

17/09/2026

רופא/ה נכבד/ה
רוקח/ת נכבד/ה

הנדון:

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

חברת J-C Health Care Ltd מבקשת להודיעכם כי העלונים לרופא ולצרכן של התכשיר שבנדון התעדנו
בספטמבר 2026.

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://israel drugs.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

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	
All patients			
Step-up dosing schedule ^b	Day 1	Step-up dose 1	0.06 mg/kg SC single dose
	Day 3 ^c	Step-up dose 2	0.3 mg/kg SC single dose
	Day 5 ^d	First maintenance dose	1.5 mg/kg SC single dose
Weekly dosing schedule ^b	One week after first maintenance dose and weekly thereafter ^e	Subsequent maintenance doses	1.5 mg/kg SC once weekly
Patients who have a complete response or better for a minimum of 6 months			
<u>Q2W</u> Biweekly (every two weeks) dosing schedule ^b	Consider reducing the dosing frequency to 1.5 mg/kg SC every two weeks		

^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.

^c Step-up dose 2 may be given between two to seven days after Step-up dose 1..

^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).

^e Maintain a minimum of five days between weekly maintenance doses.

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Pre-treatment medicinal products

The following pre-treatment medicinal products must be administered 1 to 3 hours before each dose of the TECVAYLI step-up dosing schedule (see Table 1) to reduce the risk of cytokine release syndrome (see sections 4.4 and 4.8).

- Corticosteroid (oral or intravenous dexamethasone 16 mg)
- Antihistamine (oral or intravenous diphenhydramine 50 mg, or equivalent)
- Antipyretics (oral or intravenous ~~acetaminophen~~ paracetamol 650 to 1 000 mg, or equivalent)

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4.4 Special warnings and precautions for use

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Cytokine release syndrome (CRS)

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Table 4: Recommendations for management of cytokine release syndrome with tocilizumab and corticosteroids

Grade ^e	Presenting symptoms	Tocilizumab ^a	Corticosteroids ^b
Grade 1	Temperature $\geq 38^{\circ}\text{C}$ ^c	May be considered	Not applicable May be considered

Grade 2	Temperature $\geq 38^{\circ}\text{C}^{\text{c}}$ with either: - Hypotension responsive to fluids and not requiring vasopressors, or - Oxygen requirement of low-flow nasal cannula^d or blow-by	Administer tocilizumab ^b 8 mg/kg intravenously over 1 hour (not to exceed 800 mg). Repeat tocilizumab every 8 hours as needed, if not responsive to intravenous fluids or increasing supplemental oxygen. Limit to a maximum of 3 doses in a 24-hour period; maximum total of 4 doses.	If no improvement within 24 hours of starting tocilizumab, administer methylprednisolone 1 mg/kg intravenously twice daily, or dexamethasone 10 mg intravenously every 6 hours. Continue corticosteroid use until the event is Grade 1 or less, then taper over 3 days.
Grade 3	Temperature $\geq 38^{\circ}\text{C}^{\text{c}}$ with either: - Hypotension requiring one vasopressor with or without vasopressin, or - Oxygen requirement of high-flow nasal cannula^d, facemask, non-rebreather mask, or Venturi mask	Administer tocilizumab 8 mg/kg intravenously over 1 hour (not to exceed 800 mg). Repeat tocilizumab every 8 hours as needed, if not responsive to intravenous fluids or increasing supplemental oxygen. Limit to a maximum of 3 doses in a 24-hour period; maximum total of 4 doses.	If no improvement, administer methylprednisolone 1 mg/kg intravenously twice daily, or dexamethasone 10 mg intravenously every 6 hours. Continue corticosteroid use until the event is Grade 1 or less, then taper over 3 days.
Grade 4	Temperature $\geq 38^{\circ}\text{C}^{\text{c}}$ with either: - Hypotension requiring multiple vasopressors (excluding vasopressin), or - Oxygen requirement of positive pressure (e.g., continuous positive airway pressure [CPAP], bilevel positive airway pressure [BiPAP], intubation, and mechanical ventilation)	Administer tocilizumab 8 mg/kg intravenously over 1 hour (not to exceed 800 mg). Repeat tocilizumab every 8 hours as needed if not responsive to intravenous fluids or increasing supplemental oxygen. Limit to a maximum of 3 doses in a 24-hour period; maximum total of 4 doses.	As above, or administer methylprednisolone 1 000 mg intravenously per day for 3 days, per physician discretion. If no improvement or if condition worsens, consider alternate immunosuppressants ^b .

^a Refer to tocilizumab prescribing information for details.

^b Treat unresponsive CRS per institutional guidelines.

^c Attributed to CRS. Fever may not always be present concurrently with hypotension or hypoxia as it may be masked by interventions such as antipyretics or anticytokine therapy (e.g., tocilizumab or corticosteroids).

^d Low-flow nasal cannula is ≤ 6 L/min, and high-flow nasal cannula is > 6 L/min.

^e Based on ASTCT grading for CRS (Lee et al 2019).

Neurologic toxicities, including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS)

Serious, life-threatening or fatal neurologic toxicities, including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) occurred following treatment with TECVAYLI.

Patients should be monitored for signs or symptoms of ICANS neurologic toxicities during treatment and treated promptly.

Patients should be counselled to seek medical attention should signs or symptoms of ICANS neurologic toxicity occur. At the first sign of neurologic toxicity, including ICANS, patients should be immediately evaluated and treated based on severity. Patients who experience Grade 2 or higher ICANS or first

occurrence of Grade 3 ICANS with the previous dose of TECVAYLI should be instructed to remain within proximity of a healthcare facility and monitored for signs and symptoms daily for 48 hours.

For ICANS ~~and other neurologic toxicities~~, treatment with TECVAYLI should be withheld as indicated in Table 3 (see section 4.2).

Due to the potential for ICANS, patients should be advised not to drive or operate heavy machinery during the TECVAYLI step-up dosing schedule and for 48 hours after completing the TECVAYLI step-up dosing schedule and in the event of new onset of any neurological symptoms (see section 4.7).

Management of ~~ICANS~~ ~~neurologic toxicities~~

At the first sign of ~~neurologic toxicity, including~~ ICANS, neurology evaluation should be considered. Other causes of neurologic symptoms should be ruled out. TECVAYLI should be withheld until adverse reaction resolves (see Table 3). Intensive care and supportive therapy should be provided for severe or life-threatening ~~ICANS~~ ~~neurologic toxicities~~. General management for ~~neurologic toxicity (e.g., ICANS~~ with or without concurrent CRS) is summarised in Table 5.

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Hypogammaglobulinaemia

Hypogammaglobulinaemia has been reported in patients receiving TECVAYLI (see section 4.8).

Immunoglobulin levels should be monitored during treatment with TECVAYLI. Intravenous or subcutaneous immunoglobulin therapy ~~should be used to maintain the serum IgG levels >400 mg/dL. was used to treat hypogammaglobulinaemia in 39% of patients. Patients should be treated according to local institutional guidelines, including~~ infection precautions, ~~and antimicrobials, including~~ antibiotic or antiviral prophylaxis, ~~should be used according to local institutional guidelines, and administration of immunoglobulin replacement.~~

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4.8 Undesirable effects

Summary of safety profile

The most frequent adverse reactions of any grade in patients were hypogammaglobulinaemia ~~neutropenia, cytokine release syndrome, upper respiratory tract infection, musculoskeletal pain, diarrhoea, anaemia, cough, fatigue, injection site reaction, thrombocytopenia, pneumonia, COVID-19, lymphopenia, pyrexia, pain, nausea, headache, and hypokalaemia.~~ (75%), cytokine release syndrome (72%), neutropenia (71%), anaemia (55%), musculoskeletal pain (52%), fatigue (41%), thrombocytopenia (40%), injection site reaction (38%), upper respiratory tract infection (37%), lymphopenia (35%), diarrhoea (28%), pneumonia (28%), nausea (27%), pyrexia (27%), headache (24%), cough (24%), constipation (21%) and pain (21%).

Serious adverse reactions were reported in 65% of patients who received TECVAYLI, including pneumonia (22.4%), COVID-19 (14.5%), ~~cytokine release syndrome (11%), upper respiratory tract infection (7%), cytokine release syndrome (8%), sepsis (6.7%), pyrexia (3.5%), febrile neutropenia (3.1%), diarrhoea (2.3%) and~~ musculoskeletal pain (2.3%), ~~acute kidney injury (4.8%), diarrhoea (3.0%), cellulitis (2.4%), hypoxia (2.4%), febrile neutropenia (2.4%), and encephalopathy (2.4%).~~

Tabulated list of adverse reactions

The adverse reaction frequencies are based on all-cause adverse event frequencies, from patients with multiple myeloma exposed to teclistamab, when after thorough assessment, a causal relationship between the medicinal product and the adverse event is at least a reasonable possibility.

The safety data of TECVAYLI was evaluated in MajesTEC-1, which included 165 adult patients with multiple myeloma who received the recommended dosing regimen of TECVAYLI as monotherapy. The median duration of TECVAYLI treatment was 8.5 (Range: 0.2 to 24.4) months.

Table 6 summarises adverse reactions reported in patients in MajesTEC-1, MajesTEC-9 and MajesTEC-3 studies and postmarketing, who received TECVAYLI. The safety data of TECVAYLI was also evaluated in the all treated population (N=302) with no additional adverse reactions identified.

Adverse reactions observed during clinical studies are listed below by frequency category. Adverse reactions are listed in Table 6 by system organ class and by frequency. Frequency categories are defined as follows: very common ($\geq 1/10$); common ($\geq 1/100$ to $< 1/10$); uncommon ($\geq 1/1\,000$ to $< 1/100$); rare ($\geq 1/10\,000$ to $< 1/1\,000$); very rare ($< 1/10\,000$) and not known (frequency cannot be estimated from the available data).

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 6: Adverse reactions in patients with multiple myeloma treated with TECVAYLI in MajesTEC 1 at the recommended dose for monotherapy use

System Organ Class	Adverse Reaction	Frequency (All grades)	N=165 n (%)	
			Any Grade	Grade 3 or 4
Infections and infestations	Pneumonia ¹	Very common	46 (28%)	32 (19%)
	Sepsis ²	Common	13 (7.9%)	11 (6.7%)
	COVID-19 ³	Very common	30 (18%)	20 (12%)
	Upper respiratory tract infection ⁴	Very common	61 (37%)	4 (2.4%)
	Cellulitis	Common	7 (4.2%)	5 (3.0%)
	Urinary tract infection ^{5, 21}	Very common	23 (14%)	10 (6.1%)
	Progressive multifocal leukoencephalopathy ²¹	Uncommon	1 (0.6%)	1 (0.6%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Tumour flare ²²	Not known		
Blood and lymphatic system disorders	Neutropenia	Very common	117 (71%)	106 (64%)
	Febrile neutropenia	Common	6 (3.6%)	5 (3.0%)
	Thrombocytopenia	Very common	66 (40%)	35 (21%)
	Lymphopenia	Very common	57 (35%)	54 (33%)
	Anaemia ⁶	Very common	90 (55%)	61 (37%)
	Leukopenia	Very common	29 (18%)	12 (7.3%)
	Hypofibrinogenaemia	Common	16 (9.7%)	2 (1.2%)
Immune system disorders	Cytokine release syndrome	Very common	119 (72%)	1 (0.6%)
	Hypogammaglobulinaemia ⁷	Very common	123 (75%)	3 (1.8%)

Metabolism and nutrition disorders	Hyperamylasaemia	Common	6 (3.6%)	4 (2.4%)
	Hyperkalaemia	Common	8 (4.8%)	2 (1.2%)
	Hypercalcaemia	Very common	19 (12%)	5 (3.0%)
	Hyponatraemia	Common	13 (7.9%)	8 (4.8%)
	Hypokalaemia	Very common	23 (14%)	8 (4.8%)
	Hypocalcaemia	Common	12 (7.3%)	0
	Hypophosphataemia	Very common	20 (12%)	10 (6.1%)
	Hypoalbuminaemia	Common	4 (2.4%)	1 (0.6%)
	Hypomagnesaemia	Very common	22 (13%)	0
	Decreased appetite	Very common	20 (12%)	1 (0.6%)
	Hypoglycaemia ²¹	Common	4 (2.4%)	0
Nervous system disorders	Immune effector cell-associated neurotoxicity syndrome	Common	5 (3.0%)	0
	Encephalopathy ⁸	Common	16 (9.7%)	0
	Neuropathy peripheral ⁹	Very common	26 (16%)	1 (0.6%)
	Headache	Very common	39 (24%)	1 (0.6%)
Vascular disorders	Haemorrhage ¹⁰	Very common	20 (12%)	5 (3.0%)
	Hypertension ¹¹	Very common	21 (13%)	9 (5.5%)
	Hypotension ²¹	Very common	18 (11%)	4 (2.4%)
Respiratory, thoracic and mediastinal disorders	Hypoxia	Common	16 (9.7%)	6 (3.6%)
	Dyspnoea ¹²	Very common	22 (13%)	3 (1.8%)
	Cough ¹³	Very common	39 (24%)	0
Gastrointestinal disorders	Diarrhoea	Very common	47 (28%)	6 (3.6%)
	Abdominal pain ^{14, 21}	Very common	20 (12%)	2 (1.2%)
	Vomiting	Very common	21 (13%)	1 (0.6%)
	Nausea	Very common	45 (27%)	1 (0.6%)
	Constipation	Very common	34 (21%)	0
Musculoskeletal and connective tissue disorders	Musculoskeletal pain ¹⁵	Very common	85 (52%)	14 (8.5%)
	Muscle spasms ²¹	Very common	17 (10%)	0
General disorders and administration site conditions	Pyrexia	Very common	45 (27%)	1 (0.6%)
	Injection site reaction ¹⁶	Very common	62 (38%)	1 (0.6%)
	Pain ¹⁷	Very common	34 (21%)	3 (1.8%)
	Oedema ¹⁸	Very common	23 (14%)	0

	Fatigue ¹⁹	Very common	67 (41%)	5 (3.0%)
Investigations	Blood creatinine increased	Common	9 (5.5%)	0
	Transaminase elevation ²⁰	Common	16 (9.7%)	4 (2.4%)
	Lipase increased	Common	10 (6.1%)	2 (1.2%)
	Blood alkaline phosphatase increased	Very common	18 (11%)	3 (1.8%)
	Gamma glutamyltransferase increased	Common	16 (9.7%)	5 (3.0%)
	Activated partial thromboplastin time prolonged	Common	13 (7.9%)	2 (1.2%)
	International normalised ratio increased	Common	10 (6.1%)	2 (1.2%)

Adverse events are coded using MedDRA Version 24.0.

Note: The output includes the diagnosis of CRS and ICANS; the symptoms of CRS or ICANS are excluded.

- ¹—Pneumonia includes Enterobacter pneumonia, lower respiratory tract infection, lower respiratory tract infection viral, Metapneumovirus pneumonia, Pneumocystis jirovecii pneumonia, pneumonia, Pneumonia adenoviral, Pneumonia bacterial, Pneumonia klebsiella, Pneumonia moraxella, Pneumonia pneumococcal, Pneumonia pseudomonal, Pneumonia respiratory syncytial viral, Pneumonia staphylococcal and Pneumonia viral.
- ²—Sepsis includes bacteraemia, Meningococcal sepsis, neutropenic sepsis, Pseudomonal bacteraemia, Pseudomonal sepsis, sepsis and Staphylococcal bacteraemia.
- ³—COVID-19 includes asymptomatic COVID-19 and COVID-19.
- ⁴—Upper respiratory tract infection includes bronchitis, nasopharyngitis, pharyngitis, respiratory tract infection, respiratory tract infection bacterial, rhinitis, rhinovirus infection, sinusitis, tracheitis, upper respiratory tract infection and viral upper respiratory tract infection.
- ⁵—Urinary tract infection includes Cystitis, Cystitis escherichia, Cystitis klebsiella, Escherichia urinary tract infection, Urinary tract infection and Urinary tract infection bacterial.
- ⁶—Anaemia includes anaemia, iron deficiency and iron deficiency anaemia.
- ⁷—Hypogammaglobulinaemia includes patients with adverse events of hypogammaglobulinaemia, hypoglobulinaemia, immunoglobulins decreased, and/or patients with laboratory IgG levels below 500 mg/dL following treatment with teclistamab.
- ⁸—Encephalopathy includes confusional state, depressed level of consciousness, lethargy, memory impairment and somnolence.
- ⁹—Neuropathy peripheral includes dysaesthesia, hypoaesthesia, hypoaesthesia oral, neuralgia, paraesthesia, paraesthesia oral, peripheral sensory neuropathy and sciatica.
- ¹⁰—Haemorrhage includes conjunctival haemorrhage, epistaxis, haematoma, haematuria, haemoperitoneum, haemorrhoidal haemorrhage, lower gastrointestinal haemorrhage, melaena, mouth haemorrhage and subdural haematoma.
- ¹¹—Hypertension includes essential hypertension and hypertension.
- ¹²—Dyspnoea includes acute respiratory failure, dyspnoea and dyspnoea exertional.
- ¹³—Cough includes allergic cough, cough, productive cough and upper airway cough syndrome.
- ¹⁴—Abdominal pain includes Abdominal discomfort, Abdominal pain and Abdominal pain upper.
- ¹⁵—Musculoskeletal pain includes arthralgia, back pain, bone pain, musculoskeletal chest pain, musculoskeletal pain, myalgia, neck pain and pain in extremity.
- ¹⁶—Injection site reaction includes injection site bruising, injection site cellulitis, injection site discomfort, injection site erythema, injection site haematoma, injection site induration, injection site inflammation, injection site oedema, injection site pruritus, injection site rash, injection site reaction and injection site swelling.
- ¹⁷—Pain includes ear pain, flank pain, groin pain, non-cardiac chest pain, oropharyngeal pain, pain, pain in jaw, toothache and tumour pain.
- ¹⁸—Oedema includes face oedema, fluid overload, oedema peripheral and peripheral swelling.
- ¹⁹—Fatigue includes asthenia, fatigue and malaise.
- ²⁰—Transaminase elevation includes alanine aminotransferase increased and aspartate aminotransferase increased.
- ²¹—New adverse reaction terms identified using long term follow-up from MajesTEC-1.
- ²²—Based on post-marketing experience.

Table 6: Adverse reactions in multiple myeloma patients treated with TECVAYLI in clinical trials and postmarketing.

System Organ Class	Adverse Reaction	Frequency	N=739
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		(all grades)	Any Grade (%)	Grade 3 or 4 (%)
Infections and infestations	Upper respiratory tract infection ¹	Very common	60	9
	Pneumonia ²	Very common	34	24
	COVID-19 ³	Very common	31	13
	Urinary tract infection ⁴	Very common	15	4.1
	Sepsis ⁵	Common	9	6
	Cellulitis	Common	2	1.1
	Progressive multifocal leukoencephalopathy	Uncommon	0.1	0.1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Tumour flare ⁵	Not known		
Blood and lymphatic system disorders	Neutropenia	Very common	71	65
	Anaemia ⁶	Very common	44	23
	Thrombocytopenia	Very common	34	17
	Lymphopenia	Very common	26	24
	Leukopenia	Very common	19	10
	Febrile neutropenia	Common	4.9	4.6
Immune system disorders	Hypogammaglobulinaemia ⁷	Very common	76	3.8
	Cytokine release syndrome	Very common	65	0.4
Metabolism and nutrition disorders	Hypokalaemia	Very common	20	7
	Decreased appetite	Very common	14	0.7
	Hypophosphataemia	Common	9	2.4
	Hyponatraemia	Common	7	2
	Hyperkalaemia	Common	3.5	0.8
	Hyperamylasaemia	Common	3.2	0.9
Nervous system disorders	Headache	Very common	21	0.9
	Neuropathy peripheral ⁸	Very common	15	0.4
	Encephalopathy ⁹	Common	6	0.5
	Immune effector cell-associated neurotoxicity syndrome	Common	2.7	0.3
Vascular disorders	Haemorrhage ¹⁰	Very common	10	1.8
	Hypertension ¹¹	Very common	10	4.9
	Hypotension	Common	7	1.1
Respiratory, thoracic and mediastinal disorders	Cough ¹²	Very common	40	0.5

	Dyspnoea ¹³	Very common	11	2.4
	Hypoxia	Common	3.9	1.8
Gastrointestinal disorders	Diarrhoea ¹⁴	Very common	45	4.2
	Nausea	Very common	22	0.4
	Constipation	Very common	16	0.1
	Vomiting	Very common	16	0.5
	Abdominal pain ¹⁵	Very common	12	0.5
Musculoskeletal and connective tissue disorders	Musculoskeletal pain ¹⁶	Very common	45	3.4
	Muscle spasms	Common	6	0
General disorders and administration site conditions	Injection site reaction ¹⁷	Very common	37	0.1
	Fatigue ¹⁸	Very common	37	3.2
	Pyrexia	Very common	25	0.7
	Pain ¹⁹	Very common	24	0.9
	Oedema ²⁰	Very common	12	0.3
Investigations	Transaminase elevation ²¹	Very common	16	2.8
	Weight decreased	Very common	13	2
	Gamma-glutamyltransferase increased	Common	10	2.3
	Lipase increased	Common	8	1.1

Note: Adverse events are graded according to the NCI-CTCAE Version 5.0, with the exception of ICANS and CRS, which were graded by ASTCT consensus grading system (Lee et al 2019).

- ¹ Upper respiratory tract infection includes Acute sinusitis, Adenoviral upper respiratory infection, Bacterial rhinitis, Bronchiolitis, Bronchitis, Bronchitis bacterial, Bronchitis chronic, Bronchitis haemophilus, Bronchitis viral, Chronic sinusitis, Herpes simplex bronchitis, Nasopharyngitis, Pharyngitis, Pharyngitis streptococcal, Respiratory syncytial virus infection, Respiratory tract infection, Respiratory tract infection bacterial, Respiratory tract infection fungal, Respiratory tract infection viral, Rhinitis, Rhinovirus infection, Sinobronchitis, Sinusitis, Sinusitis bacterial, Tracheitis, Tracheobronchitis, Upper respiratory fungal infection, Upper respiratory tract infection, Upper respiratory tract infection bacterial, Viral rhinitis, Viral sinusitis and Viral upper respiratory tract infection.
- ² Pneumonia includes Atypical pneumonia, Candida pneumonia, Coronavirus pneumonia, Enterobacter pneumonia, Lower respiratory tract infection, Lower respiratory tract infection bacterial, Lower respiratory tract infection viral, Metapneumovirus pneumonia, Pneumocystis jirovecii pneumonia, Pneumonia, Pneumonia adenoviral, Pneumonia bacterial, Pneumonia chlamydial, Pneumonia cryptococcal, Pneumonia cytomegaloviral, Pneumonia escherichia, Pneumonia fungal, Pneumonia haemophilus, Pneumonia influenzal, Pneumonia klebsiella, Pneumonia legionella, Pneumonia moraxella, Pneumonia mycoplasmal, Pneumonia parainfluenzae viral, Pneumonia pneumococcal, Pneumonia pseudomonal, Pneumonia respiratory syncytial viral, Pneumonia staphylococcal, Pneumonia streptococcal, Pneumonia viral and Stenotrophomonas maltophilia pneumonia.
- ³ COVID-19 includes COVID-19 and COVID-19 pneumonia.
- ⁴ Urinary tract infection includes Cystitis, Cystitis escherichia, Cystitis haemorrhagic, Cystitis klebsiella, Escherichia urinary tract infection, Genitourinary tract infection, Klebsiella urinary tract infection, Pyelonephritis, Pyelonephritis acute, Pyuria, Urinary tract candidiasis, Urinary tract infection, Urinary tract infection bacterial, Urinary tract infection enterococcal, Urinary tract infection fungal and Urinary tract infection staphylococcal.
- ⁵ Sepsis includes Abdominal sepsis, Acinetobacter bacteraemia, Bacillus bacteraemia, Bacteraemia, Bacterial sepsis, Campylobacter bacteraemia, Campylobacter sepsis, Citrobacter bacteraemia, Corynebacterium bacteraemia, Device related bacteraemia, Enterococcal bacteraemia, Enterococcal sepsis, Escherichia bacteraemia, Escherichia sepsis, Haemophilus sepsis, Klebsiella sepsis, Meningococcal sepsis, Neutropenic sepsis, Pseudomonal bacteraemia, Pseudomonal sepsis, Pulmonary sepsis, Sepsis, Septic shock, Staphylococcal bacteraemia, Staphylococcal sepsis, Streptococcal sepsis and Urosepsis.
- ⁶ Anaemia includes Anaemia, Iron deficiency anaemia, Leukoerythroblastic anaemia and Microcytic anaemia
- ⁷ Hypogammaglobulinaemia includes patients with adverse events of hypogammaglobulinaemia, hyperglobulinaemia, immunoglobulins decreased; and/or patients with laboratory IgG levels below 400 mg/dL following treatment with TECVAYLI.
- ⁸ Neuropathy peripheral includes Dysaesthesia, Hypoaesthesia, Hypoaesthesia oral, Neuralgia, Neuropathy peripheral, Paraesthesia, Paraesthesia oral, Peripheral motor neuropathy, Peripheral sensory neuropathy and Sciatica.
- ⁹ Encephalopathy includes Amnesia, Brain fog, Cognitive disorder, Confusional state, Depressed level of consciousness, Lethargy, Memory impairment and Somnolence.
- ¹⁰ Haemorrhage includes Anal haemorrhage, Conjunctival haemorrhage, Epistaxis, Eye haemorrhage, Eyelid bleeding, Eyelid haematoma, Gastrointestinal haemorrhage, Gingival bleeding, Haematochezia, Haematoma, Haematuria, Haemoperitoneum, Haemoptysis, Haemorrhoidal haemorrhage, Haemorrhoids, Hepatic haemorrhage, Lower gastrointestinal haemorrhage, Melaena, Mouth haemorrhage, Post procedural haemorrhage, Postmenopausal haemorrhage, Pulmonary alveolar haemorrhage, Rectal haemorrhage, Subdural haematoma, Upper gastrointestinal haemorrhage and Vitreous haemorrhage.
- ¹¹ Hypertension includes Blood pressure increased, Essential hypertension, Hypertension, Hypertensive crisis, Mean arterial pressure increased and Systolic hypertension.
- ¹² Cough includes Allergic cough, Cough, Productive cough and Upper-airway cough syndrome.
- ¹³ Dyspnoea includes Acute respiratory failure, Dyspnoea, Dyspnoea exertional and Respiratory failure.
- ¹⁴ Diarrhoea includes Bacterial diarrhoea, Diarrhoea and Viral diarrhoea.
- ¹⁵ Abdominal pain includes Abdominal discomfort, Abdominal pain, Abdominal pain lower, Abdominal pain upper, Epigastric discomfort and Gastrointestinal pain.
- ¹⁶ Musculoskeletal pain includes Arthralgia, Back pain, Bone pain, Musculoskeletal chest pain, Musculoskeletal pain, Myalgia, Neck pain, Pain in extremity and Sacral pain.
- ¹⁷ Injection site reaction includes Administration site pruritus, Administration site reaction, Application site erythema, Injection site bruising, Injection site cellulitis, Injection site discolouration, Injection site discomfort, Injection site eczema, Injection site erythema, Injection site haematoma, Injection site hyperaesthesia, Injection site induration, Injection site inflammation, Injection site irritation, Injection site oedema, Injection site pain, Injection site paraesthesia, Injection site pruritus, Injection site rash, Injection site reaction, Injection site swelling, Injection site vesicles and Injection site warmth.
- ¹⁸ Fatigue includes Asthenia, Fatigue and Malaise.
- ¹⁹ Pain includes Axillary pain, Breast pain, Cancer pain, Chest pain, Ear pain, Eye pain, Facial pain, Flank pain, Gingival pain, Groin pain, Laryngeal pain, Non-cardiac chest pain, Oesophageal pain, Oral pain, Oropharyngeal pain, Pain, Pain in jaw, Pain of skin, Pelvic pain, Perineal pain, Periorbital pain, Sinus pain, Spinal pain, Testicular pain, Toothache and Tumour pain.
- ²⁰ Oedema includes Eyelid oedema, Face oedema, Localised oedema, oedema, oedema peripheral, Periorbital oedema, Peripheral swelling, Skin oedema, Swelling, Swelling face and Testicular swelling.
- ²¹ Transaminase elevation includes Alanine aminotransferase increased, Aspartate aminotransferase, Aspartate aminotransferase increased, Hypertransaminasaemia and Transaminase increased.
- * Based on post-marketing experience.

Description of selected adverse reactions

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Neurologic toxicities, including ICANS

In MajesTEC-1 (N=165), ~~ICANS neurologic toxicity events~~ were reported in 15% of patients receiving TECVAYLI. ~~ICANS Neurologic toxicity events~~ were Grade 1 (8.5%), Grade 2 (5.5%), or Grade 4 (<1%). The most frequently reported ~~ICANS neurologic toxicity event~~ was headache (8%).

ICANS, including Grade 3 and higher, were reported in clinical trials and with post-marketing experience. The most frequent clinical manifestation of ICANS were confusional state, decreased level of consciousness, disorientation, dysgraphia, aphasia, apraxia, and somnolence. The onset of ~~ICANS neurologic toxicity~~ can be concurrent with CRS, following resolution of CRS, or in the absence of CRS. The observed time to onset of ICANS ranged from 0 to 21 days after the most recent dose.

In monotherapy clinical trials (MajesTEC-1 and MajesTEC-9), 186 patients were less than 65 years of age, 165 patients were 65 to less than 75 years of age, and 105 patients were 75 years of age or older. Serious adverse events occurred in 65% of patients less than 65 years of age, compared with 63% in those aged 65 to less than 75 years of age and 52% in those 75 years of age or older.

Immunogenicity

~~Patients treated with subcutaneous teclistamab monotherapy (N=238) in MajesTEC-1 were evaluated for antibodies to teclistamab using an electrochemiluminescence-based immunoassay. One subject (0.4%) developed neutralising antibodies to teclistamab of low titre.~~

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form: <https://reportsideffect.health.gov.il/drugs/home>
<https://sideeffects.health.gov.il>

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5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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Immunogenicity

Anti-drug antibodies (ADA) were very rarely detected. No evidence of ADA impact on pharmacokinetics, efficacy or safety was observed.

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5.2 Pharmacokinetic properties

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Renal impairment

No formal studies of TECVAYLI in patients with renal impairment have been conducted. Results of population pharmacokinetic analyses indicate that mild renal impairment ($60 \text{ mL/min/1.73 m}^2 \leq \text{estimated glomerular filtration rate (eGFR)} < 90 \text{ mL/min/1.73 m}^2$) or moderate renal impairment ($30 \text{ mL/min/1.73 m}^2 \leq \text{eGFR} < 60 \text{ mL/min/1.73 m}^2$) did not significantly influence the pharmacokinetics of teclistamab. Limited data are available from patients with severe renal impairment.

Hepatic impairment

No formal studies of TECVAYLI in patients with hepatic impairment have been conducted. Results of population pharmacokinetic analyses indicate that mild hepatic impairment (total bilirubin >1 to 1.5 times upper limit of normal (ULN) and any aspartate aminotransferase (AST), or total bilirubin $\leq$ ULN and $\text{AST} > \text{ULN}$) did not significantly influence the pharmacokinetics of teclistamab. Limited data are available in patients with moderate hepatic impairment and ~~No~~ data are available in patients with ~~moderate and~~ severe hepatic impairment.

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6.4 Special precautions for storage

Store in a refrigerator (2 °C - 8 °C).

Do not freeze.

Store in the original carton in order to protect from light. Do not shake.

העדכון בעלון לצרכן הינו:

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תופעות לוואי

תופעות לוואי שכיחות מאוד – תופעות שמופיעות ביותר ממשתמש אחד מעשרה:

- כאב
- זיהום בריאות (דלקת ריאות)
- זיהום קוביד-19 (COVID-19) הנגרם על ידי נגיף קורונה (SARS-CoV-2)
- זיהום באף, בסינוסים או בגרון (זיהום בדרכי הנשימה העליונות)
- דלקת בדרכי השתן
- רמות נמוכות של תאי דם אדומים (אנמיה)
- רמות נמוכות של טסיות בדם (תאים העוזרים בקרישת דם; תרומבוציטופניה)
- מספר נמוך של תאי דם לבנים (לויקופניה)
- רמות נמוכות של תאי דם לבנים מסוג מסוים (לימפופניה)
- רמה נמוכה של פוספט, מגנזיום או אשלגן בדם (היפופוספטמיה, היפומגנזמיה או היפוקלמיה)
- רמה מוגברת של אנזימי כבד מסוג "טרנסאמינאזות" בדם
- אובדן משקל
- עלייה ברמת הסיידן בדם (היפרקלצמיה)
- עלייה ברמת אלקליין פוספטאז בדם
- תיאבון ירוד
- בחילות, שלשול, עצירות, הקאות, כאב בטן
- כאב ראש
- פגיעה עצבית העלולה לגרום לעקצוץ, לחוסר תחושה, לכאב או לאובדן תחושת הכאב
- התכווצויות שרירים
- לחץ דם גבוה (יתר לחץ דם)
- דימום העלול להיות חמור
- לחץ דם נמוך
- שיעול
- קוצר נשימה (דיספנאה)
- חום
- תחושת עייפות חמורה
- כאבים או כאבי שרירים.
- נפיחות בכפות הידיים, בקרסוליים או בכפות הרגליים (בצקת)
- תגובות עוריות במקום ההזרקה או בקרבתו, לרבות אודם בעור, גרד, נפיחות, כאב, חבורות, פריחה, דימום

תופעות לוואי שכיחות – תופעות שמופיעות בעד משתמש אחד מעשרה:

- זיהום חמור המפושט בכל הגוף (אלח דם [ספסיס])
- זיהום עורי הגורם לאודם (צלוליטיס)
- מספר נמוך של תאי דם לבנים מסוג מסוים המלווה בחום (נויטרופניה המלווה בחום - חום נויטרופני)
- רמות נמוכות של פיברינוגן, סוג של חלבון בדם, אשר מקשות על יצירת קרישים
- שינוי בתפקוד המוח (אנצפלופתיה)

• לחץ דם נמוך

• רמה נמוכה של פוספט-סייד או נתרן בדם (היפוקלצמיה-היפופוספטמיה או היפונתרמיה)

• רמה גבוהה של אשלגן בדם (היפרקלמיה)

• רמה נמוכה של אלבומין בדם (היפואלבומינמיה)

• רמה נמוכה של סוכר בדם (היפוגליקמיה)

• רמה נמוכה של חמצן בדם (היפוקסיה)

• התכווצויות שרירים

• רמה מוגברת של גמא-גלוטמיל-טרנספראז בדם

• רמה מוגברת של אנזימי כבד (אנזימי-טרנסאמינאז) בדם

• רמה מוגברת של קריאטינין בדם

• רמה מוגברת של עמילאז בדם (היפרעמילאזמיה)

• רמה מוגברת של ליפאז בדם (היפרליפאזמיה)

• בדיקות הדם עלולות להדגים כי נדרש פרק-זמן ממושך יותר לקרישת דם (INR מוגבר והארכת PTT)

אם הופיעה תופעת לוואי, אם אחת מתופעות הלוואי מחמירה או כאשר אתה סובל מתופעת לוואי שלא צוינה בעלון, עליך להתייעץ עם הרופא.

ניתן לדווח על תופעות לוואי למשרד הבריאות באמצעות לחיצה על הקישור "דיווח על תופעות לוואי עקב טיפול תרופתי" שנמצא בדף הבית של אתר משרד הבריאות (www.health.gov.il) המפנה לטופס המקוון לדיווח על תופעות לוואי, או על ידי בניהול קישור:

<https://reportsideeffect.health.gov.il/drugs/home> <https://sideeffects.health.gov.il>

1. איך לאחסן את התרופה?

מנע הרעלה! תרופה זו וכל תרופה אחרת יש לשמור במקום סגור מחוץ להישג ידם וטווח ראייתם של ילדים ו/או תינוקות ועל ידי כך תמנע הרעלה. אל תגרום להקאה ללא הוראה מפורשת מהרופא. אין להשתמש בתרופה אחרי תאריך התפוגה (exp. date) המופיע על גבי האריזה/תווית. תאריך התפוגה מתייחס ליום האחרון של אותו חודש.

תנאי אחסון:

טקוואילי יאוחסן בבית החולים או במרפאה על ידי הרופא.

יש לאחסן במקרר (2°C-8°C). אין להקפיא. יש לאחסן באריזה המקורית כדי להגן מאור. אין לנער

אין להשליך את התרופה לשפכים או לפסולת הביתית. הצוות הרפואי ישליך את התרופות שאינן בשימוש עוד. אמצעים אלה יסייעו בהגנה על הסביבה.

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