

# Dosing and Administration Guide



## INDICATION AND USAGE

TECVAYLI™ (teclistamab-cqyv) is a bispecific B-cell maturation antigen (BCMA)-directed CD3 T-cell engager indicated for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody.

This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

## IMPORTANT SAFETY INFORMATION

**WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGIC TOXICITY including IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME**

Cytokine release syndrome (CRS), including life-threatening or fatal reactions, can occur in patients receiving TECVAYLI™. Initiate treatment with TECVAYLI™ step-up dosing schedule to reduce risk of CRS. Withhold TECVAYLI™ until CRS resolves or permanently discontinue based on severity.

Neurologic toxicity, including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) and serious and life-threatening reactions, can occur in patients receiving TECVAYLI™. Monitor patients for signs or symptoms of neurologic toxicity, including ICANS, during treatment and treat promptly. Withhold TECVAYLI™ until neurologic toxicity resolves or permanently discontinue based on severity.

TECVAYLI™ is available only through a restricted program called the TECVAYLI™ Risk Evaluation and Mitigation Strategy (REMS).

## WARNINGS AND PRECAUTIONS

**Cytokine Release Syndrome** - TECVAYLI™ can cause cytokine release syndrome (CRS), including life-threatening or fatal reactions. In the clinical trial, CRS occurred in 72% of patients who received TECVAYLI™ at the recommended dose, with Grade 1 CRS occurring in 50% of patients, Grade 2 in 21%, and Grade 3 in 0.6%. Recurrent CRS occurred in 33% of patients. Most patients experienced CRS following step-up dose 1 (42%), step-up dose 2 (35%), or the initial treatment dose (24%). Less than 3% of patients developed first occurrence of CRS following subsequent doses of TECVAYLI™. The median time to onset of CRS was 2 (range: 1 to 6) days after the most recent dose with a median duration of 2 (range: 1 to 9) days. Clinical signs and symptoms of CRS included, but were not limited to, fever, hypoxia, chills, hypotension, sinus tachycardia, headache, and elevated liver enzymes (aspartate aminotransferase and alanine aminotransferase elevation).

Initiate therapy according to TECVAYLI™ step-up dosing schedule to reduce risk of CRS. Administer pretreatment medications to reduce risk of CRS and monitor patients following administration of TECVAYLI™ accordingly. At the first sign of CRS, immediately evaluate patient for hospitalization. Administer supportive care based on severity and consider further management per current practice guidelines. Withhold or permanently discontinue TECVAYLI™ based on severity.

TECVAYLI™ is available only through a restricted program under a REMS.

Please see full Important Safety Information on pages 20-23.

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## WARNINGS AND PRECAUTIONS (cont'd)

**Neurologic Toxicity including ICANS** - TECVAYLI™ can cause serious or life-threatening neurologic toxicity, including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS).

In the clinical trial, neurologic toxicity occurred in 57% of patients who received TECVAYLI™ at the recommended dose, with Grade 3 or 4 neurologic toxicity occurring in 2.4% of patients. The most frequent neurologic toxicities were headache (25%), motor dysfunction (16%), sensory neuropathy (15%), and encephalopathy (13%). With longer follow-up, Grade 4 seizure and fatal Guillain-Barré syndrome (one patient each) occurred in patients who received TECVAYLI™.

In the clinical trial, ICANS was reported in 6% of patients who received TECVAYLI™ at the recommended dose. Recurrent ICANS occurred in 1.8% of patients. Most patients experienced ICANS following step-up dose 1 (1.2%), step-up dose 2 (0.6%), or the initial treatment dose (1.8%). Less than 3% of patients developed first occurrence of ICANS following subsequent doses of TECVAYLI™. The median time to onset of ICANS was 4 (range: 2 to 8) days after the most recent dose with a median duration of 3 (range: 1 to 20) days. The most frequent clinical manifestations of ICANS reported were confusional state and dysgraphia. The onset of ICANS can be concurrent with CRS, following resolution of CRS, or in the absence of CRS.

Monitor patients for signs and symptoms of neurologic toxicity during treatment. At the first sign of neurologic toxicity, including ICANS, immediately evaluate patient and provide supportive therapy based on severity. Withhold or permanently discontinue TECVAYLI™ based on severity per recommendations and consider further management per current practice guidelines.

Due to the potential for neurologic toxicity, patients are at risk of depressed level of consciousness. Advise patients to refrain from driving or operating heavy or potentially dangerous machinery during and for 48 hours after completion of TECVAYLI™ step-up dosing schedule and in the event of new onset of any neurologic toxicity symptoms until neurologic toxicity resolves.

TECVAYLI™ is available only through a restricted program under a REMS.

Please see full Important Safety Information on pages 20-23.

## Mechanism of Action

Teclistamab-cqyv is a bispecific T-cell engaging antibody that binds to the CD3 receptor expressed on the surface of T-cells and B-cell maturation antigen (BCMA) expressed on the surface of multiple myeloma cells and some healthy B-lineage cells.

*In vitro*, teclistamab-cqyv activated T-cells, caused the release of various proinflammatory cytokines, and resulted in the lysis of multiple myeloma cells.

## Clinical Studies

The efficacy of TECVAYLI™ was evaluated in patients with relapsed or refractory multiple myeloma in a single-arm, open-label, multi-center study (MajesTEC-1, NCT03145181 [Phase 1] and NCT04557098 [Phase 2]). The study included patients who had previously received at least three prior therapies, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody. The study excluded patients who had stroke, seizure, allogeneic stem cell transplantation within the past 6 months, Eastern Cooperative Oncology Group (ECOG) performance score of 2 or higher, known active CNS involvement or clinical signs of meningeal involvement of multiple myeloma, or active or documented history of autoimmune disease, with the exception of vitiligo, Type 1 diabetes, and prior autoimmune thyroiditis.

Efficacy was established based on overall response rate (ORR) as determined by the Independent Review Committee (IRC) assessment using International Myeloma Working Group (IMWG) 2016 criteria (see Table 13 in the full Prescribing Information).

The median time to first response was 1.2 months (range: 0.2 to 5.5 months). With a median follow-up of 7.4 months among responders, the estimated duration of response (DOR) rate was 90.6% (95% CI: 80.3%, 95.7%) at 6 months and 66.5% (95% CI: 38.8%, 83.9%) at 9 months.

## Efficacy Results for MajesTEC-1

	N=110
<b>Overall response rate (ORR: sCR+CR+VGPR+PR) n(%)</b>	68 (61.8)
95% CI (%)	(52.1, 70.9)
Complete response (CR) or better <sup>a</sup>	31 (28.2)
Very good partial response (VGPR)	32 (29.1)
Partial response (PR)	5 (4.5)
<b>Duration of Response (DOR) (months)</b>	
DOR (Months): Median (95% CI)	NE (9.0, NE)

NE=not estimable

<sup>a</sup> Complete response or better = Stringent complete response (sCR) + complete response (CR).

 **TECVAYLI™**  
(teclistamab-cqyv) Injection for  
subcutaneous use  
10 mg/mL and 90 mg/mL

## Recommended Pretreatment Medications

Administer the following pretreatment medications 1 to 3 hours before each dose of the TECVAYLI™ step-up dosing schedule, which includes step-up dose 1, step-up dose 2, and the first treatment dose (see Table 1 in the full Prescribing Information), to reduce the risk of CRS [see *Warnings and Precautions (5.1) and Adverse Reactions (6.1) in the full Prescribing Information*].

- Corticosteroid (oral or intravenous dexamethasone 16 mg)
- Histamine-1 (H1) receptor antagonist (oral or intravenous diphenhydramine 50 mg or equivalent)
- Antipyretics (oral or intravenous acetaminophen 650 mg to 1,000 mg or equivalent)

Administration of pretreatment medications may be required prior to administration of subsequent doses of TECVAYLI™ in the following patients:

- Patients who repeat doses within the TECVAYLI™ step-up dosing schedule following a dose delay [see *Dosage and Administration (2.3) in the full Prescribing Information*].
- Patients who experienced CRS following the prior dose of TECVAYLI™ [see *Dosage and Administration (2.4) in the full Prescribing Information*].

## Prophylaxis for Herpes Zoster Reactivation

Prior to starting treatment with TECVAYLI™, consider initiation of antiviral prophylaxis to prevent herpes zoster reactivation per guidelines.

## WARNINGS AND PRECAUTIONS (cont'd)

**TECVAYLI™ REMS** - TECVAYLI™ is available only through a restricted program under a REMS called the TECVAYLI™ REMS because of the risks of CRS and neurologic toxicity, including ICANS.

**Hepatotoxicity** - TECVAYLI™ can cause hepatotoxicity, including fatalities. In patients who received TECVAYLI™ at the recommended dose in the clinical trial, there was one fatal case of hepatic failure. Elevated aspartate aminotransferase (AST) occurred in 34% of patients, with Grade 3 or 4 elevations in 1.2%. Elevated alanine aminotransferase (ALT) occurred in 28% of patients, with Grade 3 or 4 elevations in 1.8%. Elevated total bilirubin occurred in 6% of patients with Grade 3 or 4 elevations in 0.6%. Liver enzyme elevation can occur with or without concurrent CRS.

Monitor liver enzymes and bilirubin at baseline and during treatment as clinically indicated. Withhold TECVAYLI™ or consider permanent discontinuation of TECVAYLI™ based on severity.

Please see full Important Safety Information on pages 20-23.

## Recommended Dosage

For subcutaneous injection only.

The recommended dosing schedule for TECVAYLI™ is provided in Table 1 of the full Prescribing Information. The recommended dosage of TECVAYLI™ is step-up doses of 0.06 mg/kg and 0.3 mg/kg followed by 1.5 mg/kg once weekly until disease progression or unacceptable toxicity.

Administer pretreatment medications prior to each dose of the TECVAYLI™ step-up dosing schedule, which includes step-up dose 1, step-up dose 2, and the first treatment dose as described in Table 1 [see *Dosage and Administration (2.2) in the full Prescribing Information*].

Administer TECVAYLI™ subcutaneously according to the step-up dosing schedule in Table 1 of the full Prescribing Information to reduce the incidence and severity of cytokine release syndrome (CRS). Due to the risk of CRS and neurologic toxicity, including ICANS, patients should be hospitalized for 48 hours after administration of all doses within the TECVAYLI™ step-up dosing schedule [see *Dosage and Administration (2.4) and Warnings and Precautions (5.1, 5.2) in the full Prescribing Information*].

## WARNINGS AND PRECAUTIONS (cont'd)

**Infections** - TECVAYLI™ can cause severe, life-threatening, or fatal infections. In patients who received TECVAYLI™ at the recommended dose in the clinical trial, serious infections, including opportunistic infections, occurred in 30% of patients, with Grade 3 or 4 infections in 35%, and fatal infections in 4.2%. Monitor patients for signs and symptoms of infection prior to and during treatment with TECVAYLI™ and treat appropriately. Administer prophylactic antimicrobials according to guidelines. Withhold TECVAYLI™ or consider permanent discontinuation of TECVAYLI™ based on severity.

Monitor immunoglobulin levels during treatment with TECVAYLI™ and treat according to guidelines, including infection precautions and antibiotic or antiviral prophylaxis.

## Recommended Dosage (cont'd)

### TECVAYLI™ Dosing Schedule

Dosing Schedule	Day	Dose	
Step-up dosing schedule <sup>a</sup>	Day 1	Step-up dose 1	0.06 mg/kg
	Day 4 <sup>b</sup>	Step-up dose 2	0.3 mg/kg
	Day 7 <sup>c</sup>	First treatment dose	1.5 mg/kg
Weekly dosing schedule <sup>a</sup>	One week after first treatment dose and weekly thereafter	Subsequent treatment doses	1.5 mg/kg once weekly

<sup>a</sup> See Table 2 in the full Prescribing Information for recommendations on restarting TECVAYLI™ after dose delays [see *Dosage and Administration (2.3) in the full Prescribing Information*].

<sup>b</sup> Step-up dose 2 may be given between 2 to 4 days after step-up dose 1 and may be given up to 7 days after step-up dose 1 to allow for resolution of adverse reactions.

<sup>c</sup> First treatment dose may be given between 2 to 4 days after step-up dose 2 and may be given up to 7 days after step-up dose 2 to allow for resolution of adverse reactions.

### WARNINGS AND PRECAUTIONS (cont'd)

**Neutropenia** - TECVAYLI™ can cause neutropenia and febrile neutropenia. In patients who received TECVAYLI™ at the recommended dose in the clinical trial, decreased neutrophils occurred in 84% of patients, with Grade 3 or 4 decreased neutrophils in 56%. Febrile neutropenia occurred in 3% of patients.

Monitor complete blood cell counts at baseline and periodically during treatment and provide supportive care per local institutional guidelines. Monitor patients with neutropenia for signs of infection. Withhold TECVAYLI™ based on severity.

Please see full Important Safety Information on pages 20-23.

## Restarting TECVAYLI™ after Dosage Delay

If a dose of TECVAYLI™ is delayed, restart therapy based on the recommendations in Table 2 in the full Prescribing Information and resume the treatment schedule accordingly [see *Dosage and Administration (2.1) in the full Prescribing Information*]. Administer pretreatment medications as indicated in Table 2 in the full Prescribing Information. Due to the risk of CRS and neurologic toxicity, including ICANS, patients should be hospitalized for 48 hours after administration of all doses within the TECVAYLI™ step-up dosing schedule [see *Dosage and Administration (2.4) and Warnings and Precautions (5.1, 5.2) in the full Prescribing Information*].

### Recommendations for Restarting Therapy with TECVAYLI™ After Dose Delay

Last dose administered	Duration of delay from the last dose administered	Action
Step-up dose 1	More than 7 days	Restart TECVAYLI™ step-up dosing schedule at step-up dose 1 (0.06 mg/kg). <sup>a</sup>
Step-up dose 2	8 days to 28 days	Repeat step-up dose 2 (0.3 mg/kg) <sup>a</sup> and continue TECVAYLI™ step-up dosing schedule.
	More than 28 days <sup>b</sup>	Restart TECVAYLI™ step-up dosing schedule at step-up dose 1 (0.06 mg/kg). <sup>a</sup>
Any treatment dose	8 days to 28 days	Continue TECVAYLI™ weekly dosing schedule at treatment dose (1.5 mg/kg).
	More than 28 days <sup>b</sup>	Restart TECVAYLI™ step-up dosing schedule at step-up dose 1 (0.06 mg/kg). <sup>a</sup>

<sup>a</sup> Administer pretreatment medications prior to TECVAYLI™ dose and monitor patients accordingly [see *Dosage and Administration (2.2, 2.5) in the full Prescribing Information*].

<sup>b</sup> Consider benefit-risk of restarting TECVAYLI™ in patients who require a dose delay of more than 28 days due to an adverse reaction.

### WARNINGS AND PRECAUTIONS (cont'd)

**Hypersensitivity and Other Administration Reactions** - TECVAYLI™ can cause both systemic administration-related and local injection-site reactions. **Systemic Reactions** - In patients who received TECVAYLI™ at the recommended dose in the clinical trial, 1.2% of patients experienced systemic-administration reactions, which included Grade 1 recurrent pyrexia and Grade 1 swollen tongue. **Local Reactions** - In patients who received TECVAYLI™ at the recommended dose in the clinical trial, injection-site reactions occurred in 35% of patients, with Grade 1 injection-site reactions in 30% and Grade 2 in 4.8%. Withhold TECVAYLI™ or consider permanent discontinuation of TECVAYLI™ based on severity.

## Preparation and Administration

TECVAYLI™ is intended for subcutaneous use by a healthcare provider only.

TECVAYLI™ should be administered by a healthcare provider with adequate medical personnel and appropriate medical equipment to manage severe reactions, including CRS and ICANS [see *Warnings and Precautions (5.1, 5.2) in the full Prescribing Information*].

TECVAYLI™ is a clear to slightly opalescent, colorless to light yellow solution. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Do not use if the solution is discolored, or cloudy, or if foreign particles are present.

TECVAYLI™ 30 mg/3 mL (10 mg/mL) vial and TECVAYLI™ 153 mg/1.7 mL (90 mg/mL) vial are supplied as ready-to-use solution that do not need dilution prior to administration.

Do not combine TECVAYLI™ vials of different concentrations to achieve treatment dose.

Use aseptic technique to prepare and administer TECVAYLI™.

### Preparation of TECVAYLI™

Refer to the following reference tables for the preparation of TECVAYLI™.

Use Table 7 in the full Prescribing Information to determine total dose, injection volume and number of vials required based on patient's actual body weight for step-up dose 1 using TECVAYLI™ 30 mg/3 mL (10 mg/mL) vial.

### Step-up Dose 1 (0.06 mg/kg) Injection Volumes using TECVAYLI™ 30 mg/3 mL (10 mg/mL) Vial

Patient Body Weight (kg)	Total Dose (mg)	Volume of Injection (mL)	Number of Vials (1 vial=3 mL)
35 to 39	2.2	0.22	1
40 to 44	2.5	0.25	1
45 to 49	2.8	0.28	1
50 to 59	3.3	0.33	1
60 to 69	3.9	0.39	1
70 to 79	4.5	0.45	1
80 to 89	5.1	0.51	1
90 to 99	5.7	0.57	1
100 to 109	6.3	0.63	1
110 to 119	6.9	0.69	1
120 to 129	7.5	0.75	1
130 to 139	8.1	0.81	1
140 to 149	8.7	0.87	1
150 to 160	9.3	0.93	1

Please see full Important Safety Information on pages 20-23.

Use Table 8 in the full Prescribing Information to determine total dose, injection volume and number of vials required based on patient's actual body weight for step-up dose 2 using TECVAYLI™ 30 mg/3 mL (10 mg/mL) vial.

### Step-up Dose 2 (0.3 mg/kg) Injection Volumes using TECVAYLI™ 30 mg/3 mL (10 mg/mL) Vial

Patient Body Weight (kg)	Total Dose (mg)	Volume of Injection (mL)	Number of Vials (1 vial=3 mL)
35 to 39	11	1.1	1
40 to 44	13	1.3	1
45 to 49	14	1.4	1
50 to 59	16	1.6	1
60 to 69	19	1.9	1
70 to 79	22	2.2	1
80 to 89	25	2.5	1
90 to 99	28	2.8	1
100 to 109	31	3.1	2
110 to 119	34	3.4	2
120 to 129	37	3.7	2
130 to 139	40	4	2
140 to 149	43	4.3	2
150 to 160	47	4.7	2

## WARNINGS AND PRECAUTIONS (cont'd)

**Embryo-Fetal Toxicity** - Based on its mechanism of action, TECVAYLI™ may cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to the fetus. Advise females of reproductive potential to use effective contraception during treatment with TECVAYLI™ and for 5 months after the last dose.

## Preparation and Administration (cont'd)

Use Table 9 in the full Prescribing Information to determine total dose, injection volume and number of vials required based on patient's actual body weight for the treatment dose using TECVAYLI™ 153 mg/1.7 mL (90 mg/mL) vial.

### Treatment Dose (1.5 mg/kg) Injection Volumes using TECVAYLI™ 153 mg/1.7 mL (90 mg/mL) Vial

Patient Body Weight (kg)	Total Dose (mg)	Volume of Injection (mL)	Number of Vials (1 vial=1.7 mL)
35 to 39	56	0.62	1
40 to 44	63	0.7	1
45 to 49	70	0.78	1
50 to 59	82	0.91	1
60 to 69	99	1.1	1
70 to 79	108	1.2	1
80 to 89	126	1.4	1
90 to 99	144	1.6	1
100 to 109	153	1.7	1
110 to 119	171	1.9	2
120 to 129	189	2.1	2
130 to 139	198	2.2	2
140 to 149	216	2.4	2
150 to 160	234	2.6	2

## WARNINGS AND PRECAUTIONS (cont'd)

**Adverse Reactions** - The most common adverse reactions ( $\geq 20\%$ ) were pyrexia, CRS, musculoskeletal pain, injection site reaction, fatigue, upper respiratory tract infection, nausea, headache, pneumonia, and diarrhea. The most common Grade 3 to 4 laboratory abnormalities ( $\geq 20\%$ ) were decreased lymphocytes, decreased neutrophils, decreased white blood cells, decreased hemoglobin, and decreased platelets.

Please see full Important Safety Information on pages 20-23.

Remove the appropriate strength TECVAYLI™ vial from refrigerated storage [ $2^{\circ}\text{C}$  to  $8^{\circ}\text{C}$  ( $36^{\circ}\text{F}$  to  $46^{\circ}\text{F}$ )].

Once removed from refrigerated storage, equilibrate TECVAYLI™ to ambient temperature [ $15^{\circ}\text{C}$  to  $30^{\circ}\text{C}$  ( $59^{\circ}\text{F}$  to  $86^{\circ}\text{F}$ )] for at least 15 minutes. Do not warm TECVAYLI™ in any other way.

Once equilibrated, gently swirl the vial for approximately 10 seconds to mix. Do not shake.

Withdraw the required injection volume of TECVAYLI™ from the vial(s) into an appropriately sized syringe using a transfer needle.

Each injection volume should not exceed 2 mL. Divide doses requiring greater than 2 mL equally into multiple syringes.

TECVAYLI™ is compatible with stainless steel injection needles and polypropylene or polycarbonate syringe material.

Replace the transfer needle with an appropriately sized needle for injection.

## Preparation and Administration (cont'd)

### Administration of TECVAYLI™

Inject the required volume of TECVAYLI™ into the subcutaneous tissue of the abdomen (preferred injection site). Alternatively, TECVAYLI™ may be injected into the subcutaneous tissue at other sites (e.g., thigh). If multiple injections are required, TECVAYLI™ injections should be at least 2 cm apart.

Do not inject into tattoos or scars or areas where the skin is red, bruised, tender, hard or not intact.

Any unused product or waste material should be disposed in accordance with local requirements.

### Storage

If the prepared dosing syringe(s) of TECVAYLI™ is not used immediately, store syringe(s) at 2°C to 8°C (36°F to 46°F) or at ambient temperature 15°C to 30°C (59°F to 86°F) for a maximum of 20 hours. Discard syringe(s) after 20 hours, if not used.

### Monitoring

Due to the risk of CRS and neurologic toxicity, including ICANS, patients should be hospitalized for 48 hours after administration of all doses within the TECVAYLI™ step-up dosing schedule [see *Dosage and Administration (2.1) and Warnings and Precautions (5.1, 5.2) in the full Prescribing Information*].

## Dosage Modifications for Adverse Reactions

Dosage reductions of TECVAYLI™ are not recommended.

Dosage delays may be required to manage toxicities related to TECVAYLI™ [see *Warnings and Precautions (5) in the full Prescribing Information*].

See Tables 3, 4, and 5 in the full Prescribing Information for recommended actions for adverse reactions of CRS, neurologic toxicity, and ICANS. See Table 6 in the full Prescribing Information for recommended actions for other adverse reactions following administration of TECVAYLI™.

### WARNINGS AND PRECAUTIONS (cont'd)

**Cytokine Release Syndrome** - TECVAYLI™ can cause cytokine release syndrome (CRS), including life-threatening or fatal reactions. In the clinical trial, CRS occurred in 72% of patients who received TECVAYLI™ at the recommended dose, with Grade 1 CRS occurring in 50% of patients, Grade 2 in 21%, and Grade 3 in 0.6%. Recurrent CRS occurred in 33% of patients. Most patients experienced CRS following step-up dose 1 (42%), step-up dose 2 (35%), or the initial treatment dose (24%). Less than 3% of patients developed first occurrence of CRS following subsequent doses of TECVAYLI™. The median time to onset of CRS was 2 (range: 1 to 6) days after the most recent dose with a median duration of 2 (range: 1 to 9) days. Clinical signs and symptoms of CRS included, but were not limited to, fever, hypoxia, chills, hypotension, sinus tachycardia, headache, and elevated liver enzymes (aspartate aminotransferase and alanine aminotransferase elevation).

## Warnings and Precautions

### Cytokine Release Syndrome

TECVAYLI™ can cause cytokine release syndrome (CRS), including life-threatening or fatal reactions [see *Adverse Reactions (6.1) in the full Prescribing Information*].

In the clinical trial, CRS occurred in 72% of patients who received TECVAYLI™ at the recommended dose, with Grade 1 CRS occurring in 50% of patients, Grade 2 in 21%, and Grade 3 in 0.6%. Recurrent CRS occurred in 33% of patients. Most patients experienced CRS following step-up dose 1 (42%), step-up dose 2 (35%), or the initial treatment dose (24%). Less than 3% of patients developed first occurrence of CRS following subsequent doses of TECVAYLI™. The median time to onset of CRS was 2 (range: 1 to 6) days after the most recent dose with a median duration of 2 (range: 1 to 9) days.

Clinical signs and symptoms of CRS included, but were not limited to, fever, hypoxia, chills, hypotension, sinus tachycardia, headache, and elevated liver enzymes (aspartate aminotransferase and alanine aminotransferase elevation).

Initiate therapy according to TECVAYLI™ step-up dosing schedule to reduce risk of CRS [see *Dosage and Administration (2.1, 2.4) in the full Prescribing Information*]. Administer pretreatment medications to reduce risk of CRS and monitor patients following administration of TECVAYLI™ accordingly [see *Dosage and Administration (2.2, 2.4) in the full Prescribing Information*].

At the first sign of CRS, immediately evaluate patient for hospitalization. Administer supportive care based on severity and consider further management per current practice guidelines. Withhold or permanently discontinue TECVAYLI™ based on severity [see *Dosage and Administration (2.4) in the full Prescribing Information*].

TECVAYLI™ is available only through a restricted program under a REMS [see *Warnings and Precautions (5.3) in the full Prescribing Information*].

### Neurologic Toxicity including ICANS

TECVAYLI™ can cause serious or life-threatening neurologic toxicity, including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) [see *Adverse Reactions (6.1) in the full Prescribing Information*].

In the clinical trial, neurologic toxicity occurred in 57% of patients who received TECVAYLI™ at the recommended dose, with Grade 3 or 4 neurologic toxicity occurring in 2.4% of patients. The most frequent neurologic toxicities were headache (25%), motor dysfunction (16%), sensory neuropathy (15%), and encephalopathy (13%).

With longer follow-up, Grade 4 seizure and fatal Guillain-Barré syndrome (one patient each) occurred in patients who received TECVAYLI™.

In the clinical trial, ICANS was reported in 6% of patients who received TECVAYLI™ at the recommended dose [see *Adverse Reactions (6.1) in the full Prescribing Information*]. Recurrent ICANS occurred in 1.8% of patients.

Please see full Important Safety Information on pages 20-23.

### Neurologic Toxicity including ICANS (cont'd)

Most patients experienced ICANS following step-up dose 1 (1.2%), step-up dose 2 (0.6%), or the initial treatment dose (1.8%). Less than 3% of patients developed first occurrence of ICANS following subsequent doses of TECVAYLI™. The median time to onset of ICANS was 4 (range: 2 to 8) days after the most recent dose with a median duration of 3 (range: 1 to 20) days. The most frequent clinical manifestations of ICANS reported were confusional state and dysgraphia. The onset of ICANS can be concurrent with CRS, following resolution of CRS, or in the absence of CRS.

Monitor patients for signs and symptoms of neurologic toxicity during treatment. At the first sign of neurologic toxicity, including ICANS, immediately evaluate patient and provide supportive therapy based on severity. Withhold or permanently discontinue TECVAYLI™ based on severity per recommendations and consider further management per current practice guidelines [see *Dosage and Administration (2.4) in the full Prescribing Information*].

Due to the potential for neurologic toxicity, patients receiving TECVAYLI™ are at risk of depressed level of consciousness [see *Adverse Reactions (6.1) in the full Prescribing Information*]. Advise patients to refrain from driving or operating heavy or potentially dangerous machinery during and for 48 hours after completion of TECVAYLI™ step-up dosing schedule and in the event of new onset of any neurologic toxicity symptoms until neurologic toxicity resolves [see *Dosage and Administration (2.1) in the full Prescribing Information*].

TECVAYLI™ is available only through a restricted program under a REMS [see *Warnings and Precautions (5.3) in the full Prescribing Information*].

### TECVAYLI™ REMS

TECVAYLI™ is available only through a restricted program under a REMS called the TECVAYLI™ REMS because of the risks of CRS and neurologic toxicity, including ICANS [see *Warnings and Precautions (5.1, 5.2) in the full Prescribing Information*].

Notable requirements of the TECVAYLI™ REMS include the following:

- Prescribers must be certified with the program by enrolling and completing training.
- Prescribers must counsel patients receiving TECVAYLI™ about the risk of CRS and neurologic toxicity, including ICANS, and provide patients with Patient Wallet Card.
- Pharmacies and healthcare settings that dispense TECVAYLI™ must be certified with the TECVAYLI™ REMS program and must verify prescribers are certified through the TECVAYLI™ REMS program.
- Wholesalers and distributors must only distribute TECVAYLI™ to certified pharmacies or healthcare settings.

Further information about the TECVAYLI™ REMS program is available at [www.TECVAYLIREMS.com](http://www.TECVAYLIREMS.com) or by telephone at 1-855-810-8064.



## Warnings and Precautions (cont'd)

### Hepatotoxicity

TECVAYLI™ can cause hepatotoxicity, including fatalities. In patients who received TECVAYLI™ at the recommended dose in the clinical trial, there was one fatal case of hepatic failure. Elevated aspartate aminotransferase (AST) occurred in 34% of patients, with Grade 3 or 4 elevations in 1.2%. Elevated alanine aminotransferase (ALT) occurred in 28% of patients, with Grade 3 or 4 elevations in 1.8%. Elevated total bilirubin occurred in 6% of patients with Grade 3 or 4 elevations in 0.6%. Liver enzyme elevation can occur with or without concurrent CRS.

Monitor liver enzymes and bilirubin at baseline and during treatment as clinically indicated. Withhold TECVAYLI™ or consider permanent discontinuation of TECVAYLI™ based on severity [see *Dosage and Administration (2.4) in the full Prescribing Information*].

### Infections

TECVAYLI™ can cause severe, life-threatening, or fatal infections. In patients who received TECVAYLI™ at the recommended dose in the clinical trial, serious infections, including opportunistic infections, occurred in 30% of patients, with Grade 3 or 4 infections in 35%, and fatal infections in 4.2% [see *Adverse Reactions (6.1) in the full Prescribing Information*].

Monitor patients for signs and symptoms of infection prior to and during treatment with TECVAYLI™ and treat appropriately. Administer prophylactic antimicrobials according to guidelines [see *Dosage and Administration (2.2) in the full Prescribing Information*].

Withhold TECVAYLI™ or consider permanent discontinuation of TECVAYLI™ based on severity [see *Dosage and Administration (2.4) in the full Prescribing Information*].

Monitor immunoglobulin levels during treatment with TECVAYLI™ and treat according to guidelines, including infection precautions and antibiotic or antiviral prophylaxis [see *Dosage and Administration (2.2) in the full Prescribing Information*].

### Neutropenia

TECVAYLI™ can cause neutropenia and febrile neutropenia. In patients who received TECVAYLI™ at the recommended dose in the clinical trial, decreased neutrophils occurred in 84% of patients, with Grade 3 or 4 decreased neutrophils in 56%. Febrile neutropenia occurred in 3% of patients [see *Adverse Reactions (6.1) in the full Prescribing Information*].

Monitor complete blood cell counts at baseline and periodically during treatment and provide supportive care per local institutional guidelines.

Monitor patients with neutropenia for signs of infection.

Withhold TECVAYLI™ based on severity [see *Dosage and Administration (2.4) in the full Prescribing Information*].

Please see full Important Safety Information on pages 20-23.

### Hypersensitivity and Other Administration Reactions

TECVAYLI™ can cause both systemic administration-related reactions and local injection-site reactions.

#### Systemic Reactions

In patients who received TECVAYLI™ at the recommended dose in the clinical trial, 1.2% of patients experienced systemic-administration reactions, which included Grade 1 recurrent pyrexia and Grade 1 swollen tongue.

#### Local Reactions

In patients who received TECVAYLI™ at the recommended dose in the clinical trial, injection-site reactions occurred in 35% of patients with Grade 1 injection-site reactions in 30% and Grade 2 in 4.8%.

Withhold TECVAYLI™ or consider permanent discontinuation of TECVAYLI™ based on severity [see *Dosage and Administration (2.4) in the full Prescribing Information*].

### Embryo-Fetal Toxicity

Based on its mechanism of action, TECVAYLI™ may cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to the fetus. Advise females of reproductive potential to use effective contraception during treatment with TECVAYLI™ and for 5 months after the last dose [see *Use in Specific Populations (8.1, 8.3) in the full Prescribing Information*].

### Adverse Reactions

The most common adverse reactions (≥20%) were pyrexia, CRS, musculoskeletal pain, injection site reaction, fatigue, upper respiratory tract infection, nausea, headache, pneumonia, and diarrhea. The most common Grade 3 to 4 laboratory abnormalities (≥20%) were decreased lymphocytes, decreased neutrophils, decreased white blood cells, decreased hemoglobin, and decreased platelets.

## Patient Counseling Information

### Advise the patient to read the FDA-approved patient labeling (Medication Guide).

#### Cytokine Release Syndrome (CRS)

Discuss the signs and symptoms associated with CRS, including fever, hypoxia, chills, hypotension, sinus tachycardia, headache, and elevated liver enzymes. Advise patients to immediately contact their healthcare provider if they experience any signs or symptoms of CRS. Advise patients that they will be hospitalized for 48 hours after administration of all doses within the TECVAYLI™ step-up dosing schedule [see *Dosage and Administration (2.4) and Warnings and Precautions (5.1) in the full Prescribing Information*].

#### Neurologic Toxicity including ICANS

Discuss the signs and symptoms associated with neurologic toxicity, including ICANS, including headache, confusion, dysgraphia, motor dysfunction, neuropathy, or encephalopathy. Advise patients to immediately contact their healthcare provider if they experience any signs or symptoms of neurologic toxicity. Advise patients to refrain from driving or operating heavy or potentially dangerous machinery during and for 48 hours after completion of TECVAYLI™ step-up dosing schedule and in the event of new onset of any neurologic toxicity symptoms until neurologic toxicity resolves [see *Dosage and Administration (2.4) and Warnings and Precautions (5.2) in the full Prescribing Information*].

#### TECVAYLI™ REMS

TECVAYLI™ is available only through a restricted program called TECVAYLI™ REMS. Inform patients that they will be given a TECVAYLI™ Patient Wallet Card that they should carry with them at all times and show to all of their healthcare providers. This card describes signs and symptoms of CRS and neurologic toxicity which, if experienced, should prompt the patient to immediately seek medical attention [see *Warnings and Precautions (5.3) in the full Prescribing Information*].

#### Hepatotoxicity

Advise patients that liver enzyme elevations may occur and that they should report symptoms that may indicate liver toxicity, including fatigue, anorexia, right upper abdominal discomfort, dark urine, or jaundice [see *Warnings and Precautions (5.4) in the full Prescribing Information*].

#### Infections

Discuss the signs and symptoms of infection [see *Dosage and Administration (2.4) and Warnings and Precautions (5.5) in the full Prescribing Information*].

#### Neutropenia

Discuss the signs and symptoms associated with neutropenia and febrile neutropenia [see *Dosage and Administration (2.4) and Warnings and Precautions (5.6) in the full Prescribing Information*].

#### Hypersensitivity and Other Administration Reactions

Advise patients to immediately seek medical attention for any signs and symptoms of systemic administration-related reactions. Advise patients that local injection-site reactions may occur and to report any severe reactions [see *Warnings and Precautions (5.7) in the full Prescribing Information*].

#### Embryo-Fetal Toxicity

Advise pregnant women to inform their healthcare provider if they are pregnant or become pregnant. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception during treatment with TECVAYLI™ and for 5 months after the last dose [see *Warnings and Precautions (5.8) and Use in Specific Populations (8.1, 8.3) in the full Prescribing Information*].

#### Lactation

Advise women not to breastfeed during treatment with TECVAYLI™ and for 5 months after the last dose [see *Use in Specific Populations (8.2) in the full Prescribing Information*].

## Important Safety Information

### INDICATION AND USAGE

TECVAYLI™ (teclistamab-cqyv) is a bispecific B-cell maturation antigen (BCMA)-directed CD3 T-cell engager indicated for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody.

This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

### IMPORTANT SAFETY INFORMATION

**WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGIC TOXICITY including IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME**

Cytokine release syndrome (CRS), including life-threatening or fatal reactions, can occur in patients receiving TECVAYLI™. Initiate treatment with TECVAYLI™ step-up dosing schedule to reduce risk of CRS. Withhold TECVAYLI™ until CRS resolves or permanently discontinue based on severity.

Neurologic toxicity, including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) and serious and life-threatening reactions, can occur in patients receiving TECVAYLI™. Monitor patients for signs or symptoms of neurologic toxicity, including ICANS, during treatment and treat promptly. Withhold TECVAYLI™ until neurologic toxicity resolves or permanently discontinue based on severity.

TECVAYLI™ is available only through a restricted program called the TECVAYLI™ Risk Evaluation and Mitigation Strategy (REMS).

### WARNINGS AND PRECAUTIONS

**Cytokine Release Syndrome** - TECVAYLI™ can cause cytokine release syndrome (CRS), including life-threatening or fatal reactions. In the clinical trial, CRS occurred in 72% of patients who received TECVAYLI™ at the recommended dose, with Grade 1 CRS occurring in 50% of patients, Grade 2 in 21%, and Grade 3 in 0.6%. Recurrent CRS occurred in 33% of patients. Most patients experienced CRS following step-up dose 1 (42%), step-up dose 2 (35%), or the initial treatment dose (24%). Less than 3% of patients developed first occurrence of CRS following subsequent doses of TECVAYLI™. The median time to onset of CRS was 2 (range: 1 to 6) days after the most recent dose with a median duration of 2 (range: 1 to 9) days. Clinical signs and symptoms of CRS included, but were not limited to, fever, hypoxia, chills, hypotension, sinus tachycardia, headache, and elevated liver enzymes (aspartate aminotransferase and alanine aminotransferase elevation).

Initiate therapy according to TECVAYLI™ step-up dosing schedule to reduce risk of CRS. Administer pretreatment medications to reduce risk of CRS and monitor patients following administration of TECVAYLI™ accordingly. At the first sign of CRS, immediately evaluate patient for hospitalization. Administer supportive care based on severity and consider further management per current practice guidelines. Withhold or permanently discontinue TECVAYLI™ based on severity.

TECVAYLI™ is available only through a restricted program under a REMS.

**Neurologic Toxicity including ICANS** - TECVAYLI™ can cause serious or life-threatening neurologic toxicity, including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS).

In the clinical trial, neurologic toxicity occurred in 57% of patients who received TECVAYLI™ at the recommended dose, with Grade 3 or 4 neurologic toxicity occurring in 2.4% of patients. The most frequent neurologic toxicities were headache (25%), motor dysfunction (16%), sensory neuropathy (15%), and encephalopathy (13%). With longer follow-up, Grade 4 seizure and fatal Guillain-Barré syndrome (one patient each) occurred in patients who received TECVAYLI™.

In the clinical trial, ICANS was reported in 6% of patients who received TECVAYLI™ at the recommended dose. Recurrent ICANS occurred in 1.8% of patients. Most patients experienced ICANS following step-up dose 1 (1.2%), step-up dose 2 (0.6%), or the initial treatment dose (1.8%). Less than 3% of patients developed first occurrence of ICANS following subsequent doses of TECVAYLI™. The median time to onset of ICANS was 4 (range: 2 to 8) days after the most recent dose with a median duration of 3 (range: 1 to 20) days. The most frequent clinical manifestations of ICANS reported were confusional state and dysgraphia. The onset of ICANS can be concurrent with CRS, following resolution of CRS, or in the absence of CRS.

Monitor patients for signs and symptoms of neurologic toxicity during treatment. At the first sign of neurologic toxicity, including ICANS, immediately evaluate patient and provide supportive therapy based on severity. Withhold or permanently discontinue TECVAYLI™ based on severity per recommendations and consider further management per current practice guidelines.

## Important Safety Information (cont'd)

### WARNINGS AND PRECAUTIONS (cont'd)

**Neurologic Toxicity including ICANS (cont'd)** - Due to the potential for neurologic toxicity, patients are at risk of depressed level of consciousness. Advise patients to refrain from driving or operating heavy or potentially dangerous machinery during and for 48 hours after completion of TECVAYLI™ step-up dosing schedule and in the event of new onset of any neurologic toxicity symptoms until neurologic toxicity resolves.

TECVAYLI™ is available only through a restricted program under a REMS.

**TECVAYLI™ REMS** - TECVAYLI™ is available only through a restricted program under a REMS called the TECVAYLI™ REMS because of the risks of CRS and neurologic toxicity, including ICANS.

**Hepatotoxicity** - TECVAYLI™ can cause hepatotoxicity, including fatalities. In patients who received TECVAYLI™ at the recommended dose in the clinical trial, there was one fatal case of hepatic failure. Elevated aspartate aminotransferase (AST) occurred in 34% of patients, with Grade 3 or 4 elevations in 1.2%. Elevated alanine aminotransferase (ALT) occurred in 28% of patients, with Grade 3 or 4 elevations in 1.8%. Elevated total bilirubin occurred in 6% of patients with Grade 3 or 4 elevations in 0.6%. Liver enzyme elevation can occur with or without concurrent CRS.

Monitor liver enzymes and bilirubin at baseline and during treatment as clinically indicated. Withhold TECVAYLI™ or consider permanent discontinuation of TECVAYLI™ based on severity.

**Infections** - TECVAYLI™ can cause severe, life-threatening, or fatal infections. In patients who received TECVAYLI™ at the recommended dose in the clinical trial, serious infections, including opportunistic infections, occurred in 30% of patients, with Grade 3 or 4 infections in 35%, and fatal infections in 4.2%. Monitor patients for signs and symptoms of infection prior to and during treatment with TECVAYLI™ and treat appropriately. Administer prophylactic antimicrobials according to guidelines. Withhold TECVAYLI™ or consider permanent discontinuation of TECVAYLI™ based on severity.

Monitor immunoglobulin levels during treatment with TECVAYLI™ and treat according to guidelines, including infection precautions and antibiotic or antiviral prophylaxis.

**Neutropenia** - TECVAYLI™ can cause neutropenia and febrile neutropenia. In patients who received TECVAYLI™ at the recommended dose in the clinical trial, decreased neutrophils occurred in 84% of patients, with Grade 3 or 4 decreased neutrophils in 56%. Febrile neutropenia occurred in 3% of patients.

Monitor complete blood cell counts at baseline and periodically during treatment and provide supportive care per local institutional guidelines. Monitor patients with neutropenia for signs of infection. Withhold TECVAYLI™ based on severity.

**Hypersensitivity and Other Administration Reactions** - TECVAYLI™ can cause both systemic administration-related and local injection-site reactions. **Systemic Reactions** - In patients who received TECVAYLI™ at the recommended dose in the clinical trial, 1.2% of patients experienced systemic-administration reactions, which included Grade 1 recurrent pyrexia and Grade 1 swollen tongue. **Local Reactions** - In patients who received TECVAYLI™ at the recommended dose in the clinical trial, injection-site reactions occurred in 35% of patients, with Grade 1 injection-site reactions in 30% and Grade 2 in 4.8%. Withhold TECVAYLI™ or consider permanent discontinuation of TECVAYLI™ based on severity.

**Embryo-Fetal Toxicity** - Based on its mechanism of action, TECVAYLI™ may cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to the fetus. Advise females of reproductive potential to use effective contraception during treatment with TECVAYLI™ and for 5 months after the last dose.

**Adverse Reactions** - The most common adverse reactions (≥20%) were pyrexia, CRS, musculoskeletal pain, injection site reaction, fatigue, upper respiratory tract infection, nausea, headache, pneumonia, and diarrhea. The most common Grade 3 to 4 laboratory abnormalities (≥20%) were decreased lymphocytes, decreased neutrophils, decreased white blood cells, decreased hemoglobin, and decreased platelets.

Please read full [Prescribing Information](#), including **Boxed WARNING**, for TECVAYLI™.

cp-322928v1

### Reference:

1. TECVAYLI™ (teclistamab-cqyv) Prescribing Information. Janssen Biotech, Inc., Horsham, PA 19044.

Learn more at  
[TECVAYLIHCP.com](https://TECVAYLIHCP.com)



Please see full Important Safety Information on pages 20-23.