adult patients with relapsed and refractory multiple myeloma, who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy.

מרכיב פעיל: Teclistamab 10mg/ml , Teclistamab 90mg/ml

העלונים המעודכנים נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות:
https://israeldrugs.health.gov.il/#!/byDrug.

כמו כן, מצורפים לפרסום זה וניתן לקבל העתק מודפס שלהם באמצעות פנייה לבעל הרישום: J-C Health Care Ltd, קיבוץ שפיים, 6099000, טל': 09-9591111.

בברכה,

יעל לפידות מללי
רוקחת ממונה
J-C Health Care Ltd

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העדכון בעלון לרופא הינו:

4.2 Posology and method of administration

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Table 1: TECVAYLI dosing schedule

Dosing schedule	Day	Dose[a]	
Step-up dosing schedule[~~e~~b]	Day 1	Step-up dose 1	0.06 mg/kg single dose
	Day 3[~~b~~c]	Step-up dose 2	0.3 mg/kg single dose
	Day 5[~~e~~d]	First maintenance dose	1.5 mg/kg single dose
Weekly dosing schedule[~~e~~b]	One week after first maintenance dose and weekly thereafter[~~d~~e]	Subsequent maintenance doses	1.5 mg/kg once weekly

a Dose is based on actual body weight and should be administered subcutaneously.

b See Table 2 for recommendations on restarting TECVAYLI after dose delays.~~Step-up dose 2 may be given between 2 to 7 days after Step-up dose 1.~~

c Step-up dose 2 may be given between two to seven days after Step-up dose 1.~~First maintenance dose may be given between 2 to 7 days after Step-up dose 2. This is the first full treatment dose (1.5 mg/kg)~~.

d First maintenance dose may be given between two to seven days after Step-up dose 2. This is the first full maintenance dose (1.5 mg/kg).~~Maintain a minimum of five days between weekly maintenance doses.~~

e Maintain a minimum of five days between weekly maintenance doses.~~See Table 2 for recommendations on restarting TECVAYLI after dose delays.~~

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4.6 Fertility, pregnancy and lactation

Women of child-bearing potential/Contraception in males and females

Pregnancy status for females of child-bearing potential should be verified prior to starting treatment with TECVAYLI.

Women of child-bearing potential should use effective contraception during treatment and for five ~~3~~ months after the final dose of TECVAYLI. In clinical studies, male patients with a female partner of child-bearing potential used effective contraception during treatment and for three months after the last dose of teclistamab.

Pregnancy

There are no available data on the use of teclistamab in pregnant women or animal data to assess the risk of teclistamab in pregnancy. Human IgG is known to cross the placenta after the first trimester of pregnancy. Therefore, teclistamab, a humanised IgG4-based antibody, has the potential to be transmitted from the mother to the developing foetus. TECVAYLI is not recommended for women who are pregnant. TECVAYLI is associated with hypogammaglobulinaemia, therefore, assessment of immunoglobulin levels in newborns of mothers treated with TECVAYLI should be considered.

Breast-feeding

It is not known whether teclistamab is excreted in human or animal milk, affects breast-fed infants or affects milk production. Because of the potential for serious adverse reactions in

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breast-fed infants from TECVAYLI, patients should be advised not to breast-feed during treatment with TECVAYLI and for at least five ~~three~~ months after the last dose.
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5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other monoclonal antibodies and antibody drug conjugates ~~(group)~~, ATC code: L01FX24 ~~not yet assigned~~
…

5.2 Pharmacokinetic properties

Teclistamab exhibited approximately dose-proportional pharmacokinetics following subcutaneous administration across a dose range of 0.08 mg/kg to 3 mg/kg (0.05 to 2.0 times the recommended dose). ~~The mean accumulation ratio following subcutaneous weekly dosing of teclistamab at steady state (based on the 7th weekly maintenance dose), was 2.71- and 3.05-fold for C_{max} and AUC_{tau}, respectively. The mean bioavailability following teclistamab subcutaneous administration was 69%, relative to intravenous dosing.~~ Ninety percent of steady state exposure was achieved after 12 weekly maintenance doses. The mean accumulation ratio between the first and 13th weekly maintenance dose of teclistamab 1.5 mg/kg was 4.2-fold for C_{max}, 4.1-fold for C_{trough}, and 5.3-fold for AUC_{tau}.

~~Pharmacokinetic parameters of teclistamab following the 1st and 7th recommended maintenance dose of 1.5 mg/kg are shown in Table 8.~~ The C_{max}, C_{trough}, and AUC_{tau} of teclistamab are presented in Table 8.

Table 8: Pharmacokinetic parameters of teclistamab for the 13th recommended weekly maintenance dose (1.5 mg/kg) in patients with relapsed or refractory multiple myeloma in MajesTEC-1

Pharmacokinetic Parameter	Teclistamab Geometric Mean (CV%)
C_{max} (µg/mL)	23.8 (55%)
C_{trough} (µg/mL)	21.1 (63%)
AUC_{tau} (µg·h/mL)	3 838 (57%)

C_{max} = Maximum serum teclistamab concentration; C_{trough} = Serum teclistamab concentration prior to next dose; CV = geometric coefficient of variation; AUC_{tau} = Area under the concentration-time curve over the weekly dosing interval.

Absorption

The mean bioavailability of teclistamab was 72% when administered subcutaneously. The median (range) T_{max} of teclistamab after the first and 13th maintenance doses were 139 (19 to 168) hours and 72 (24 to 168) hours, respectively.

Distribution

The mean volume of distribution was 5.63 L (29% coefficient of variation (CV)).

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Elimination

Teclistamab clearance decreases over time, with a mean (CV%) maximal reduction from baseline to the 13th maintenance dose of 40.8% (56%). The geometric mean (CV%) clearance is 0.472 L/day (64%) at the 13th maintenance dose. Patients who discontinue teclistamab after the 13th maintenance dose are expected to have a 50% reduction from C_{max} in teclistamab concentration at a median (5th to 95th percentile) time of 15 (7 to 33) days after T_{max} and a 97% reduction from C_{max} in teclistamab concentration at a median time of 69 (32 to 163) days after T_{max}.

Population pharmacokinetic analysis (based on MajesTEC-1) showed that soluble BCMA did not impact teclistamab serum concentrations.

~~**Table 8: Pharmacokinetic parameters of teclistamab following the at first and seventh recommended maintenance dose (1.5 mg/kg) in patients with relapsed or refractory multiple myeloma in MajesTEC-1**~~

~~Pharmacokinetic Parameters~~	~~1st maintenance dose of 1.5 mg/kg~~	~~7th maintenance dose of 1.5 mg/kg (steady-state)~~
~~T_{max} (hours)~~	~~72.0 (45.8 – 193) (n=40)~~	~~48.9 (0.0 – 166) (n=15)~~
~~C_{max} (µg/mL)~~	~~8.74 ± 3.65 (n=40)~~	~~25.3 ± 11.1 (n=15)~~
~~C_{trough} (µg/mL)~~	~~7.67 ± 3.52 (n=38)~~	~~22.1 ± 10.9 (n=27)~~
~~AUC_{tau} (µg·h/mL)~~	~~1 169 ± 481 (n=38)~~	~~3 905 ± 1 748 (n=13)~~

~~T_{max} = Time to reach the C_{max}; C_{max} = Maximum observed serum teclistamab concentration; C_{trough} = Observed serum teclistamab concentration prior to next dose; AUC_{tau} = Area under the concentration-time curve over the weekly dosing interval. Data are presented as mean ± standard deviation, except for T_{max} which is presented as median (minimum, maximum).~~

~~*Distribution*~~

~~Based on the population pharmacokinetic model, mean volume of distribution was 4.13 L (48.8% CV (coefficient of variation)) for the central compartment, and 1.34 L for the peripheral compartment.~~

~~*Excretion*~~

~~Teclistamab exhibited both time-independent and time-dependent clearance. Based on the population pharmacokinetic model, the mean time-independent clearance of teclistamab is 0.449 L/day (53.6% CV), with the median of time-dependent clearance contributing approximately 43% of the total clearance at baseline and decreasing rapidly thereafter to less than 10% after Week 8.~~

~~Based on non-compartmental analysis, the mean half-life (SD) was 3.8 (1.7) days (individual values ranging up to 8.8 days) following the first treatment intravenous dose of teclistamab.~~

~~Population pharmacokinetic analysis (based on MajesTEC-1) showed that soluble BCMA did not impact teclistamab serum concentrations.~~

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העדכון בעלון לצרכן הינו:

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קבוצה תרפויטית: נוגדנים חד שבטיים אחרים ונוגדנים מצומדי תרופה (antibody drug conjugates),
L01FX24~~טרם הוגדרה~~.

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היריון והנקה

לא ידוע אם טקוואילי משפיע על העובר או עובר לחלב אם.

מידע לנשים לגבי היריון

דווחי לרופא או לאחות שלך טרם קבלת טקוואילי אם את בהיריון, חושבת שאת עשויה להיות בהיריון או מתכננת להרות.

אם תהרי במהלך הטיפול בתרופה זו, דווחי לרופא או לאחות שלך מייד. טקוואילי קשור להיפוגמגלבולינמיה (hypogammaglobulinaemia), לכן יש לשקול הערכת רמות אימונוגלובולינים בילודים של אמהות שטופלו בטקוואילי.

מידע לגברים לגבי היריון

אם בת זוגך תהרה במהלך הטיפול שלך בתרופה זו, דווח לרופא שלך מייד.

אמצעי מניעה- מידע עבור נשים המסוגלות להרות

אם את מסוגלת להרות, עליך להשתמש באמצעי מניעה יעילים במהלך הטיפול ובמשך 5 חודשים לאחר הפסקת הטיפול בטקוואילי.

אמצעי מניעה- מידע עבור גברים (הנוטלים טקוואילי)

אם ~~את או~~ בת זוגתך ~~(עבור גברים הנוטלים טקוואילי)~~ מסוגלת להרות, עלייך/~~עליה~~ להשתמש באמצעי מניעה יעילים במהלך הטיפול ובמשך 3 חודשים לאחר הפסקת הטיפול בטקוואילי.

הנקה

לא ידוע האם טקוואילי עוברת לחלב אם. אין להניק במהלך הטיפול בטקוואילי. אם הוחלט על הפסקת הטיפול בטקוואילי, עלייך להימנע מהנקה במשך ~~3~~ 5 חודשים לאחר הפסקת הטיפול.

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