**Category**

Best Biotechnology Product

**General Information**

**Company Name ***

Johnson & Johnson Services, Inc.

**Product/Solution Name ***

TALVEY™ (talquetamab-tgvs)

**Compound/Tech Name***

talquetamab-tgvs

**Trade Name ***

TALVEY™

**Corporate Name ***

Johnson & Johnson

**Date of Approval ***

2023-08-09

**Indications ***

In the United States, TALVEYTM (talquetamab-tgvs) is a G protein-coupled receptor class C group 5 member D (GPRC5D)-directed CD3 T-cell engager approved in the United States of America as a monotherapy for the treatment of adult patients with relapsed or refractory MM (RRMM) who have received at least 4 prior lines of therapy including a proteasome inhibitor (PI), an immunomodulatory agent (IMiD), and an anti-CD38 monoclonal antibody (mAb). This indication is approved under accelerated approval based on response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

In the European Union, TALVEYTM is approved as a monotherapy for the treatment of adult patients with RRMM who have received at least 3 prior therapies including a PI, an IMiD, and an anti-CD38 mAb, and have demonstrated disease progression on the last therapy.

Australia: Provisional approval for the treatment of adult patients with RRMM who have previously received ≥4 prior therapies, including a PI, an IMiD, and an anti-CD38 mAb.

Bahrain, Costa Rica, Dominican Republic, Hong Kong, Iceland, Israel, Mexico, Norway, Panama, Peru, Qatar, Singapore, Switzerland, Syria, Thailand, and the United Kingdom: Indicated as monotherapy for the treatment of adult patients with RRMM who have received ≥3 prior therapies, including a PI, an IMiD, and an anti-CD38 mAb and have demonstrated disease progression on the last therapy.

Brazil: Indicated for the treatment of adult patients with RRMM who have received ≥3 prior therapies, including a PI, an IMiD, and an anti-CD38 mAb and have demonstrated disease progression on the last therapy.

Canada: Indicated for the treatment of adult patients with RRMM who have received ≥3 prior lines of therapy, including a PI, an IMiD, and an anti-CD38 mAb, and have demonstrated disease progression on or after the last therapy.

China and Korea: Indicated as monotherapy for the treatment of adult patients with RRMM who have received ≥3 prior therapies, including a PI, an IMiD, and an anti-CD38 mAb.

Japan: Indicated as monotherapy for the treatment of adult patients with RRMM (limit the use to patients for whom standard treatment is difficult).

Kuwait, Oman, Saudi Arabia, Serbia, and United Arab Emirates: Indicated as monotherapy for the treatment of adult patients with RRMM who have received≥3 prior therapies, including a PI, an IMiD, and an anti-CD38 mAb and have demonstrated disease progression or did not respond to the last therapy.

Taiwan: Indicated for the treatment of adult patients with RRMM who have received ≥4 prior lines of therapy, including an IMiD, a PI, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy.

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**Therapeutic Areas ***

Oncology: multiple myeloma (MM)

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- TALVEY Prix Galien_30June2025 FOR SUBMISSION_1.pdf

**Background information and need for drug / device**
**(please be as specific as possible in your description; limit 500 words)**

Multiple myeloma is a hematologic malignancy characterized by the uncontrolled proliferation of plasma cells and overproduction of abnormal immunoglobulins. In 2023, an estimated 35,730 new MM cases and 12,590 deaths were reported in the U.S. MM primarily affects the elderly, with a median diagnosis age of 69 and a median age of 75 at death. Considered to be incurable, MM carries a high symptom burden and a 5-year relative survival rate of 59.8%.

MM is a complex disease characterized by genomic heterogeneity; the genetic aberrations that arise lead to treatment resistance and disease progression, with many patients exhausting the most effective agents early in treatment. Moreover, infections are a leading cause of mortality in MM due to both disease- and treatment-related immune suppression. Overall, real-world studies have found a median survival of only 12.4 months once patients have been exposed to the standard classes of therapy (proteasome inhibitors [PIs], immunomodulatory drugs [IMiDs], and anti-CD38 antibodies). The introduction of B cell maturation antigen (BCMA)-targeted T-cell-redirecting immunotherapies for patients with relapsed and refractory MM, including chimeric antigen receptor (CAR)-T cell therapies and bispecific antibodies, have significantly expanded the treatment landscape of MM. However, manufacturing CAR-T cells takes several weeks, and BCMA-targeted bispecifics have been associated with a high risk of severe infections, which is a significant cause of mortality in patients with MM. Those treated with a BCMA-targeted therapy also tend to have poor outcomes when treated with a second BCMA-targeted therapy, and outcomes continue to decline with each successive treatment. Available therapies with novel therapeutic targets are therefore critical to improve outcomes in heavily pretreated patients.

TALVEYTM, with its novel GPRC5D target, high response rates in difficult-to-treat patients, and versatility in combination regimens, shows potential to address unmet needs in MM.

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**History of the development of the solution/product ***
**(please be as specific as possible in your description; 500 words)**

TALVEYTM is a novel GPRC5D-directed T-cell-redirecting bispecific antibody and is the first approved therapy to target GPRC5D. TALVEYTM has two antigen binding sites: CD3, expressed by all CD8+ and CD4+ T cells, and the novel myeloma target GPRC5D. TALVEYTM induces T-cell-mediated cytotoxicity of myeloma cells via recruitment of CD3-expressing T cells into close proximity with GPRC5D-expressing cells (primarily tumor cells), leading to T-cell activation and subsequent target cell lysis.75,76

GPRC5D is an orphan G protein-coupled receptor with no known ligand, signaling mechanism, or function in normal tissues.77 Outside the immune cell compartment, GPRC5D expression is largely restricted to subsets of cells in epithelial tissues. In cells of the immune system, expression levels are low or nonexistent on normal B cells, T cells, natural killer cells, monocytes, granulocytes, and bone marrow progenitors; however, GPRC5D is highly expressed on myeloma cells and is abundant in the bone marrow from patients with MM to smoldering MM.77

US Food and Drug Administration's (FDA) approval of TALVEYTM was based on MonumenTAL-1, a phase 1/2, open-label, multicenter study of TALVEYTM monotherapy in patients with RRMM. Patients in MonumenTAL-1 were heavily pretreated individuals with historically poor outcomes, including a cohort of patients who received prior T-cell-redirecting therapy. MonumenTAL-1 investigated two

doses of TALVEYTM (0.4 mg/kg weekly [QW] or 0.8 mg/kg every other week [Q2W]).78 TALVEYTM demonstrated high ORRs of 74.1% in the QW cohort, 69.5% in the Q2W cohort, and 66.7% in patients with prior exposure to novel T-cell-redirecting therapy.79 TALVEYTM had a clinically manageable safety profile. Adverse events associated with GPRC5D targeting, such as changes in taste and issues affecting the skin and nails were clinically manageable and did not lead to high rates of treatment discontinuation. TALVEYTM also demonstrated sustained, clinically meaningful improvements in quality of life, including general health, physical and role function, fatigue, and pain symptoms.

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**Why this drug or device is innovative, the broad implications for future research, and/or how it will improve the human condition ***

TALVEY™ is an innovative bispecific antibody targeting GPRC5D, a novel antigen with a distinct expression profile. It has received Breakthrough and Orphan drug designations from multiple countries, highlighting its unique potential in RRMM.

TALVEY™ has shown low treatment discontinuation rates and a favorable infection profile compared with BCMA-targeted bispecific antibodies. TALVEY™ preserves immune function due to limited GPRC5D expression on normal B-cell precursors or plasma cells, resulting in lower rates of severe infection with preservation of B-cell and immunoglobulin levels.

Unlike other approved bispecific antibodies, the pharmacokinetic profile of TALVEY™ allows for both QW and Q2W dosing from the initiation of therapy. Together with SC administration, which patients and providers prefer over intravenous administration, the less frequent Q2W dosing with TALVEYTM reduces the treatment burden by shortening the time for administration, reducing the need for active clinical intervention by the provider, and limiting healthcare resource use. Notably, some responders in MonumenTAL-1 who experienced AEs maintained efficacy after dose reductions, with a trend toward improved resolution of GPRC5D-related AEs, suggesting that dosing flexibility with TALVEY™ can enhance patient experience and convenience.

Due to its unique mechanism of action, TALVEY™ is demonstrating its potential as a first-in-class, versatile partner for sequencing (ie, therapy order) and combination regimens with other myeloma therapies. Recent findings from the TRIMM-2, RedirecTT-1, and MonumenTAL-2 studies highlight the strong therapeutic potential of dual-targeting with TALVEY™ combinations to maximize efficacy and overcome heterogeneous mechanisms of resistance, including in patients with EMD.107-109 The relative preservation of immune function with TALVEYTM allows for effective combinations without exacerbating risks of serious infections.77 Trials are exploring the potential of TALVEY™ in earlier lines of therapy, in patients with aggressive disease or high risk of progression, and in bispecific-exposed patients, with the goal of transforming the treatment landscape and pursuing a potential cure for patients with MM.

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**Please provide appropriate references (PubMed, Abstract, Website) ***

Please see uploaded PDF for full reference list.

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