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For Immediate Release

Johnson & Johnson highlights its preeminent leadership in hematology through differentiated blood cancer portfolio and pipeline with new clinical and real-world data at ASH

Data highlights strength of multi-target, multi-platform multiple myeloma portfolio and continued innovation in B-cell malignancies to transform patient outcomes

RARITAN, N.J., November 29, 2023 – Johnson & Johnson announced today that more than 85 presentations from the Company's robust hematology portfolio and pipeline will be presented at the 65th Annual American Society of Hematology (ASH) Annual Meeting in San Diego from December 9-12. Clinical and real-world data will highlight the Company's differentiated portfolio and pipeline across the spectrum of hematologic malignancies, further expanding its leadership in multiple myeloma and B-cell malignancies and as a pioneer in the discovery and development of new therapeutic targets. The late-breaking abstract session will include the first presentation of results from the Phase 3 PERSEUS study evaluating a quadruplet regimen of DARZALEX *FASPRO*® (daratumumab and hyaluronidase-fihj) and doublet maintenance regimen in the treatment of patients with newly diagnosed multiple myeloma (NDMM) who are transplant-eligible (TE).

"Our presence at this year's ASH represents our deep scientific focus in hematology and unwavering commitment to developing new options to help improve outcomes for patients facing a blood cancer diagnosis," said Yusri Elsayed, M.D., M.H.Sc., Ph.D., Vice President, Disease Area Leader, Hematologic Malignancies, Johnson & Johnson Innovative Medicine. "We continue our focus on working to advance standards of care in multiple myeloma and B-cell malignancies for every patient, at every stage of disease – with the ultimate goal of delivering cures."

"The real-world data we're presenting across our blood cancer portfolio at ASH complement our extensive clinical trial program by providing further evidence about the promise and use of our medicines in clinical practice," said Tyrone Brewer, U.S. President, Oncology, Johnson & Johnson Innovative Medicine. "We intend to lead where hematology is going so patients can ultimately live longer, better lives."

Accelerating innovative therapies across all lines of treatment in multiple myeloma

Of the more than 85 abstracts presented at this year's meeting, over 60 presentations will highlight data from an industry-leading pipeline and portfolio of multiple myeloma treatments, underscoring a commitment to bringing complementary and combinable therapies to address patient needs from the frontline to relapsed/refractory settings.

In the treatment of newly diagnosed multiple myeloma, highlights will include:

- The first presentation of data from the Phase 3 PERSEUS study, a collaborative study with the European Myeloma Network and a late-breaking abstract, will be featured as an oral presentation. The study evaluates DARZALEX *FASPRO*® in a quadruple therapy combination with bortezomib, lenalidomide and dexamethasone (D-VRd) and DARZALEX *FASPRO*® and lenalidomide (DR) maintenance compared with bortezomib, lenalidomide and dexamethasone (V-Rd) and lenalidomide (R) maintenance in TE NDMM (Abstract #LBA-1).
- An oral presentation will evaluate time to next treatment or death in a retrospective cohort study in transplant-ineligible (TIE) NDMM comparing DARZALEX®, lenalidomide and dexamethasone (D-Rd) to V-Rd alone (Abstract #543).
- A systematic literature review and meta-analysis of comparative clinical evidence evaluating D-Rd in TIE NDMM compared to V-Rd alone will be highlighted in a poster presentation (Abstract #1963).

In the treatment of smoldering multiple myeloma (SMM), key presentations will include:

- An oral presentation will highlight results from the final analysis of the Phase 2 CENTAURUS study evaluating the efficacy and safety of DARZALEX® (daratumumab) monotherapy in intermediate-risk or high-risk SMM (Abstract #210).

- An oral presentation will report on results from the randomized Phase 2 Immuno-PRISM platform study evaluating bispecific antibodies, including TECVAYLI® (teclistamab-cqyv), in high-risk SMM (Abstract #206).

In the treatment of relapsed or refractory multiple myeloma (RRMM), highlights will include:

- Two oral presentations will assess TALVEY™ (talquetamab-tgvs) in the treatment of patients with RRMM, including patients who were previously treated with B-cell maturation antigen (BCMA)-directed therapies. This includes:
    - Additional results from the Phase 1/2 MonumenTAL-1 study evaluating the efficacy and safety of less frequent and reduced dosing of TALVEY™ (Abstract #1010); and
    - Preliminary results from the MonumenTAL-2 study evaluating the efficacy and safety of TALVEY™ in combination with pomalidomide (Abstract #1014).
- A poster presentation will strengthen sequencing evidence and support the versatility of TALVEY™ to be used before or after BCMA-directed chimeric antigen receptor-T (CAR-T) cell therapy and bispecific antibody therapies in tripe-class exposed RRMM (Abstract #3377).
- An oral presentation will examine mechanisms of response to inform the evaluation of combination treatments with TECVAYLI® in earlier lines of treatment via longitudinal correlative profiles, including immune fitness and T-cell function, in patients with RRMM who responded, did not respond or relapsed following treatment with TECVAYLI® in the MajesTEC-1 study (Abstract #455).
- Six poster presentations will cover real-world experience with TECVAYLI® in an outpatient setting (Abstracts #3374, #4736, #5087 and #5154), in a U.S. hospital setting (Abstract #3792), and for patients on dialysis (Abstract #4739). Together, these data provide further context to the replicability of safety and efficacy results from MajesTEC-1 in varied real-world settings among patients who did not participate in the clinical trial.
- An oral presentation will focus on patient-reported outcomes (PROs) from the CARTITUDE-4 study of CARVYKTI® (ciltacabtagene autoleucel; cilta-cel) for the treatment of patients with lenalidomide-refractory multiple myeloma who have had one to three prior lines of treatment (Abstract #1063).
- An oral presentation will include further analysis from the CARTITUDE-2 study Cohorts A and B, evaluating the safety and efficacy of CARVYKTI® in patients with RRMM who received one prior line of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent and had disease progression within 12 months of treatment with autologous stem cell transplant (ASCT), or within 12 months of the start of anti-myeloma therapy for patients who have not had ASCT (Abstract #1021).
- A poster presentation featuring data and analyses from the CARTITUDE-4 study will include updated safety and efficacy findings among patients who received CARVYKTI® as study treatment (Abstract #4866).
- Analyses on real-world treatment patterns and clinical outcomes among triple-class-exposed and BCMA-exposed patients with RRMM compare real-world outcomes among patients who started a subsequent line of therapy, to better understand the need for effective treatments for heavily pretreated patients with multiple myeloma (Abstract #542).

Demonstrating long-term scientific innovation in B-cell malignancies

The research to be presented at ASH represents our continued commitment to advancing the science of IMBRUVICA® (ibrutinib) and will add to the robust clinical data that has supported it as an innovative treatment for patients with B-cell malignancies for almost a decade, including:

- Oral presentations will feature long-term follow-up data from the Phase 3 GLOW study (Abstract #634) and Phase 2 CAPTIVATE study (Abstract #633) evaluating sustained efficacy of the first-line, fixed-duration combination treatment with IMBRUVICA® + venetoclax (I+V) in first-line chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL).
    - A nearly five-year follow-up study from GLOW in older patients with comorbidities will include an analysis of I+V treatment in comparison to chlorambucil plus obinutuzumab (Clb+O) demonstrating sustained overall survival (OS) and progression-free survival (PFS).
    - Updated five-year data from the CAPTIVATE study in patients up to 70 years of age with previously untreated CLL or SLL, which used a similar I+V schedule as GLOW, will report on survival outcomes and response rates for patients who need subsequent therapy with IMBRUVICA® as a monotherapy.
- The first presentation of data from the Phase 3 SYMPATICO study, a late-breaking abstract, will be featured as an oral presentation. The study evaluates I+V in patients with relapsed/refractory mantle cell lymphoma (MCL) (Abstract #LBA-2).

- Oral and poster presentations on real-world value evidence from phased clinical studies KOMODO (Abstract #270) and ACENTRUS (Abstract #1915) will showcase clinical efficacy and long-term results of dose modification in a first-line setting for patients with CLL/SLL and will evaluate flexibility for patients to adjust their daily dose to maintain treatment response and reduce recurrence or worsening of adverse events.

Deepening commitment to innovation through pioneering new targets across hematologic malignancies

New data from early pipeline therapies underscore the Company's commitment to investigating new targets and modalities and advancing novel options for patients living with hematologic malignancies.

Results from longer-term follow-up studies of next-generation chimeric antigen receptor (CAR) T-cell therapies recently licensed by Janssen for the treatment of B-cell non-Hodgkin's lymphoma (NHL) will be shared at ASH, including:

- An oral presentation will report on data from the open-label, dose-escalation study of C-CAR039, an autologous anti-CD20/CD19 bispecific CAR-T cell therapy, in patients with relapsed or refractory B-cell non-Hodgkin's lymphoma (NHL) (Abstract #1025).
- A poster will feature two-year follow-up results of C-CAR066, a novel anti-CD20 CAR-T cell therapy, in patients with relapsed or refractory large B-cell lymphoma after failure of anti-CD19 CAR-T therapy (Abstract #2115).

Additional reporting on data from early pipeline assets will include:

- An oral presentation on results from a first-in-human study of a Menin-KMT2A inhibitor among patients with acute myeloid leukemia harboring certain genetic alterations (Abstract #57).
- An oral presentation on preclinical studies of JNJ-79635322, a novel BCMA x GPRC5D x CD3 T-Cell redirecting trispecific antibody, an investigational therapy being studied in multiple myeloma (Abstract #456).

Company-sponsored oral and poster abstracts include*:

Multiple myeloma	
DARZALEX® (daratumumab) and DARZALEX *FASPRO*® (daratumumab and hyaluronidase-fihj)	
Oral sessions	
Abstract #LBA-1	Phase 3 randomized study of daratumumab (DARA) + bortezomib, lenalidomide, and dexamethasone (V-Rd) versus V-Rd alone in patients (Pts) with newly diagnosed multiple myeloma (NDMM) who are eligible for autologous stem cell transplantation (ASCT): primary results of the PERSEUS trial
Abstract #210	Efficacy and safety of daratumumab monotherapy in patients with intermediate-risk or high-risk SMM: final analysis of the Phase 2 CENTAURUS study
Abstract #543	Comparison of time to next treatment or death between front-line daratumumab, lenalidomide, and dexamethasone (D-Rd) and bortezomib, lenalidomide, and dexamethasone (V-Rd) in transplant-ineligible patients with multiple myeloma
Poster sessions	
Abstract #1963	Systematic literature review and meta-analysis of comparative clinical evidence investigating daratumumab, lenalidomide, and dexamethasone (D-Rd) versus bortezomib, lenalidomide, and dexamethasone (V-Rd) as first-line treatment for transplant-ineligible NDMM
Abstract #4785	Phase 2 study of daratumumab plus bortezomib, cyclophosphamide, and dexamethasone (D-VCd) in a diverse patient population with newly diagnosed amyloid light chain (AL) amyloidosis: AQUARIUS
Abstract #2006	Subgroup analyses of progression-free survival from the Phase 3 OCTANS and ALCYONE studies in transplant-ineligible patients with NDMM treated with bortezomib, melphalan, and prednisone with or without daratumumab

Abstract #3388	Daratumumab, bortezomib, melphalan, and prednisone (D-VMP) versus bortezomib, melphalan, and prednisone (V-MP) alone in transplant-ineligible Asian patients with NDMM: final analysis of the Phase 3 OCTANS study
TALVEY™ (talquetamab-tgvs)	
Oral sessions	
Abstract #542	Real-world treatment patterns and clinical outcomes among triple-class exposed and BCMA exposed multiple myeloma patients
Abstract #1010	Efficacy and safety of less frequent/lower intensity dosing of talquetamab in patients with RRMM: results from the Phase 1/2 MonumenTAL-1 study
Abstract #1014	Talquetamab + pomalidomide in patients with RRMM: safety and preliminary efficacy results from the Phase 1b MonumenTAL-2 study
Poster sessions	
Abstract #1933	Mechanisms of resistance and relapse with talquetamab in patients with RRMM from the Phase 1/2 MonumenTAL-1 study
Abstract #2007	Clinical outcomes of subsequent therapies in patients with RRMM following talquetamab treatment: analyses from the Phase 1/2 MonumenTAL-1 study
Abstract #3377	Updated results of talquetamab, a GPRC5D x CD3 bispecific antibody, in patients with RRMM with prior exposure to T-cell redirecting therapies from the Phase 1/2 MonumenTAL-1 study
TECVAYLI® (teclistamab-cqyv)	
Oral sessions	
Abstract #206	Immuno-PRISM: a randomized Phase 2 platform study of bispecific antibodies in high-risk smoldering myeloma
Abstract #455	Longitudinal correlative profiles of responders, non-responders, and those with relapse on treatment with teclistamab in the Phase 1/2 MajesTEC-1 study of patients with RRMM
Poster sessions	
Abstract #3374	OPTEC: a Phase 2 study to evaluate outpatient administration of teclistamab, a BCMA-targeting bispecific antibody, in patients with multiple myeloma
Abstract #3792	Real-world patient profile and step-up dosing process of early initiators of teclistamab for multiple myeloma in US hospitals – an updated analysis using premier healthcare database
Abstract #4670	Model-based exploration of the impact of prophylactic tocilizumab on IL-6 dynamics in multiple myeloma patients receiving teclistamab treatment
Abstract #4698	Outcomes of patients with extramedullary disease in triple-class exposed RRMM from the LocoMMotion & MoMMent studies
Abstract #4736	French monocentric experience of outpatient step-up dosing of teclistamab in relapsed refractory multiple myeloma
Abstract #4739	Teclistamab in RRMM patients on dialysis: a French experience
Abstract #5087	Evolving real-world characteristics and step-up dosing among early initiators of teclistamab for multiple myeloma – a national all-payer claims database study
Abstract #5154	Real-world treatment outcomes of teclistamab under an outpatient model for step-up dosing administration
CARVYKTI® (ciltacabtagene autoleucel; cilta-cel)	
Oral sessions	

Abstract #1021	The Phase 2 CARTITUDE-2 trial: updated efficacy and safety of ciltacabtagene autoleucel in patients with multiple myeloma and 1-3 prior lines of therapy (cohort A) and with early relapse after first line treatment (cohort B)
Abstract #1063	Patient-reported outcomes in the Phase 3 CARTITUDE-4 study of ciltacabtagene autoleucel versus standard of care in patients with lenalidomide-refractory multiple myeloma after 1-3 lines of therapy
Poster sessions	
Abstract #2099	Biomarker correlates of response to ciltacabtagene autoleucel in patients with RRMM from CARTITUDE-1, a Phase 1b/2 open-label study, at the ~3-year follow-up
Abstract #2141	Comparative efficacy of ciltacabtagene autoleucel versus idecabtagene vicleucel in the treatment of patients with RRMM previously treated with 2-4 prior lines of therapy using matching-adjusted indirect comparison
Abstract #3501	Clinical experience with cranial nerve impairment in the CARTITUDE-1, CARTITUDE-2 cohorts A, B and C, and CARTITUDE-4 studies of ciltacabtagene autoleucel
Abstract #4866	Efficacy and safety in patients with lenalidomide-refractory multiple myeloma after 1-3 prior lines who received a single infusion of ciltacabtagene autoleucel as study treatment in the Phase 3 CARTITUDE-4 trial
Abstract #5083	Cost per responder analysis of patients with lenalidomide-refractory multiple myeloma who received ciltacabtagene autoleucel from the CARTITUDE-4 trial
Abstract #5088	Personal financial burdens of multiple myeloma: a deep dive into the patient's journey using qualitative interview
Multiple myeloma pipeline	
Oral session	
Abstract #456	Characterization of JNJ-79635322, a novel BCMA x GPRC5D x CD3 T-cell redirecting trispecific antibody, for the treatment of multiple myeloma
B-cell malignancies	
IMBRUVICA® (ibrutinib)	
Oral sessions	
Abstract #LBA-2	Ibrutinib combined with venetoclax in patients with relapsed/refractory mantle cell lymphoma: primary analysis results from the randomized Phase 3 SYMPATICO study
Abstract #269	Impact of ibrutinib dose reduction on duration of therapy in patients with CLL/SLL
Abstract #270	Comparative effectiveness of ibrutinib flexible dosing treatment strategies on time to next treatment in a largely community-based claims database: a target trial emulation study
Abstract #633	Relapse after first-line fixed duration ibrutinib + venetoclax: high response rates to ibrutinib retreatment and absence of BTK mutations in patients with CLL/ SLL with up to 5 years of follow-up in the Phase 2 CAPTIVATE study
Abstract #634	First-line fixed-duration ibrutinib plus venetoclax (Ibr+Ven) versus chlorambucil plus obinutuzumab (Clb+O): 55-month follow-up from the GLOW study
Poster sessions	
Abstract #1915	Ibrutinib dose adjustment does not impact time to next treatment in first-line patients with CLL: a real-world analysis of electronic medical records from academic and non-teaching hospitals using target trial emulation
Abstract #2348	Healthcare resource utilization and costs among newly diagnosed and relapsed/refractory acute myeloid leukemia (AML) patients: a retrospective cohort study using contemporary US claims

Abstract #2428	Real-world treatment patterns and overall survival among newly diagnosed and relapsed/refractory AML patients: a retrospective cohort study using claims data
Abstract #2817	Combination of ibrutinib with CD19 CAR-T cells suggests greater contribution to CAR T-cell efficacy than other approved BTK inhibitors in the preclinical setting
Abstract #3278	Overall survival outcomes in CLL/SLL patients with high-risk molecular-cytogenetic features treated with 1L ibrutinib: a comparative effectiveness study using the Flatiron health data
Abstract #3780	Real-world outcomes following dose modifications of first-line ibrutinib in patients with Waldenström Macroglobulinemia
B-cell malignancies pipeline	
Oral session	
Abstract #1025**	C-CAR039, a novel anti-CD20/CD19 bi-specific CAR T-Cell therapy shows deep and durable clinical benefits in patients with relapsed or refractory (r/r) B-cell non-Hodgkin lymphoma (B-NHL) in long-term follow-up
Poster session	
Abstract #2115**	Two-year follow-up results of C-CAR066, a novel anti-CD20 chimeric antigen receptor cell therapy (CAR-T) in relapsed or refractory large B-cell lymphoma (LBCL) patients after failure of CD19 CAR-T therapy
Additional pipeline assets	
Oral session	
Abstract #57	A first-in-human Phase 1 study of the Menin-KMT2A (MLL1) inhibitor JNJ-75276617 in adult patients with relapsed/refractory acute leukemia harboring KMT2A or NPM1 alterations
Poster session	
Abstract #1777	Discovery of JNJ-88549968, a novel, first-in-class CALRmut x CD3 T-cell redirecting antibody for the treatment of myeloproliferative neoplasms
Abstract #2348	Healthcare resource utilization and costs among newly diagnosed and relapsed/refractory AML patients: a retrospective cohort study using contemporary US claims
Abstract #2428	Real-world treatment patterns and overall survival among newly diagnosed and relapsed/refractory AML patients: a retrospective cohort study using claims data
Abstract #4167	Preclinical efficacy of Menin-KMT2A inhibitor JNJ-75276617 in combination with venetoclax and azacitidine in AML

*18 additional abstracts accepted for publication only in the supplement to *Blood.*

**In collaboration with and presented by AbelZeta Pharma, Inc.

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.[1] In multiple myeloma, these plasma cells change, spread rapidly and replace normal cells in the bone marrow with tumors.[2] Multiple myeloma is the third most common blood cancer and remains an incurable disease.[3,4] In 2023, it is estimated that more than 35,000 people will be diagnosed with multiple myeloma in the U.S. and more than 12,000 people will die from the disease.[5] People living with multiple myeloma have a 5-year relative survival rate of 59.8 percent.[6] 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 and kidney problems or infections.[7,8]

About DARZALEX *FASPRO*® and DARZALEX®

DARZALEX *FASPRO*® (daratumumab and hyaluronidase-fihj) received U.S. FDA approval in May 2020 and is approved for eight indications in multiple myeloma, three of which are for frontline treatment in newly diagnosed patients who are transplant eligible or ineligible.[9] It is the only subcutaneous CD38-directed antibody approved to treat patients with MM. DARZALEX *FASPRO*® is co-formulated with recombinant human hyaluronidase PH20 (rHuPH20), Halozyme's ENHANZE® drug delivery technology.

DARZALEX® (daratumumab) received U.S. FDA approval in November 2015 and is approved in eight indications, three of which are in the frontline setting, including newly diagnosed patients who are transplant eligible and ineligible.[10]

DARZALEX® is the first CD38-directed antibody approved to treat multiple myeloma.[11] DARZALEX®-based regimens have been used in the treatment of more than 422,000 patients worldwide and more than 68,000 patients in the U.S. alone.

In August 2012, Janssen Biotech, Inc. and Genmab A/S entered a worldwide agreement, which granted Johnson & Johnson an exclusive license to develop, manufacture and commercialize daratumumab.

Since 2020, the National Comprehensive Cancer Network® (NCCN®) has recommended daratumumab-based combination regimens for the treatment of newly diagnosed multiple myeloma and relapsed and refractory multiple myeloma.† For newly diagnosed multiple myeloma, the NCCN® guidelines recommend daratumumab in combination with lenalidomide and dexamethasone as a Category 1 preferred regimen in non-transplant candidates; daratumumab in combination with bortezomib, melphalan, and prednisone as another recommended Category 1 regimen for non-transplant candidates; and daratumumab in combination with bortezomib, thalidomide and dexamethasone as a Category 2A regimen useful in certain circumstances for transplant candidates. In relapsed/refractory myeloma, four daratumumab regimens are listed as Category 1 preferred regimens for early relapses (1-3 prior therapies): daratumumab in combination with lenalidomide and dexamethasone; daratumumab in combination with bortezomib and dexamethasone; daratumumab in combination with carfilzomib and dexamethasone; and daratumumab in combination with pomalidomide and dexamethasone [after one prior therapy including lenalidomide and a proteasome inhibitor (PI)]. The NCCN® also recommends daratumumab in combination with cyclophosphamide, bortezomib and dexamethasone as another Category 2A regimen for early relapses (1-3 prior therapies) and as monotherapy as a Category 2A regimen useful in certain circumstances for early relapse patients after at least three prior therapies, including a PI and an immunomodulatory agent, or for patients who are double refractory to a PI and an immunomodulatory agent.

For more information, visit www.DARZALEX.com.

About TALVEY™

TALVEY™ (talquetamab-tgvs) received approval from the U.S. FDA in August 2023 as a first-in-class bispecific antibody 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 antibody.[12] The European Commission (EC) has granted conditional marketing authorization (CMA) of TALVEY™ (talquetamab-tgvs) in August 2023 as monotherapy for the treatment of adult patients with relapsed and refractory multiple myeloma (RRMM) who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody, and have demonstrated disease progression on the last therapy.[13]

TALVEY™ is a bispecific T-cell engaging antibody that binds to the CD3 receptor expressed on the surface of T cells and G protein-coupled receptor class C group 5 member D (GPRC5D), a novel multiple myeloma target which is highly expressed on the surface of multiple myeloma cells and non-malignant plasma cells, as well as some healthy tissues such as epithelial cells of the skin and tongue.

For more information, visit www.TALVEY.com.

About TECVAYLI®

TECVAYLI® (teclistamab-cqyv) received approval from the U.S. FDA in October 2022 as an off-the-shelf (or ready-to-use) antibody that is administered as a subcutaneous treatment for adult patients with relapsed or refractory multiple myeloma (RRMM) who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 antibody.[14] The European Commission (EC) granted TECVAYLI® conditional marketing authorization (CMA) in August 2022 as monotherapy for the treatment of adult patients with RRMM who have received at least three prior therapies, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 antibody, and have demonstrated disease progression since the last therapy.[15] In August 2023, the EC granted the approval of a Type II variation application for TECVAYLI®, providing the option for a reduced dosing frequency of 1.5 mg/kg every two weeks in patients who have achieved a complete response (CR) or better for a minimum of six months.[15] TECVAYLI® is a first-in-class, bispecific T-cell engager antibody therapy that 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.[16]

For more information, visit www.TECVAYLI.com.

About CARVYKTI®

CARVYKTI® (cilta-cel) received U.S. Food and Drug Administration approval in February 2022 for the treatment of adults with relapsed or refractory multiple myeloma after four or more prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.[17] In May 2022, the European Commission granted conditional marketing authorization of CARVYKTI® (cilta-cel) for the treatment of adults with relapsed and refractory multiple myeloma who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 antibody, and have demonstrated disease progression on the last therapy.

CARVYKTI® is a BCMA-directed, genetically modified autologous T-cell immunotherapy, which involves reprogramming a patient's own T-cells with a transgene encoding chimeric antigen receptor (CAR) that directs the CAR-positive T-cells to eliminate cells that express BCMA. BCMA is primarily expressed on the surface of malignant multiple myeloma B-lineage cells, as well as late-stage B cells and plasma cells. The CARVYKTI® CAR protein features two BCMA-targeting single domains designed to confer high avidity against human BCMA. Upon binding to BCMA-expressing cells, the CAR promotes T-cell activation, expansion, and elimination of target cells.

In December 2017, Janssen Biotech, Inc., entered into an exclusive worldwide license and collaboration agreement with Legend Biotech USA, Inc. to develop and commercialize CARVYKTI®.

For more information, visit www.CARVYKTI.com.

About IMBRUVICA®

IMBRUVICA® (ibrutinib) is a once-daily oral medication that is jointly developed and commercialized by Janssen Biotech, Inc., and Pharmacyclics LLC, an AbbVie company. IMBRUVICA® blocks the BTK protein, which is needed by normal and abnormal B cells, including specific cancer cells, to multiply and spread. By blocking BTK, IMBRUVICA® may help move abnormal B cells out of their nourishing environments and inhibit their proliferation.[18,19,20]

IMBRUVICA® is approved in more than 100 countries and has been used to treat nearly 300,000 patients worldwide over the last decade. There are more than 50 company-sponsored clinical trials, including 18 Phase 3 studies, and more than 11 years evaluating the efficacy and safety of IMBRUVICA®.

IMBRUVICA® was first approved by the U.S. FDA in November 2013, and today is indicated for adult patients in four disease areas, including three hematologic cancers. These include indications to treat adults with chronic lymphocytic leukemia (CLL)/ small lymphocytic lymphoma (SLL) with or without 17p deletion (del17p); adults with Waldenström's macroglobulinemia (WM); and adult and pediatric patients aged one year and older with previously treated chronic graft-versus-host disease (cGVHD) after failure of one or more lines of systemic therapy.[21]

For more information, visit www.IMBRUVICA.com.

All information below is applicable to the U.S. FDA indications.

DARZALEX *FASPRO*® IMPORTANT SAFETY INFORMATION

INDICATIONS

DARZALEX *FASPRO*® (daratumumab and hyaluronidase-fihj) is indicated for the treatment of adult patients with multiple myeloma:

- In combination with bortezomib, melphalan, and prednisone in newly diagnosed patients who are ineligible for autologous stem cell transplant
- In combination with lenalidomide and dexamethasone in newly diagnosed patients who are ineligible for autologous stem cell transplant and in patients with relapsed or refractory multiple myeloma who have received at least one prior therapy
- In combination with bortezomib, thalidomide, and dexamethasone in newly diagnosed patients who are eligible for autologous stem cell transplant
- In combination with pomalidomide and dexamethasone in patients who have received at least one prior line of therapy including lenalidomide and a proteasome inhibitor
- In combination with carfilzomib and dexamethasone in patients with relapsed or refractory multiple myeloma who have received one to three prior lines of therapy
- In combination with bortezomib and dexamethasone in patients who have received at least one prior therapy
- As monotherapy in patients who have received at least three prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent or who are double-refractory to a PI and an immunomodulatory agent

CONTRAINDICATIONS

DARZALEX *FASPRO*® is contraindicated in patients with a history of severe hypersensitivity to daratumumab, hyaluronidase, or any of the components of the formulation.

WARNINGS AND PRECAUTIONS

Hypersensitivity and Other Administration Reactions

Both systemic administration-related reactions, including severe or life-threatening reactions, and local injection-site reactions can occur with DARZALEX *FASPRO*®. Fatal reactions have been reported with daratumumab-containing products, including DARZALEX *FASPRO*®.

Systemic Reactions

In a pooled safety population of 898 patients with multiple myeloma (N=705) or light chain (AL) amyloidosis (N=193) who received DARZALEX *FASPRO*® as monotherapy or in combination, 9% of patients experienced a systemic administration-related reaction (Grade 2: 3.2%, Grade 3: 1%). Systemic administration-related reactions occurred in 8% of patients with the first injection, 0.3% with the second injection, and cumulatively 1% with subsequent injections. The median time to onset was 3.2 hours (range: 4 minutes to 3.5 days). Of the 140 systemic administration-related reactions that occurred in 77 patients, 121 (86%) occurred on the day of DARZALEX *FASPRO*® administration. Delayed systemic administration-related reactions have occurred in 1% of the patients.

Severe reactions included hypoxia, dyspnea, hypertension, tachycardia, and ocular adverse reactions, including choroidal effusion, acute myopia, and acute angle closure glaucoma. Other signs and symptoms of systemic administration-related reactions may include respiratory symptoms, such as bronchospasm, nasal congestion, cough, throat irritation, allergic rhinitis, and wheezing, as well as anaphylactic reaction, pyrexia, chest pain, pruritus, chills, vomiting, nausea, hypotension, and blurred vision.

Pre-medicate patients with histamine-1 receptor antagonist, acetaminophen, and corticosteroids. Monitor patients for systemic administration-related reactions, especially following the first and second injections. For anaphylactic reaction or life-threatening (Grade 4) administration-related reactions, immediately and permanently discontinue DARZALEX *FASPRO*®. Consider administering corticosteroids and other medications after the administration of DARZALEX *FASPRO*® depending on dosing regimen and medical history to minimize the risk of delayed (defined as occurring the day after administration) systemic administration-related reactions.

Ocular adverse reactions, including acute myopia and narrowing of the anterior chamber angle due to ciliochoroidal effusions with potential for increased intraocular pressure or glaucoma, have occurred with daratumumab-containing products. If ocular symptoms occur, interrupt DARZALEX *FASPRO*® and seek immediate ophthalmologic evaluation prior to restarting DARZALEX *FASPRO*®.

Local Reactions

In this pooled safety population, injection-site reactions occurred in 8% of patients, including Grade 2 reactions in 0.7%. The most frequent (>1%) injection-site reaction was injection-site erythema. These local reactions occurred a median of 5 minutes (range: 0 minutes to 6.5 days) after starting administration of DARZALEX *FASPRO*®. Monitor for local reactions and consider symptomatic management.

Neutropenia

Daratumumab may increase neutropenia induced by background therapy. Monitor complete blood cell counts periodically during treatment according to manufacturer's prescribing information for background therapies. Monitor patients with neutropenia for signs of infection. Consider withholding DARZALEX *FASPRO*® until recovery of neutrophils. In lower body weight patients receiving DARZALEX *FASPRO*®, higher rates of Grade 3-4 neutropenia were observed.

Thrombocytopenia

Daratumumab may increase thrombocytopenia induced by background therapy. Monitor complete blood cell counts periodically during treatment according to manufacturer's prescribing information for background therapies. Consider withholding DARZALEX *FASPRO*® until recovery of platelets.

Embryo-Fetal Toxicity

Based on the mechanism of action, DARZALEX *FASPRO*® can cause fetal harm when administered to a pregnant woman. DARZALEX *FASPRO*® may cause depletion of fetal immune cells and decreased bone density. Advise pregnant women of the potential risk to a fetus. Advise females with reproductive potential to use effective contraception during treatment with DARZALEX *FASPRO*® and for 3 months after the last dose.

The combination of DARZALEX *FASPRO*® with lenalidomide, thalidomide, or pomalidomide is contraindicated in pregnant women because lenalidomide, thalidomide, and pomalidomide may cause birth defects and death of the unborn child. Refer to the lenalidomide, thalidomide, or pomalidomide prescribing information on use during pregnancy.

Interference with Serological Testing

Daratumumab binds to CD38 on red blood cells (RBCs) and results in a positive indirect antiglobulin test (indirect Coombs test). Daratumumab-mediated positive indirect antiglobulin test may persist for up to 6 months after the last daratumumab administration. Daratumumab bound to RBCs masks detection of antibodies to minor antigens in the patient's serum. The determination of a patient's ABO and Rh blood type are not impacted.

Notify blood transfusion centers of this interference with serological testing and inform blood banks that a patient has received DARZALEX *FASPRO*®. Type and screen patients prior to starting DARZALEX *FASPRO*®.

Interference With Determination of Complete Response

Daratumumab is a human immunoglobulin G (IgG) kappa monoclonal antibody that can be detected on both the serum protein electrophoresis (SPE) and immunofixation (IFE) assays used for the clinical monitoring of endogenous M-protein. This interference can impact the determination of complete response and of disease progression in some DARZALEX *FASPRO*®-treated patients with IgG kappa myeloma protein.

ADVERSE REACTIONS

In multiple myeloma, the most common adverse reaction (≥20%) with DARZALEX *FASPRO*® monotherapy is upper respiratory tract infection. The most common adverse reactions with combination therapy (≥20% for any combination) include fatigue, nausea, diarrhea, dyspnea, insomnia, headache, pyrexia, cough, muscle spasms, back pain, vomiting, hypertension, upper respiratory tract infection, peripheral sensory neuropathy, constipation, pneumonia, and peripheral edema.

The most common hematology laboratory abnormalities (≥40%) with DARZALEX *FASPRO*® are decreased leukocytes, decreased lymphocytes, decreased neutrophils, decreased platelets, and decreased hemoglobin.

Please click here to see the full Prescribing Information.

DARZALEX® IMPORTANT SAFETY INFORMATION

INDICATIONS

DARZALEX® (daratumumab) is indicated for the treatment of adult patients with multiple myeloma:

- In combination with lenalidomide and dexamethasone in newly diagnosed patients who are ineligible for autologous stem cell transplant and in patients with relapsed or refractory multiple myeloma who have received at least one prior therapy
- In combination with bortezomib, melphalan, and prednisone in newly diagnosed patients who are ineligible for autologous stem cell transplant
- In combination with bortezomib, thalidomide, and dexamethasone in newly diagnosed patients who are eligible for autologous stem cell transplant
- In combination with bortezomib and dexamethasone in patients who have received at least one prior therapy
- In combination with carfilzomib and dexamethasone in patients with relapsed or refractory multiple myeloma who have received one to three prior lines of therapy
- In combination with pomalidomide and dexamethasone in patients who have received at least two prior therapies including lenalidomide and a proteasome inhibitor
- As monotherapy in patients who have received at least three prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent or who are double-refractory to a PI and an immunomodulatory agent

CONTRAINDICATIONS

DARZALEX® is contraindicated in patients with a history of severe hypersensitivity (eg, anaphylactic reactions) to daratumumab or any of the components of the formulation.

WARNINGS AND PRECAUTIONS

Infusion-Related Reactions

DARZALEX® can cause severe and/or serious infusion-related reactions including anaphylactic reactions. These reactions can be life-threatening, and fatal outcomes have been reported. In clinical trials (monotherapy and combination: N=2066), infusion-related reactions occurred in 37% of patients with the Week 1 (16 mg/kg) infusion, 2% with the Week 2 infusion, and cumulatively 6% with subsequent infusions. Less than 1% of patients had a Grade 3/4 infusion-related reaction at Week 2 or subsequent infusions. The median time to onset was 1.5 hours (range: 0 to 73 hours). Nearly all reactions occurred during infusion or within 4 hours of completing DARZALEX®. Severe reactions have occurred, including bronchospasm, hypoxia, dyspnea, hypertension, tachycardia, headache, laryngeal edema, pulmonary edema, and ocular adverse reactions, including choroidal effusion, acute myopia, and acute angle closure glaucoma. Signs and symptoms may include respiratory symptoms, such as nasal congestion, cough, throat irritation, as well as chills, vomiting, and nausea. Less common signs and symptoms were wheezing, allergic rhinitis, pyrexia, chest discomfort, pruritus, hypotension, and blurred vision.

When DARZALEX® dosing was interrupted in the setting of ASCT (CASSIOPEIA) for a median of 3.75 months (range: 2.4 to 6.9 months), upon re-initiation of DARZALEX®, the incidence of infusion-related reactions was 11% for the first infusion following ASCT. Infusion-related reactions occurring at re-initiation of DARZALEX® following ASCT were consistent in terms of symptoms and severity (Grade 3 or 4: <1%) with those reported in previous studies at Week 2 or subsequent infusions. In EQUULEUS, patients receiving combination treatment (n=97) were administered the first 16 mg/kg dose at Week 1 split over two days, ie, 8 mg/kg on Day 1 and Day 2, respectively. The incidence of any grade infusion-related reactions was 42%, with 36% of patients experiencing infusion-related reactions on Day 1 of Week 1, 4% on Day 2 of Week 1, and 8% with subsequent infusions.

Pre-medicate patients with antihistamines, antipyretics, and corticosteroids. Frequently monitor patients during the entire infusion. Interrupt DARZALEX® infusion for reactions of any severity and institute medical management as needed. Permanently discontinue DARZALEX® therapy if an anaphylactic reaction or life-threatening (Grade 4) reaction occurs and institute appropriate emergency care. For patients with Grade 1, 2, or 3 reactions, reduce the infusion rate when re-starting the infusion.

To reduce the risk of delayed infusion-related reactions, administer oral corticosteroids to all patients following DARZALEX® infusions. Patients with a history of chronic obstructive pulmonary disease may require additional post-infusion medications to manage respiratory complications. Consider prescribing short- and long-acting bronchodilators and inhaled corticosteroids for patients with chronic obstructive pulmonary disease.

Ocular adverse reactions, including acute myopia and narrowing of the anterior chamber angle due to ciliochoroidal effusions with potential for increased intraocular pressure or glaucoma, have occurred with DARZALEX® infusion. If ocular symptoms occur, interrupt DARZALEX® infusion and seek immediate ophthalmologic evaluation prior to restarting DARZALEX®.

Interference With Serological Testing

Daratumumab binds to CD38 on red blood cells (RBCs) and results in a positive indirect antiglobulin test (indirect Coombs test). Daratumumab-mediated positive indirect antiglobulin test may persist for up to 6 months after the last daratumumab infusion. Daratumumab bound to RBCs masks detection of antibodies to minor antigens in the patient's serum. The determination of a patient's ABO and Rh blood type is not impacted. Notify blood transfusion centers of this interference with serological testing and inform blood banks that a patient has received DARZALEX®. Type and screen patients prior to starting DARZALEX®.

Neutropenia and Thrombocytopenia

DARZALEX® may increase neutropenia and thrombocytopenia induced by background therapy. Monitor complete blood cell counts periodically during treatment according to manufacturer's prescribing information for background therapies. Monitor patients with neutropenia for signs of infection. Consider withholding DARZALEX® until recovery of neutrophils or for recovery of platelets.

Interference With Determination of Complete Response

Daratumumab is a human immunoglobulin G (IgG) kappa monoclonal antibody that can be detected on both the serum protein electrophoresis (SPE) and immunofixation (IFE) assays used for the clinical monitoring of endogenous M-protein. This interference can impact the determination of complete response and of disease progression in some patients with IgG kappa myeloma protein.

Embryo-Fetal Toxicity

Based on the mechanism of action, DARZALEX® can cause fetal harm when administered to a pregnant woman. DARZALEX® may cause depletion of fetal immune cells and decreased bone density. Advise pregnant women of the potential risk to a fetus. Advise females with reproductive potential to use effective contraception during treatment with DARZALEX® and for 3 months after the last dose.

The combination of DARZALEX® with lenalidomide, pomalidomide, or thalidomide is contraindicated in pregnant women because lenalidomide, pomalidomide, and thalidomide may cause birth defects and death of the unborn child. Refer to the lenalidomide, pomalidomide, or thalidomide prescribing information on use during pregnancy.

ADVERSE REACTIONS

The most frequently reported adverse reactions (incidence ≥20%) were upper respiratory infection, neutropenia, infusion-related reactions, thrombocytopenia, diarrhea, constipation, anemia, peripheral sensory neuropathy, fatigue, peripheral edema, nausea, cough, pyrexia, dyspnea, and asthenia. The most common hematologic laboratory abnormalities (≥40%) with DARZALEX® are neutropenia, lymphopenia, thrombocytopenia, leukopenia, and anemia.

Please click here to see the full Prescribing Information.

TALVEY™ 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 TALVEY™. Initiate TALVEY™ treatment with step-up dosing to reduce the risk of CRS. Withhold TALVEY™ until CRS resolves or permanently discontinue based on severity.

Neurologic toxicity, including immune effector cell-associated neurotoxicity syndrome (ICANS), and serious and life-threatening or fatal reactions, can occur with TALVEY™. Monitor patients for signs and symptoms of neurologic toxicity including ICANS during treatment. Withhold or discontinue TALVEY™ based on severity.

Because of the risk of CRS and neurologic toxicity, including ICANS, TALVEY™ is available only through a restricted program called the TECVAYLI® and TALVEY™ Risk Evaluation and Mitigation Strategy (REMS).

INDICATION AND USAGE

TALVEY™ (talquetamab-tgvs) is 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 and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

CONTRAINDICATIONS: None.

WARNINGS AND PRECAUTIONS

Cytokine Release Syndrome (CRS): TALVEY™ can cause cytokine release syndrome, including life-threatening or fatal reactions. In the clinical trial, CRS occurred in 76% of patients who received TALVEY™ at the recommended dosages, with Grade 1 CRS occurring in 57% of patients, Grade 2 in 17%, and Grade 3 in 1.5%. Recurrent CRS occurred in 30% of patients. CRS occurred in 33% of patients with step-up dose 3 in the biweekly dosing schedule (N=153). CRS occurred in 30% of patients with the first 0.4 mg/kg treatment dose and in 12% of patients treated with the first 0.8 mg/kg treatment dose. The CRS rate for both dosing schedules combined was less than 3% for each of the remaining doses in Cycle 1 and less than 3% cumulatively from Cycle 2 onward. The median time to onset of CRS was 27 (range: 0.1 to 167) hours from the last dose, and the median duration was 17 (range: 0 to 622) hours. Clinical signs and symptoms of CRS include but are not limited to pyrexia, hypotension, chills, hypoxia, headache, and tachycardia. Potentially life-threatening complications of CRS may include cardiac dysfunction, acute respiratory distress syndrome, neurologic toxicity, renal and/or hepatic failure, and disseminated intravascular coagulation (DIC).

Initiate therapy with step-up dosing and administer pre-treatment medications (corticosteroids, antihistamine, and antipyretics) prior to each dose of TALVEY™ in the step-up dosing schedule to reduce the risk of CRS. Monitor patients following administration accordingly. In patients who experience CRS, pre-treatment medications should be administered prior to the next TALVEY™ dose.

Counsel patients to seek medical attention should signs or symptoms of CRS occur. At the first sign of CRS, immediately evaluate patient for hospitalization and institute treatment with supportive care based on severity, and consider further management per current practice guidelines. Withhold TALVEY™ until CRS resolves or permanently discontinue based on severity.

Neurologic Toxicity including ICANS: TALVEY™ can cause serious, life-threatening or fatal neurologic toxicity, including immune effector cell-associated neurotoxicity syndrome (ICANS), including fatal reactions. In the clinical trial, neurologic toxicity including ICANS occurred in 55% of patients

who received the recommended dosages, with Grade 3 or 4 neurologic toxicity occurring in 6% of patients. The most frequent neurologic toxicities were headache (20%), encephalopathy (15%), sensory neuropathy (14%), and motor dysfunction (10%).

ICANS was reported in 9% of 265 patients where ICANS was collected and who received the recommended dosages. Recurrent ICANS occurred in 3% of patients. Most patients experienced ICANS following step-up dose 1 (3%), step-up dose 2 (3%), step-up dose 3 of the biweekly dosing schedule (1.8%), or the initial treatment dose of the weekly dosing schedule (2.6%) (N=156) or the biweekly dosing schedule (3.7%) (N=109). The median time to onset of ICANS was 2.5 (range: 1 to 16) days after the most recent dose with a median duration of 2 (range: 1 to 22) days. The onset of ICANS can be concurrent with CRS, following resolution of CRS, or in the absence of CRS. Clinical signs and symptoms of ICANS may include but are not limited to confusional state, depressed level of consciousness, disorientation, somnolence, lethargy, and bradyphrenia.

Monitor patients for signs and symptoms of neurologic toxicity during treatment. At the first sign of neurologic toxicity, including ICANS, immediately evaluate the patient and provide supportive care based on severity; withhold or permanently discontinue TALVEY™ based on severity and consider further management per current practice guidelines (*see Dosage and Administration [2.5]*).

Due to the potential for neurologic toxicity, patients receiving TALVEY™ are at risk of depressed level of consciousness. Advise patients to refrain from driving or operating heavy or potentially dangerous machinery during the step-up dosing schedule and for 48 hours after completion of the step-up dosing schedule, and in the event of new onset of any neurological symptoms, until symptoms resolve.

TECVAYLI® and TALVEY™ REMS: TALVEY™ 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.

Further information about the TECVAYLI® and TALVEY™ REMS program is available at www.TEC-TALREMS.com or by telephone at 1-855-810-8064.

Oral Toxicity and Weight Loss: TALVEY™ can cause oral toxicities, including dysgeusia, dry mouth, dysphagia, and stomatitis. In the clinical trial, 80% of patients had oral toxicity, with Grade 3 occurring in 2.1% of patients who received the recommended dosages. The most frequent oral toxicities were dysgeusia (49%), dry mouth (34%), dysphagia (23%), and ageusia (18%). The median time to onset of oral toxicity was 15 (range: 1 to 634) days, and the median time to resolution to baseline was 43 (1 to 530) days. Oral toxicity did not resolve to baseline in 65% of patients.

TALVEY™ can cause weight loss. In the clinical trial, 62% of patients experienced weight loss of 5% or greater, regardless of having an oral toxicity, including 28% of patients with Grade 2 (10% or greater) weight loss and 2.7% of patients with Grade 3 (20% or greater) weight loss. The median time to onset of Grade 2 or higher weight loss was 67 (range: 6 to 407) days, and the median time to resolution was 50 (range: 1 to 403) days. Weight loss did not resolve in 57% of patients who reported weight loss.

Monitor patients for signs and symptoms of oral toxicity. Counsel patients to seek medical attention should signs or symptoms of oral toxicity occur and provide supportive care as per current clinical practice, including consultation with a nutritionist. Monitor weight regularly during therapy. Evaluate clinically significant weight loss further. Withhold TALVEY™ or permanently discontinue based on severity.

Infections: TALVEY™ can cause infections, including life-threatening or fatal infections. Serious infections occurred in 16% of patients, with fatal infections in 1.5% of patients. Grade 3 or 4 infections occurred in 17% of patients. The most common serious infections reported were bacterial infection (8%), which included sepsis and COVID-19 (2.7%).

Monitor patients for signs and symptoms of infection prior to and during treatment with TALVEY™ and treat appropriately. Administer prophylactic antimicrobials according to local guidelines. Withhold or permanently discontinue TALVEY™ as recommended, based on severity.

Cytopenias: TALVEY™ can cause cytopenias, including neutropenia and thrombocytopenia. In the clinical trial, Grade 3 or 4 decreased neutrophils occurred in 35% of patients, and Grade 3 or 4 decreased platelets occurred in 22% of patients who received TALVEY™. The median time to onset for Grade 3 or 4 neutropenia was 22 (range: 1 to 312) days, and the median time to resolution to Grade 2 or lower was 8 (range: 1 to 79) days. The median time to onset for Grade 3 or 4 thrombocytopenia was 12 (range: 2 to 183) days, and the median time to resolution to Grade 2 or lower was 10 (range: 1 to 64) days. Monitor complete blood counts during treatment and withhold TALVEY™ as recommended, based on severity.

Skin Toxicity: TALVEY™ can cause serious skin reactions, including rash, maculo-papular rash, erythema, and erythematous rash. In the clinical trial, skin reactions occurred in 62% of patients, with grade 3 skin reactions in 0.3%. The median time to onset was 25 (range: 1 to 630) days. The median time to improvement to grade 1 or less was 33 days.

Monitor for skin toxicity, including rash progression. Consider early intervention and treatment to manage skin toxicity. In the clinical trial, supportive care included topical steroids (15%). Oral steroid tapers (4.4%) were typically administered for Grade 3 skin reactions. Withhold or permanently discontinue TALVEY™, based on severity.

Hepatotoxicity: TALVEY™ can cause hepatoxicity. Elevated ALT occurred in 33% of patients, with grade 3 or 4 ALT elevation occurring in 2.7%; elevated AST occurred in 31% of patients, with grade 3 or 4 AST elevation occurring in 3.3%. Grade 3 or 4 elevations of total bilirubin occurred in 0.3% of patients. Liver enzyme elevation can occur with or without concurrent CRS.

Monitor liver enzymes and bilirubin at baseline and during treatment as clinically indicated. Withhold TALVEY™ or consider permanent discontinuation of TALVEY™, based on severity (*see Dosage and Administration [2.5]*).

Embryo-Fetal Toxicity: Based on its mechanism of action, TALVEY™ 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 TALVEY™ and for 3 months after the last dose.

Adverse Reactions: The most common adverse reactions (≥20%) are pyrexia, CRS, dysgeusia, nail disorder, musculoskeletal pain, skin disorder, rash, fatigue, weight decreased, dry mouth, xerosis, dysphagia, upper respiratory tract infection, diarrhea, hypotension, and headache.

The most common Grade 3 or 4 laboratory abnormalities (≥30%) are lymphocyte count decreased, neutrophil count decreased, white blood cell decreased, and hemoglobin decreased.

Please read full Prescribing Information, including Boxed Warning, for TALVEY™.

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. 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).

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).

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® 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.

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

CARVYKTI® IMPORTANT SAFETY INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME, NEUROLOGIC TOXICITIES, HLH/MAS, and PROLONGED and RECURRENT CYTOPENIA

Cytokine Release Syndrome (CRS), including fatal or life-threatening reactions, occurred in patients following treatment with CARVYKTI®. Do not administer CARVYKTI® to patients with active infection or inflammatory disorders. Treat severe or life-threatening CRS with tocilizumab or tocilizumab and corticosteroids.

Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS), which may be fatal or life-threatening, occurred following treatment with CARVYKTI®, including before CRS onset, concurrently with CRS, after CRS resolution, or in the absence of CRS. Monitor for neurologic events after treatment with CARVYKTI®. Provide supportive care and/or corticosteroids as needed.

Parkinsonism and Guillain-Barré syndrome and their associated complications resulting in fatal or life-threatening reactions have occurred following treatment with CARVYKTI®.

Hemophagocytic Lymphohistiocytosis/Macrophage Activation Syndrome (HLH/MAS), including fatal and life-threatening reactions, occurred in patients following treatment with CARVYKTI®. HLH/MAS can occur with CRS or neurologic toxicities.

Prolonged and/or recurrent cytopenias with bleeding and infection and requirement for stem cell transplantation for hematopoietic recovery occurred following treatment with CARVYKTI®.

CARVYKTI® is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the CARVYKTI® REMS Program.

WARNINGS AND PRECAUTIONS

Cytokine Release Syndrome (CRS) including fatal or life-threatening reactions, occurred following treatment with CARVYKTI® in 95% (92/97) of patients receiving ciltacabtagene autoleucel. Grade 3 or higher CRS (2019 ASTCT grade) occurred in 5% (5/97) of patients, with Grade 5 CRS reported in 1 patient. The median time to onset of CRS was 7 days (range: 1–12 days). The most common manifestations of CRS included pyrexia (100%), hypotension (43%), increased aspartate aminotransferase (AST) (22%), chills (15%), increased alanine aminotransferase (ALT) (14%) and sinus tachycardia (11%). Grade 3 or higher events associated with CRS included increased AST and ALT, hyperbilirubinemia, hypotension, pyrexia, hypoxia,

respiratory failure, acute kidney injury, disseminated intravascular coagulation and hemorrhage, HLH/MAS, angina pectoris, supraventricular and ventricular tachycardia, malaise, myalgias, increased C-reactive protein, ferritin, blood alkaline phosphatase and gamma-glutamyl transferase.

Identify CRS based on clinical presentation. Evaluate for and treat other causes of fever, hypoxia, and hypotension. CRS has been reported to be associated with findings of HLH/MAS, and the physiology of the syndromes may overlap. HLH/MAS is a potentially life-threatening condition. In patients with progressive symptoms of CRS or refractory CRS despite treatment, evaluate for evidence of HLH/MAS. One patient with CRS and suspected HLH/MAS developed a fatal retroperitoneal hemorrhage in the setting of thrombocytopenia, coagulopathy and anticoagulation.

Sixty-nine of 97 (71%) patients received tocilizumab and/or a corticosteroid for CRS after infusion of ciltacabtagene autoleucel. Forty-four (45%) patients received only tocilizumab, of whom 33 (34%) received a single dose and 11 (11%) received more than one dose; 24 patients (25%) received tocilizumab and a corticosteroid, and one patient (1%) received only corticosteroids. Ensure that a minimum of two doses of tocilizumab are available prior to infusion of CARVYKTI®.

Monitor patients at least daily for 10 days following CARVYKTI® infusion at a REMS-certified healthcare facility for signs and symptoms of CRS. Monitor patients for signs or symptoms of CRS for at least 4 weeks after infusion. At the first sign of CRS, immediately institute treatment with supportive care, tocilizumab, or tocilizumab and corticosteroids.

Counsel patients to seek immediate medical attention should signs or symptoms of CRS occur at any time.

Neurologic toxicities, which may be severe, life-threatening or fatal, occurred following treatment with CARVYKTI®. Neurologic toxicities included ICANS, neurologic toxicity with signs and symptoms of parkinsonism, Guillain-Barré Syndrome, immune mediated myelitis, peripheral neuropathies, and cranial nerve palsies. Counsel patients on the signs and symptoms of these neurologic toxicities, and on the delayed nature of onset of some of these toxicities. Instruct patients to seek immediate medical attention for further assessment and management if signs or symptoms of any of these neurologic toxicities occur at any time.

Overall, one or more subtypes of neurologic toxicity described below occurred following ciltacabtagene autoleucel in 26% (25/97) of patients, of which 11% (11/97) of patients experienced Grade 3 or higher events. These subtypes of neurologic toxicities were also observed in two ongoing studies.

Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS): Patients may experience fatal or life-threatening ICANS following treatment with CARVYKTI®, including before CRS onset, concurrently with CRS, after CRS resolution, or in the absence of CRS. ICANS occurred in 23% (22/97) of patients receiving ciltacabtagene autoleucel including Grade 3 or 4 events in 3% (3/97) and Grade 5 (fatal) events in 2% (2/97). The median time to onset of ICANS was 8 days (range 1-28 days). All 22 patients with ICANS had CRS. The most frequent (≥5%) manifestation of ICANS included encephalopathy (23%), aphasia (8%) and headache (6%).

Monitor patients at least daily for 10 days following CARVYKTI® infusion at the REMS certified healthcare facility for signs and symptoms of ICANS. Rule out other causes of ICANS symptoms. Monitor patients for signs or symptoms of ICANS for at least 4 weeks after infusion and treat promptly. Neurologic toxicity should be managed with supportive care and/or corticosteroids as needed.

Parkinsonism: Of the 25 patients in the CARTITUDE-1 study experiencing any neurotoxicity, five male patients had neurologic toxicity with several signs and symptoms of parkinsonism, distinct from immune effector cell-associated neurotoxicity syndrome (ICANS). Neurologic toxicity with parkinsonism has been reported in other ongoing trials of ciltacabtagene autoleucel. Patients had parkinsonian and non-parkinsonian symptoms that included tremor, bradykinesia, involuntary movements, stereotypy, loss of spontaneous movements, masked facies, apathy, flat affect, fatigue, rigidity, psychomotor retardation, micrographia, dysgraphia, apraxia, lethargy, confusion, somnolence, loss of consciousness, delayed reflexes, hyperreflexia, memory loss, difficulty swallowing, bowel incontinence, falls, stooped posture, shuffling gait, muscle weakness and wasting, motor dysfunction, motor and sensory loss, akinetic mutism, and frontal lobe release signs. The median onset of parkinsonism in the 5 patients in CARTITUDE-1 was 43 days (range 15-108) from infusion of ciltacabtagene autoleucel.

Monitor patients for signs and symptoms of parkinsonism that may be delayed in onset and managed with supportive care measures. There is limited efficacy information with medications used for the treatment of Parkinson's disease, for the improvement or resolution of parkinsonism symptoms following CARVYKTI® treatment.

Guillain-Barré Syndrome: A fatal outcome following Guillain-Barré Syndrome (GBS) has occurred in another ongoing study of ciltacabtagene autoleucel despite treatment with intravenous immunoglobulin (IVIG). Symptoms reported include those consistent with Miller-Fisher variant of GBS, encephalopathy, motor weakness, speech disturbances and polyradiculoneuritis.

Monitor for GBS. Evaluate patients presenting with peripheral neuropathy for GBS. Consider treatment of GBS with supportive care measures and in conjunction with immunoglobulin and plasma exchange, depending on severity of GBS.

Immune Mediated Myelitis: Grade 3 myelitis has occurred 25 days following treatment in another ongoing study. Symptoms reported included hypoesthesia of the lower extremities and the lower abdomen with impaired sphincter control. Symptoms improved with the use of corticosteroids and intravenous immunoglobulin. Myelitis was ongoing at the time of death from other cause.

Peripheral Neuropathy: Six patients in CARTITUDE-1 developed peripheral neuropathy. These neuropathies presented as sensory, motor or sensorimotor neuropathies. Median time of onset of symptoms was 62 days (range 4-136 days), median duration of peripheral neuropathies was 256 days (range 2-465 days) including those with ongoing neuropathy. Patients who experienced peripheral neuropathy also experienced cranial nerve palsies or GBS in other ongoing trials of ciltacabtagene autoleucel. Monitor patients for signs and symptoms of peripheral neuropathies.

Cranial Nerve Palsies: Three patients (3.1%) experienced cranial nerve palsies in CARTITUDE-1. All three patients had 7th cranial nerve palsy; one patient had 5th cranial nerve palsy as well. Median time to onset was 26 days (range 21-101 days) following infusion of ciltacabtagene autoleucel. Occurrence of 3rd and 6th cranial nerve palsy, bilateral 7th cranial nerve palsy, worsening of cranial nerve palsy after improvement, and occurrence of peripheral neuropathy in patients with cranial nerve palsy have also been reported in ongoing trials of ciltacabtagene autoleucel. Monitor patients for signs and symptoms of cranial nerve palsies. Consider management with systemic corticosteroids, depending on the severity and progression of signs and symptoms.

Hemophagocytic Lymphohistiocytosis (HLH)/Macrophage Activation Syndrome (MAS): Fatal HLH occurred in one patient (1%), 99 days after ciltacabtagene autoleucel. The HLH event was preceded by prolonged CRS lasting 97 days. The manifestations of HLH/MAS include hypotension, hypoxia with diffuse alveolar damage, coagulopathy, cytopenia, and multi-organ dysfunction, including renal dysfunction.

One patient with Grade 4 HLH/MAS developed fatal intracerebral and gastrointestinal hemorrhage in the setting of coagulopathy and thrombocytopenia 12 days after treatment in another ongoing study. Patients who develop HLH/MAS have an increased risk of severe bleeding. Monitor hematological parameters in patients with HLH/MAS and transfuse per institutional guidelines.

HLH is a life-threatening condition with a high mortality rate if not recognized and treated early. Treatment of HLH/MAS should be administered per institutional standards.

CARVYKTI® REMS: Because of the risk of CRS and neurologic toxicities, CARVYKTI® is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the CARVYKTI® REMS.

Further information is available at https://www.carvyktirems.com/ or 1-844-672-0067.

Prolonged and Recurrent Cytopenias: Patients may exhibit prolonged and recurrent cytopenias following lymphodepleting chemotherapy and CARVYKTI® infusion. One patient underwent autologous stem cell therapy for hematopoietic reconstitution due to prolonged thrombocytopenia.

In CARTITUDE-1, 30% (29/97) of patients experienced prolonged Grade 3 or 4 neutropenia and 41% (40/97) of patients experienced prolonged Grade 3 or 4 thrombocytopenia that had not resolved by Day 30 following ciltacabtagene autoleucel infusion.

Recurrent Grade 3 or 4 neutropenia, thrombocytopenia, lymphopenia and anemia were seen in 63% (61/97), 18% (17/97), 60% (58/97), and 37% (36/97) after recovery from initial Grade 3 or 4 cytopenia following infusion. After Day 60 following ciltacabtagene autoleucel infusion, 31%, 12% and 6% of patients had a recurrence of Grade 3 or higher lymphopenia, neutropenia and thrombocytopenia, respectively, after initial recovery of their Grade 3 or 4 cytopenia. Eighty-seven percent (84/97) of patients had one, two, or three or more recurrences of Grade 3 or 4 cytopenias after initial recovery of Grade 3 or 4 cytopenia. Six and 11 patients had Grade 3 or 4 neutropenia and thrombocytopenia, respectively, at the time of death.

Monitor blood counts prior to and after CARVYKTI® infusion. Manage cytopenias with growth factors and blood product transfusion support according to local institutional guidelines.

Infections: CARVYKTI® should not be administered to patients with active infection or inflammatory disorders. Severe, life-threatening or fatal infections occurred in patients after CARVYKTI® infusion.

Infections (all grades) occurred in 57 (59%) patients. Grade 3 or 4 infections occurred in 23% (22/97) of patients; Grade 3 or 4 infections with an unspecified pathogen occurred in 17%, viral infections in 7%, bacterial infections in 1%, and fungal infections in 1% of patients. Overall, four patients had Grade 5 infections: lung abscess (n=1), sepsis (n=2) and pneumonia (n=1).

Grade 5 infections reported in other studies include bronchopulmonary aspergillosis, pneumocystis jirovecii pneumonia, and CMV colitis (with HSV-1 hepatitis). Another patient developed mycotic aneurysm due to cerebral aspergillosis and died of subarachnoid hemorrhage.

Monitor patients for signs and symptoms of infection before and after CARVYKTI® infusion and treat patients appropriately. Administer prophylactic, pre-emptive and/or therapeutic antimicrobials according to the standard institutional guidelines. Febrile neutropenia was observed in 10% of patients after ciltacabtagene autoleucel infusion, and may be concurrent with CRS. In the event of febrile neutropenia, evaluate for infection and manage with broad-spectrum antibiotics, fluids and other supportive care, as medically indicated.

In a randomized controlled study of relapsed or refractory multiple myeloma (CARTITUDE-4), patients treated with ciltacabtagene autoleucel had an increased rate of fatal COVID-19 infections compared to the standard therapy arm. Counsel patients on the importance of prevention measures. Follow institutional guidelines for the vaccination and management of immunocompromised patients with COVID-19.

Viral Reactivation: Hepatitis B virus (HBV) reactivation, in some cases resulting in fulminant hepatitis, hepatic failure and death, can occur in patients with hypogammaglobulinemia. Perform screening for Cytomegalovirus (CMV), HBV, hepatitis C virus (HCV), and human immunodeficiency virus (HIV), or any other infectious agents if clinically indicated in accordance with clinical guidelines before collection of cells for manufacturing. Consider antiviral therapy to prevent viral reactivation per local institutional guidelines/clinical practice.

Hypogammaglobulinemia was reported as an adverse event in 12% (12/97) of patients; laboratory IgG levels fell below 500 mg/dL after infusion in 92% (89/97) of patients. Monitor immunoglobulin levels after treatment with CARVYKTI® and administer IVIG for IgG <400 mg/dL. Manage per local institutional guidelines, including infection precautions and antibiotic or antiviral prophylaxis.

Use of Live Vaccines: The safety of immunization with live viral vaccines during or following CARVYKTI® treatment has not been studied. Vaccination with live virus vaccines is not recommended for at least 6 weeks prior to the start of lymphodepleting chemotherapy, during CARVYKTI® treatment, and until immune recovery following treatment with CARVYKTI®.

Hypersensitivity Reactions have occurred in 5% (5/97) of patients following ciltacabtagene autoleucel infusion. Serious hypersensitivity reactions, including anaphylaxis, may be due to the dimethyl sulfoxide (DMSO) in CARVYKTI®. Patients should be carefully monitored for 2 hours after infusion for signs and symptoms of severe reaction. Treat promptly and manage appropriately according to the severity of the hypersensitivity reaction.

Secondary Malignancies: Patients may develop secondary malignancies. Monitor life-long for secondary malignancies. In the event that a secondary malignancy occurs, contact Janssen Biotech, Inc., at 1-800-526-7736 for reporting and to obtain instructions on collection of patient samples for testing of secondary malignancy of T cell origin.

Effects on Ability to Drive and Use Machines: Due to the potential for neurologic events, including altered mental status, seizures, neurocognitive decline, or neuropathy, patients are at risk for altered or decreased consciousness or coordination in the 8 weeks following CARVYKTI® infusion. Advise patients to refrain from driving and engaging in hazardous occupations or activities, such as operating heavy or potentially dangerous machinery during this initial period, and in the event of new onset of any neurologic toxicities.

ADVERSE REACTIONS

The most common non-laboratory adverse reactions (incidence greater than 20%) are pyrexia, cytokine release syndrome, hypogammaglobulinemia, hypotension, musculoskeletal pain, fatigue, infections of unspecified pathogen, cough, chills, diarrhea, nausea, encephalopathy, decreased appetite, upper respiratory tract infection, headache, tachycardia, dizziness, dyspnea, edema, viral infections, coagulopathy, constipation, and vomiting. The most common laboratory adverse reactions (incidence greater than or equal to 50%) include thrombocytopenia, neutropenia, anemia, aminotransferase elevation, and hypoalbuminemia.

Please read full Prescribing Information, including Boxed Warning, for CARVYKTI®.

IMBRUVICA® IMPORTANT SAFETY INFORMATION

INDICATIONS

IMBRUVICA® is a kinase inhibitor indicated for the treatment of:

- Adult patients with chronic lymphocytic leukemia (CLL)/Small lymphocytic lymphoma (SLL).
- Adult patients with chronic lymphocytic leukemia (CLL)/Small lymphocytic lymphoma (SLL) with 17p deletion.
- Adult patients with Waldenström's macroglobulinemia (WM).

WARNINGS AND PRECAUTIONS

Hemorrhage: Fatal bleeding events have occurred in patients who received IMBRUVICA®. Major hemorrhage (≥ Grade 3, serious, or any central nervous system events; e.g., intracranial hemorrhage [including subdural hematoma], gastrointestinal bleeding, hematuria, and post procedural hemorrhage) occurred in 4.2% of patients, with fatalities occurring in 0.4% of 2,838 patients who received IMBRUVICA® in 27 clinical trials. Bleeding events of any grade including bruising and petechiae occurred in 39%, and excluding bruising and petechiae occurred in 23% of patients who received IMBRUVICA®, respectively.

The mechanism for the bleeding events is not well understood.

Use of either anticoagulant or antiplatelet agents concomitantly with IMBRUVICA® increases the risk of major hemorrhage. Across clinical trials, 3.1% of 2,838 patients who received IMBRUVICA® without antiplatelet or anticoagulant therapy experienced major hemorrhage. The addition of antiplatelet therapy with or without anticoagulant therapy increased this percentage to 4.4%, and the addition of anticoagulant therapy with or without antiplatelet therapy increased this percentage to 6.1%. Consider the risks and benefits of anticoagulant or antiplatelet therapy when co-administered with IMBRUVICA®. Monitor for signs and symptoms of bleeding.

Consider the benefit-risk of withholding IMBRUVICA® for at least 3 to 7 days pre- and post-surgery depending upon the type of surgery and the risk of bleeding.

Infections: Fatal and non-fatal infections (including bacterial, viral, or fungal) have occurred with IMBRUVICA® therapy. Grade 3 or greater infections occurred in 21% of 1,476 patients with B-cell malignancies who received IMBRUVICA® in clinical trials. Cases of progressive multifocal leukoencephalopathy (PML) and *Pneumocystis jirovecii* pneumonia (PJP) have occurred in patients treated with IMBRUVICA®. Consider prophylaxis according to standard of care in patients who are at increased risk for opportunistic infections. Monitor and evaluate patients for fever and infections and treat appropriately.

Cardiac Arrhythmias, Cardiac Failure, and Sudden Death: Fatal and serious cardiac arrhythmias and cardiac failure have occurred with IMBRUVICA®. Deaths due to cardiac causes or sudden deaths occurred in 1% of 4,896 patients who received IMBRUVICA® in clinical trials, including in patients who received IMBRUVICA® in unapproved monotherapy or combination regimens. These adverse reactions occurred in patients with and without preexisting hypertension or cardiac comorbidities. Patients with cardiac comorbidities may be at greater risk of these events.

Grade 3 or greater ventricular tachyarrhythmias were reported in 0.2%, Grade 3 or greater atrial fibrillation and atrial flutter were reported in 3.7%, and Grade 3 or greater cardiac failure was reported in 1.3% of 4,896 patients who received IMBRUVICA® in clinical trials, including in patients who received IMBRUVICA® in unapproved monotherapy or combination regimens. These events have occurred particularly in patients with cardiac risk factors including hypertension and diabetes mellitus, a previous history of cardiac arrhythmias, and in patients with acute infections.

Evaluate cardiac history and function at baseline, and monitor patients for cardiac arrhythmias and cardiac function. Obtain further evaluation (e.g., ECG, echocardiogram) as indicated for patients who develop symptoms of arrhythmia (e.g., palpitations, lightheadedness, syncope, chest pain), new onset dyspnea, or other cardiovascular concerns. Manage cardiac arrhythmias and cardiac failure appropriately, follow dose modification guidelines, and consider the risks and benefits of continued IMBRUVICA® treatment.

Hypertension: Hypertension occurred in 19% of 1,476 patients with B-cell malignancies who received IMBRUVICA® in clinical trials. Grade 3 or greater hypertension occurred in 8% of patients. Based on data from a subset of these patients (N=1,124), the median time to onset was 5.9 months (range, 0 to 24 months). In a long-term safety analysis over 5 years of 1,284 patients with B-cell malignancies treated for a median of 36 months (range, 0 to 98 months), the cumulative rate of hypertension increased over time. The prevalence for Grade 3 or greater hypertension was 4% (year 0-1), 7% (year 1-2), 9% (year 2-3), 9% (year 3-4), and 9% (year 4-5); the overall incidence for the 5-year period was 11%. Monitor blood pressure in patients treated with IMBRUVICA®, initiate or adjust anti-hypertensive medication throughout treatment with IMBRUVICA® as appropriate, and follow dosage modification guidelines for Grade 3 or higher hypertension.

Cytopenias: In 645 patients with B-cell malignancies who received IMBRUVICA® as a single agent, grade 3 or 4 neutropenia occurred in 23% of patients, grade 3 or 4 thrombocytopenia in 8% and grade 3 or 4 anemia in 2.8%, based on laboratory measurements. Monitor complete blood counts monthly.

Second Primary Malignancies: Other malignancies (10%), including non-skin carcinomas (3.9%), occurred among the 1,476 patients with B-cell malignancies who received IMBRUVICA® in clinical trials. The most frequent second primary malignancy was non-melanoma skin cancer (6%).

Tumor Lysis Syndrome: Tumor lysis syndrome has been infrequently reported with IMBRUVICA®. Assess the baseline risk (e.g., high tumor burden) and take appropriate precautions. Monitor patients closely and treat as appropriate.

Embryo-Fetal Toxicity: Based on findings in animals, IMBRUVICA® can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with IMBRUVICA® and for 1 month after the last dose. Advise males with female partners of reproductive potential to use effective contraception during the same time period.

ADVERSE REACTIONS

The most common adverse reactions (≥30%) in adult patients with B-cell malignancies were thrombocytopenia (55%)*, diarrhea (44%), fatigue (39%), musculoskeletal pain (39%), neutropenia (39%)*, rash (36%), anemia (35%)*, bruising (32%), and nausea (30%).

The most common Grade ≥ 3 adverse reactions (≥5%) in adult patients with B-cell malignancies were neutropenia (21%)*, thrombocytopenia (14%)*, pneumonia (8%), and hypertension (8%).

Approximately 9% (CLL/SLL) and 14% (WM) of adult patients had a dose reduction due to adverse reactions. Approximately 4-10% (CLL/SLL) and 5% (WM) of adult patients discontinued due to adverse reactions.

**Treatment-emergent decreases (all grades) were based on laboratory measurements.*

DRUG INTERACTIONS

CYP3A Inhibitors: Co-administration of IMBRUVICA® with strong or moderate CYP3A inhibitors may increase ibrutinib plasma concentrations. Increased ibrutinib concentrations may increase the risk of drug-related toxicity. Dose modifications of IMBRUVICA® are recommended when used concomitantly with posaconazole, voriconazole, and moderate CYP3A inhibitors. Avoid concomitant use of other strong CYP3A inhibitors. Interrupt IMBRUVICA® if strong inhibitors are used short-term (e.g., for ≤ 7 days). Avoid grapefruit and Seville oranges during IMBRUVICA® treatment, as these contain strong or moderate inhibitors of CYP3A. See dose modification guidelines in USPI sections 2.3 and 7.1.

CYP3A Inducers: Avoid coadministration with strong CYP3A inducers.

SPECIFIC POPULATIONS

Hepatic Impairment (based on Child-Pugh criteria)**:** Avoid use of IMBRUVICA® in patients with severe hepatic impairment. In patients with mild or moderate impairment, reduce recommended IMBRUVICA® dose and monitor more frequently for adverse reactions of IMBRUVICA®.

Please click here to see the full Prescribing Information.

About Johnson & Johnson

At Johnson & Johnson, we believe health is everything. Our strength in healthcare innovation empowers us to build a world where complex diseases are prevented, treated, and cured, where treatments are smarter and less invasive, and solutions are personal. Through our expertise in Innovative Medicine and MedTech, we are uniquely positioned to innovate across the full spectrum of healthcare solutions today to deliver the breakthroughs of tomorrow, and profoundly impact health for humanity. Learn more at https://www.jnj.com/ or at www.janssen.com/johnson-johnson-innovative-medicine. Follow us at @JanssenUS and @JNJInnovMed. Janssen Research & Development, LLC and Janssen Biotech, Inc. are both Johnson & Johnson companies.

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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 DARZALEX® (daratumumab), DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj), TALVEY™ (talquetamab-tgvs), TECVAYLI® (teclistamab-cqyv), CARVYKTI® (ciltacabtagene autoleucel), IMBRUVICA® (ibrutinib), C-CAR039 (JNJ-4496) and C-CAR066 (JNJ-9530). 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 Janssen Research & Development, LLC, Janssen Biotech, Inc., 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 1, 2023, 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 Janssen Research & Development, LLC, Janssen Biotech, Inc., nor Johnson & Johnson undertake to update any forward-looking statement as a result of new information or future events or developments.

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