

News Release

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U.S. FDA Approves TECVAYLI™ (teclistamab-cqyv), the First Bispecific T-cell Engager Antibody for the Treatment of Patients with Relapsed or Refractory Multiple Myeloma

TECVAYLI™, an off-the-shelf, subcutaneous therapy, is an important new medicine for patients with incurable blood cancer who face limited treatment options

HORSHAM, Pa., October 25, 2022 – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today that the U.S. Food and Drug Administration (FDA) approved TECVAYLI™ (teclistamab-cqyv) for the treatment of adult patients with relapsed or refractory multiple myeloma, who previously received four or more prior lines of therapy, including a proteasome inhibitor, immunomodulatory drug and anti-CD38 monoclonal antibody.¹ TECVAYLI™ is a first-in-class, bispecific T-cell engager antibody that is administered as a subcutaneous treatment.¹ This off-the-shelf (or ready to use) therapy uses innovative science to activate the immune system by binding to the CD3 receptor expressed on the surface of T-cells and to the B-cell maturation antigen (BCMA) expressed on the surface of multiple myeloma cells and some healthy B-lineage cells.¹

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).¹

TECVAYLI™ is Janssen's fourth approved treatment for multiple myeloma, further diversifying the company's industry-leading oncology portfolio and deepening its commitment to discovering and developing therapies for this rare blood cancer.

"We are greatly encouraged by the FDA's approval of teclistamab and Janssen's commitment to the multiple myeloma community," said Michael Andreini, President and CEO of the Multiple Myeloma Research Foundation. "Multiple myeloma is a life-threatening disease with considerable unmet need, and teclistamab is an important new treatment option for patients who have faced multiple relapses."

The pivotal Phase 2 MajesTEC-1 clinical trial included patients who had received a median of five prior lines of therapy (n=110).¹ An overall response rate (ORR) of 61.8 percent (95 percent Confidence Interval [CI]: 52.1 percent, 70.9 percent) was achieved, notably with 28.2 percent of patients achieving a complete response (CR) or better (CR or stringent complete response [sCR]).¹ 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, the estimated duration of response (DOR) rate was 90.6 percent (95 percent CI: 80.3 percent, 95.7 percent) at six months and 66.5 percent (95 percent CI: 38.8 percent, 83.9 percent) at nine months.¹ The study included heavily pretreated patients, and 78 percent of patients received four or more prior lines of therapy.¹ All patients were triple-class exposed (to a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody), and 76 percent were triple-class refractory (to a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody).¹

"Today's achievement, which marks an important addition to our diverse and growing oncology portfolio, strengthens our resolve to discover and develop much-needed cancer treatments for patients and physicians," said Peter Lebowitz, M.D., Ph.D., Global Therapeutic Area Head, Oncology, Janssen Research & Development, LLC. "The approval of TECVAYLI, which demonstrated an overall response rate of more than 60 percent in heavily pretreated patients, underscores our commitment to translate science into medicines as we strive toward our goal of one day eliminating this disease."

The Safety Information for TECVAYLI™ includes a boxed warning for Cytokine Release Syndrome (CRS) and Neurologic Toxicity including immune effector cell-associated neurotoxicity syndrome in addition to warnings and precautions for hepatotoxicity, infections, neutropenia, hypersensitivity and other administrative reactions and embryo-fetal toxicity.¹ The most common adverse reactions (>20%) in the safety population of MajesTEC-1 (n=165) were pyrexia, CRS, musculoskeletal pain, injection site reaction, fatigue, upper respiratory tract infection, nausea, headache, pneumonia, and diarrhea.¹ The most common Grade 3 to 4 laboratory abnormalities (>20%) were decreased lymphocytes, decreased neutrophils, decreased white blood cells, decreased hemoglobin and decreased platelets.¹ TECVAYLI™ is available only through a restricted program called the TECVAYLI™ Risk Evaluation and Mitigation Strategy.¹ Details of the Important Safety Information are included below. TECVAYLI™ is supplied as 30mg/3mL and 153mg/1.7mL single-dose vials.¹

“In the pivotal teclistamab study, we have continued to observe positive results in heavily pretreated patients with relapsed or refractory multiple myeloma,” said Ajai Chari, M.D., Professor of Medicine, Division of Hematology and Medical Oncology at the Icahn School of Medicine at Mount Sinai and study investigator.[‡] “As a clinician and researcher, I see first-hand the human toll of this incurable disease. The approval of teclistamab, as the first bispecific antibody in relapsed or refractory multiple myeloma, is a meaningful step in helping many of these hard-to-treat patients.”

About the MajesTEC-1 Study¹

MajesTEC-1 ([NCT04557098](#), [NCT03145181](#)), is a Phase 1/2 single-arm, open-label, multicohort, multicenter dose-escalation study to evaluate the safety and efficacy of TECVAYLI™ in adults with relapsed or refractory multiple myeloma who received three or more prior lines of therapy.

Phase 1 of the study ([NCT03145181](#)) was conducted in two parts: dose escalation (Part 1) and dose expansion (Part 2). It evaluated safety, tolerability, pharmacokinetics and preliminary efficacy of TECVAYLI™ in adult participants with relapsed or refractory multiple myeloma. Study criteria excluded patients who had stroke, seizure, allogeneic stem cell transplantation within the past six 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.

Phase 2 of the study ([NCT04557098](#)) evaluated the efficacy of TECVAYLI™ at the recommended phase 2 dose (RP2D), established at subcutaneous 1.5 mg/kg weekly, as measured by ORR. During

week one, participants received step-up doses of TECVAYLI™ subcutaneous (0.06 and 0.3 mg/kg). Subsequently, participants received weekly treatment doses of TECVAYLI™ subcutaneous 1.5 mg/kg until disease progression or unacceptable toxicity. Efficacy was established based on ORR as determined by the Independent Review Committee (IRC) assessment using International Myeloma Working Group (IMWG) 2016 criteria.

The primary endpoint was overall response rate or unacceptable toxicity. Secondary endpoints included duration of response, very good partial response, complete response, stringent complete response, time to response, minimal residual disease status, progression-free survival, overall survival, safety, pharmacokinetics, immunogenicity and patient-reported outcomes.

TECVAYLI™ 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.

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 ($\geq 20\%$) 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 read full [Prescribing Information](#) including Boxed Warning for TECVAYLI™.

About Multiple Myeloma

Multiple myeloma is an incurable blood cancer that affects a type of white blood cell called plasma cells, which are found in the bone marrow.² In multiple myeloma, these plasma cells change, spread rapidly and replace normal cells in the bone marrow with tumors.³ In 2022, it is estimated that more than 34,000 people will be diagnosed with multiple myeloma, and more than 12,000 people will die from the disease in the U.S.⁴ While some people diagnosed with multiple myeloma initially have no symptoms, most patients are diagnosed due to symptoms that can include bone fracture or pain, low red blood cell counts, tiredness, high calcium levels, kidney problems or infections.⁵

About the Janssen Pharmaceutical Companies of Johnson & Johnson

At Janssen, we're creating a future where disease is a thing of the past. We're the Pharmaceutical Companies of Johnson & Johnson, working tirelessly to make that future a reality for patients everywhere by fighting sickness with science, improving access with ingenuity, and healing hopelessness with heart. We focus on areas of medicine where we can make the biggest difference:

Cardiovascular, Metabolism, & Retina; Immunology; Infectious Diseases & Vaccines; Neuroscience; Oncology; and Pulmonary Hypertension.

Learn more at www.janssen.com. Follow us at [@JanssenGlobal](https://twitter.com/JanssenGlobal) and [@JanssenUS](https://twitter.com/JanssenUS). Janssen Research & Development, LLC and Janssen Biotech, Inc. are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

‡Dr. Chari has served as a paid consultant to Janssen; he has not been paid for any media work.

Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding product development and the potential benefits and treatment impact of TECVAYLI™ (teclistamab). The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties materialize, actual results could vary materially from the expectations and projections of Janssen Research & Development, LLC, Janssen Biotech, Inc., any of the other Janssen Pharmaceutical Companies and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; manufacturing difficulties and delays; competition, including technological advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; changes in behavior and spending patterns of purchasers of health care products and services; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and descriptions of these risks, uncertainties and other factors can be found in Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended January 2, 2022, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in Johnson & Johnson's subsequent Quarterly Reports on Form 10-Q and other filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov, www.jnj.com or on request from Johnson & Johnson. None of the Janssen Pharmaceutical Companies nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

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¹ TECVAYLI™ U.S. Prescribing Information, October 2022.

² Rajkumar SV. Multiple myeloma: 2020 update on diagnosis, risk-stratification and management. Am J Hematol. 2020;95(5):548-567. <http://www.ncbi.nlm.nih.gov/pubmed/32212178>.

³ National Cancer Institute. Plasma Cell Neoplasms. Accessed September 2022. <https://www.cancer.gov/types/myeloma/patient/myeloma-treatment-pdq>.

⁴ American Cancer Society. "Key Statistics About Multiple Myeloma." Available at: <https://www.cancer.org/cancer/multiple-myeloma/about/key-statistics.html#:~:text=Multiple%20myeloma%20is%20a%20relatively,men%20and%2015%2C370%20in%20women>). Accessed September 2022.

⁵ American Cancer Society. "What Is Multiple Myeloma?" Available at: <https://www.cancer.org/cancer/multiple-myeloma/about/what-is-multiple-myeloma.html>. Accessed September 2022.