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

NOW APPROVED IN 2L+[1]

Dosing and administration guide for

TECVAYLI®
(teclistamab-cqyv)

in combination with

DARZALEX *FASPRO*®
(daratumumab and hyaluronidase-fihj)

in adult patients with RRMM who have received at least 1 prior line of therapy, including a PI and an immunomodulatory agent[1]

2L+, second line and beyond; PI, proteasome inhibitor; RRMM, relapsed or refractory multiple myeloma.

INDICATIONS 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:

- in combination with daratumumab and hyaluronidase-fihj in patients who have received at least one prior line of therapy, including a proteasome inhibitor and an immunomodulatory agent.
- as monotherapy, in patients who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody.

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 pages 4-6 and full Prescribing Information, including Boxed WARNING, for TECVAYLI®.

TECVAYLI® + DARZALEX *FASPRO*® (daratumumab and hyaluronidase-fihj) dosing schedule[1]

	Day 0	Day 1	Day 3	Day 7	Weeks 2-8 Once weekly	Weeks 9-24 Every 2 weeks	Week 25 onward Every 4 weeks
TECVAYLI® Step-up dosing schedule	N/A	**Step-up dose 1** **0.06** mg/kg	**Step-up dose 2** **0.3** mg/kg	**1st treatment dose** **1.5** mg/kg	–	–	–
TECVAYLI® Treatment dosing	–	–	–	–	**1.5** mg/kg	**3** mg/kg	**3** mg/kg
DARZALEX *FASPRO*®	**1,800** mg/ **30,000** units	N/A	N/A	**1,800** mg/ **30,000** units	**1,800** mg/ **30,000** units	**1,800** mg/ **30,000** units	**1,800** mg/ **30,000** units

See Table 3 in the full Prescribing Information for recommendations on restarting TECVAYLI® after dose delays.

Step-up dosing schedule[1]

- The step-up dosing schedule is a component of the recommended TECVAYLI® dosage but is not applicable for the DARZALEX *FASPRO*® dosing
- **Step-up dose 1** must be administered **20 hours or more** after DARZALEX *FASPRO*®
- **Step-up dose 2** may be given between **2 to 4 days** after step-up dose 1 and, if ARs occur, may be given **up to 7 days** after step-up dose 1 to allow for resolution of ARs
- The **first treatment dose (1.5 mg/kg)** may be given between **2 to 4 days** after step-up dose 2 and, if ARs occur, may be given **up to 7 days** after step-up dose 2 to allow for resolution of ARs
- Administer **TECVAYLI®** at least **3 hours after DARZALEX *FASPRO*®** for the **first treatment dose**

Treatment dosing schedule[1]

- Administer **TECVAYLI®** at least **15 minutes after DARZALEX *FASPRO*®** for all subsequent treatment doses
- Maintain a minimum of **5 days** between **1.5 mg/kg once-weekly doses**
- Maintain a minimum of **12 days** between **3 mg/kg every-2-week doses**
- Maintain a minimum of **25 days** between **3 mg/kg every-4-week doses**

For dosage and administration instructions for DARZALEX *FASPRO*®, refer to its full Prescribing Information for the recommended dosage when used as monotherapy.

ARs, adverse reactions; N/A, not applicable.

Important dosing information[1]

TECVAYLI® and DARZALEX *FASPRO*® (daratumumab and hyaluronidase-fihj) are administered via subcutaneous injection.

Administer TECVAYLI® subcutaneously according to the step-up dosing schedule in Table 1 in the full Prescribing Information to reduce the incidence and severity of CRS.

Due to the risk of CRS and neurologic toxicity, including ICANS, patients should be hospitalized for 48 hours after administration of both step-up dose 1 and step-up dose 2. Instruct patients to remain within proximity of a healthcare facility and monitor them daily for 48 hours after the first treatment dose within the TECVAYLI® step-up dosing schedule.

Administer pretreatment medications as recommended below.

TECVAYLI® and DARZALEX *FASPRO*® should be administered until disease progression or unacceptable toxicity.

The dosage of TECVAYLI® is based on actual body weight. Please refer to Tables 8-11 in the full Prescribing Information to determine the dosage based on predetermined weight ranges.

Pretreatment medications[1]

Prior to starting treatment with TECVAYLI®

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

1-3 hours before each dose of the TECVAYLI® step-up dosing schedule (step-up doses 1 and 2, and the first treatment dose)

Administer the following pretreatment medications 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)

Prior to administration of subsequent treatment 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 TECVAYLI® step-up dosing schedule following a dose delay
- Patients who experienced CRS following the prior dose of TECVAYLI®

CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome.

IMPORTANT SAFETY INFORMATION (cont'd)
WARNINGS AND PRECAUTIONS

Cytokine Release Syndrome – TECVAYLI can cause cytokine release syndrome (CRS), including life-threatening or fatal reactions.

In the clinical trials (monotherapy and combination therapy; N=448), CRS occurred in 64% of patients who received TECVAYLI at the recommended dosage, with Grade 1 CRS occurring in 46% of patients, Grade 2 in 18%, and Grade 3 in 0.2%. Recurrent CRS occurred in 27% of patients. Most patients experienced CRS during the initial step-up dosing schedule (step-up dose 1 [37%], step-up dose 2 [32%], or the initial treatment dose [20%]). CRS first occurred following subsequent doses of TECVAYLI in 2.5% of patients. The median time to onset of CRS was 2 (range: 1 to 9) days after the most recent dose and the median duration of CRS was 2 (range: 1 to 22) 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 the patient for hospitalization. Administer supportive care based on severity and consider further management per current practice guidelines. Withhold until CRS resolves or permanently discontinue TECVAYLI based on severity.

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

Neurologic Toxicity including Immune Effector Cell-Associated Neurotoxicity Syndrome – TECVAYLI can cause serious, life-threatening, or fatal neurologic toxicity, including immune effector cell-associated neurotoxicity syndrome (ICANS).

In the clinical trials (monotherapy and combination therapy trials; N=448), neurologic toxicity occurred in 60% of patients who received TECVAYLI at the recommended dosage, with Grade 3 or 4 neurologic toxicity in 6%. Neurologic toxicities reported in ≥5% of patients included headache (27%), sensory neuropathy (16%), motor dysfunction (15%), insomnia (12%), encephalopathy (11%), and dizziness (8%). Fatal neurologic toxicity occurred in 0.4% of patients, including Guillain-Barré syndrome and status epilepticus (one patient each).

In MajesTEC-1, ICANS was reported in 6% of patients who received TECVAYLI as monotherapy at the recommended dosage. 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 TECVAYLI doses. 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.

In MajesTEC-3, ICANS was reported in 1.1% of patients who received the recommended TECVAYLI dosage in combination with daratumumab and hyaluronidase-fihj, including Grade 4 ICANS in 1 patient. All events of ICANS occurred during the step-up dosing schedule. The median time to onset of ICANS was 2 (range: 1 to 3) days after the most recent dose and the median duration of ICANS was 2 (range: 1 to 2) days. The clinical manifestations of ICANS reported were amnesia, encephalopathy and delirium.

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, including ICANS during TECVAYLI treatment. At the first sign of neurologic toxicity, including ICANS, immediately evaluate patient and provide supportive therapy based on severity. Withhold until neurologic toxicity resolves 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 receiving TECVAYLI 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. There was one fatal case of hepatic failure in MajesTEC-1. In patients who received TECVAYLI at the recommended dosage in the clinical trials (monotherapy and combination therapy trials; N=448) elevated aspartate aminotransferase (AST) occurred in 47% of patients, with Grade 3 or 4 elevations in 2.9%. Elevated alanine

IMPORTANT SAFETY INFORMATION (cont'd)
WARNINGS AND PRECAUTIONS (cont'd)

Hepatotoxicity (cont'd) - aminotransferase (ALT) occurred in 48% of patients, with Grade 3 or 4 elevations in 3.8%. Elevated total bilirubin occurred in 10% of patients with Grade 3 or 4 elevations in 0.7%. 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 MajesTEC-1 (N=165), in patients who received the recommended TECVAYLI dosage, serious infections, including opportunistic infections, occurred in 30% of patients, Grade 3 or 4 infections in 35% of patients, and fatal infections in 4.2% of patients.

In MajesTEC-3 (N=283), in patients who received TECVAYLI in combination with daratumumab and hyaluronidase-fihj at the recommended dosage, serious infections, including opportunistic infections, occurred in 54% of patients, Grade 3 or Grade 4 infections in 54% of patients, and fatal infections in 4.6% of patients.

Monitor patients for signs and symptoms of infection prior to and during treatment with TECVAYLI and treat appropriately. Administer prophylactic antimicrobials according to current practice guidelines.

Withhold TECVAYLI or consider permanent discontinuation of TECVAYLI based on severity.

Monitor immunoglobulin levels prior to and during treatment with TECVAYLI and administer subcutaneous or intravenous immunoglobulin (IVIG) to maintain the serum levels >400 mg/dL.

Neutropenia - TECVAYLI can cause neutropenia and febrile neutropenia. In patients who received TECVAYLI at the recommended dosage in the clinical trials (monotherapy and combination therapy trials; N=448), decreased neutrophils occurred in 88% of patients, with Grade 3 or 4 decreased neutrophils in 70%. Febrile neutropenia occurred in 6% 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 the recommended TECVAYLI dosage in the clinical trials (monotherapy and combination therapy trials; N=448), 2.5% of patients experienced systemic-administration reactions, which included recurrent pyrexia and rash.

Local Reactions - In patients who received TECVAYLI at the recommended dosage in the clinical trials (monotherapy and combination therapy trials; N=448), injection-site reactions occurred in 37% of patients, with Grade 1 injection-site reactions in 29% and Grade 2 in 9%.

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 patient. Advise pregnant patients 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%) in patients who received TECVAYLI monotherapy were pyrexia, CRS, musculoskeletal pain, injection site reaction, fatigue, upper respiratory tract infection, nausea, headache, pneumonia, and diarrhea. The most common adverse reactions (≥20%) in patients who received TECVAYLI in combination with daratumumab and hyaluronidase-fihj were hypogammaglobulinemia, upper respiratory tract infection, CRS, cough, diarrhea, musculoskeletal pain, COVID-19, pneumonia, injection site reaction, fatigue, pyrexia, headache, nausea, gastroenteritis, and weight decreased.

IMPORTANT SAFETY INFORMATION (cont'd)
ADVERSE REACTIONS (cont'd)

The most common Grade 3 to 4 laboratory abnormalities (≥20%) with TECVAYLI (as monotherapy or in combination with daratumumab and hyaluronidase-fihj) were decreased lymphocytes, decreased neutrophils, decreased white blood cells, decreased hemoglobin, and decreased platelets.

Please read full Prescribing Information, including Boxed WARNING, for TECVAYLI.

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