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

Recommendations for Restarting TECVAYLI® After Dose Delay

Guidance for restarting therapy with TECVAYLI® after dose interruptions.[1]

See details inside

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.

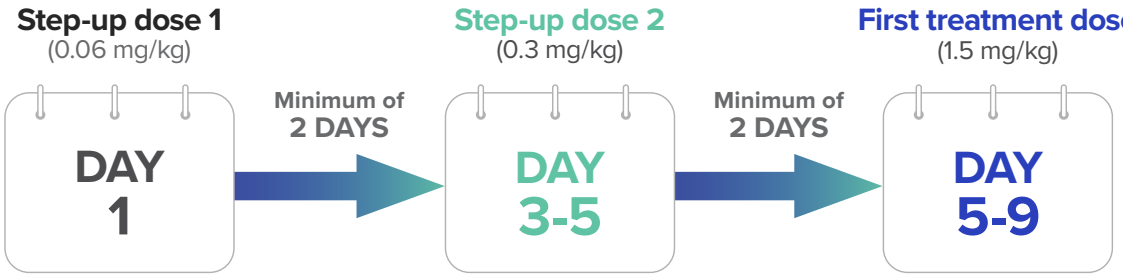
Neurologic toxicity, including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) and serious, life-threatening or fatal reactions, can occur in patients receiving TECVAYLI®. Monitor patients for signs or symptoms of neurologic toxicity, including ICANS, during treatment. Withhold TECVAYLI®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

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

Please read additional Important Safety Information on page 4 and full Prescribing Information, including Boxed WARNING, for TECVAYLI®.

A subcutaneous injection with an adaptive step-up dosing schedule and personalized weight-based dosing[1]

Step-up doses



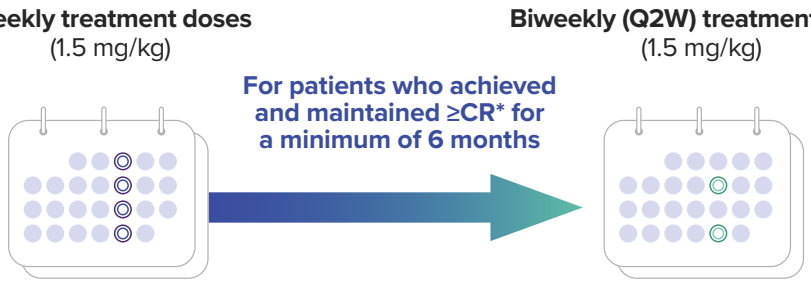
- **Step-up dose 2** may be given between **2 to 4 days after step-up dose 1** and may be given **up to 7 days after step-up dose 1** to allow for resolution of adverse reactions
- **First treatment dose** may be given between **2 to 4 days after step-up dose 2** and may be given **up to 7 days after step-up dose 2** to allow for resolution of adverse reactions

Due to the risk of cytokine release syndrome (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.

TECVAYLI® is administered by a healthcare provider according to the step-up dosing schedule to reduce the incidence and severity of CRS.

Ongoing dosing with TECVAYLI®

After step-up dosing, patients will receive weekly treatment doses with the option of switching to biweekly (Q2W) dosing if they achieve and maintain ≥CR* for a minimum of 6 months



- **Weekly dosing:** Once-weekly dosing until disease progression or unacceptable toxicity
- **Biweekly (Q2W) dosing option:** Extended dosing interval beyond 6 months. The dosing frequency may be decreased to once every 2 weeks after ≥6 months of achieving and maintaining ≥CR* during treatment until disease progression or unacceptable toxicity

Remember: Dose is personalized to each patient's actual body weight. Please refer to Tables 7-9 in the full Prescribing Information to determine the dosage based on predetermined weight ranges. Dose reductions are not recommended, and dose delays may be required to manage toxicities.

Following step-up dosing, the start of ongoing weekly dosing will begin. Certain patients will follow the biweekly (Q2W) treatment option.

*≥CR: sCR+CR.
CR, complete response; ICANS, immune effector cell-associated neurotoxicity syndrome; Q2W, every 2 weeks; sCR, stringent complete response.

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Pretreatment medications[1]

Prior to starting treatment with TECVAYLI®

Consider initiation of antiviral prophylaxis to prevent herpes zoster reactivation per local institutional guidelines.

1 to 3 hours before dose

Administer the following pretreatment medications from the TECVAYLI® step-up dosing schedule to reduce the risk of CRS:

- 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)

Prior to administration of weekly or biweekly (Q2W) doses

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 step-up dosing schedule following a dose delay
- Patients who experienced CRS following the prior dose of TECVAYLI®

Restarting TECVAYLI® after dose delay[1]

If a dose of TECVAYLI® is delayed, restart therapy based on the following recommendations and resume the treatment schedule accordingly. Administer pretreatment medications as indicated in the figure below. 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.

Last dose administered	Time since the last dose was administered	Action
Step-up dose 1	>7 days	**RESTART** TECVAYLI® step-up dosing schedule at step-up dose 1 (0.06 mg/kg)*
Step-up dose 2	8-28 days	**REPEAT** step-up dose 2 (0.3 mg/kg)† and continue TECVAYLI® step-up dosing schedule
	>28 days†	**RESTART** TECVAYLI® step-up dosing schedule at step-up dose 1 (0.06 mg/kg)*
Any weekly treatment dose	≤28 days	**CONTINUE** TECVAYLI® at last treatment dose in weekly schedule (1.5 mg/kg once weekly)
	29 days-56 days†	**RESTART** TECVAYLI® step-up dosing schedule at step-up dose 2 (0.3 mg/kg)*
	>56 days†	**RESTART** TECVAYLI® step-up dosing schedule at step-up dose 1 (0.06 mg/kg)*
Any biweekly (Q2W) treatment dose	≤63 days†	**CONTINUE** TECVAYLI® at last treatment dose in biweekly schedule (1.5 mg/kg every 2 weeks)
	64 days-112 days†	**RESTART** TECVAYLI® step-up dosing schedule at step-up dose 2 (0.3 mg/kg)*
	>112 days†	**RESTART** TECVAYLI® step-up dosing schedule at step-up dose 1 (0.06 mg/kg)*

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

†Consider benefit-risk of restarting TECVAYLI® in patients who require a dose delay of more than 28 days due to an adverse reaction.

CRS, cytokine release syndrome; ICANS, immune effector-cell associated neurotoxicity syndrome; Q2W, every 2 weeks.

Reference: 1. TECVAYLI® [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc.

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IMPORTANT SAFETY INFORMATION (continued)

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, life-threatening or fatal 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.

TECVAYLI® and TALVEY® REMS - TECVAYLI® is available only through a restricted program under a REMS called the TECVAYLI® and TALVEY® 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.

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Johnson&Johnson

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