NEW DRUG APPROVAL

Brand Name	Tecvayli™
Generic Name	teclistamab-cqyv
Drug Manufacturer	Janssen Biotech, Inc.

New Drug Approval

FDA Approval Date: October 25, 2022

Review designation: N/A; Orphan

Type of review: Biologic License Application (BLA): 761291

Dispensing restriction: N/A

Place in Therapy

DISEASE DESCRIPTION & EPIDEMIOLOGY

Multiple myeloma is a cancer of the plasma cell. Normal plasma cells are a type of white blood cell that helps make up your immune system. They are located within the bone marrow - the spongy interior of bones that produces blood cells. When your body is fighting an infection, plasma cells produce antibodies (proteins) which attack viruses and bacteria.

If a plasma cell becomes cancerous, it multiplies rapidly. This is multiple myeloma. The malignant plasma cells may crowd out normal blood-forming cells within the bone marrow, reducing the production of healthy blood cells. Additionally, rather than producing infection-fighting antibodies, the cancer cells begin to produce an abnormal antibody called a monoclonal protein (m protein) or paraproteins. In the urine, they are called Bence Jones proteins. These proteins do not fight against infection.

Multiple myeloma is a relatively uncommon cancer. In the United States, the lifetime risk of getting multiple myeloma is 1 in 132 (0.76%).

The American Cancer Society's estimates for multiple myeloma in the United States for 2022 are:

About 34,470 new cases will be diagnosed (19,100 in men and 15,370 in women).
About 12,640 deaths are expected to occur (7,090 in men and 5,550 in women).

Efficacy

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.

Patients received step-up doses of 0.06 mg/kg and 0.3 mg/kg of Tecvayli™ followed by Tecvayli™ 1.5 mg/kg subcutaneously once weekly thereafter until disease progression or unacceptable toxicity.

The efficacy population included 110 patients. The median age was 66 (range: 33 to 82) years with 16% of patients 75 years of age or older; 56% were male; 91% were White, 5% were Black or African American, 3% were Asian. The

International Staging System (ISS) at study entry was Stage I in 50%, Stage II in 38%, and Stage III in 12% of patients. High-risk cytogenetics (presence of del(17p), t(4;14) and t(14;16)) were present in 25% of patients. Seventeen percent of patients had extramedullary plasmacytomas. Patients with prior BCMA-targeted therapy were not included in the efficacy population.

The median number of prior lines of therapy was 5 (range: 2 to 14); 78% of patients had received at least 4 prior lines of therapy. Eighty-one percent of patients received prior stem cell transplantation. All patients had received prior therapy with a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody, and 76% were triple-class refractory (refractory to a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody).

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.

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.

Table 1: Efficacy Results for MajesTEC-1

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

NE=not estimable

[a] Complete response or better = Stringent complete response (sCR) + complete response (CR)

Safety

ADVERSE EVENTS

The most common adverse reactions (≥20%) are pyrexia, cytokine release syndrome, 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%) are decreased lymphocytes, decreased neutrophils, decreased white blood cells, decreased hemoglobin, and decreased platelets.

WARNINGS & PRECAUTIONS

Hepatotoxicity: Can cause hepatotoxicity, including fatalities. Monitor liver enzymes and bilirubin at baseline and during treatment as clinically indicated.

Infections: Can cause severe, life-threatening, or fatal infections. Monitor patients for signs and symptoms of infection and treat appropriately. Withhold in patients with active infection during the step-up dosing schedule.

Neutropenia: Monitor complete blood cell counts at baseline and periodically during treatment.

Hypersensitivity and Other Administration Reactions: Systemic administration-related reactions and local injection site reactions can occur. Withhold or consider permanent discontinuation based on severity.

Embryo-Fetal Toxicity: May cause fetal harm. Advise females of reproductive potential of the potential risk to the fetus and to use effective contraception.

CONTRAINDICATIONS

None reported

Clinical Pharmacology

MECHANISMS 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.

Dose & Administration

ADULTS

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

[b] 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.

[c] 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.

PEDIATRICS

The safety and efficacy of Tecvayli™ have not been established in pediatric patients.

GERIATRICS

Refer to adult dosing

RENAL IMPAIRMENT

None

HEPATIC IMPAIRMENT

None

Product Availability

DOSAGE FORM(S) & STRENGTH(S)

Injection: 30 mg/3 mL (10 mg/mL) in a single-dose vial; 153 mg/1.7 mL (90 mg/mL) in a single-dose vial