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Media Release

Johnson & Johnson ushers in the next wave of innovation in cancer care with more than 20 clinical and real-world studies at ASCO 2026

- *Late-breaking Phase 3 PROTEUS data for ERLEADA® (apalutamide) selected to open the ASCO plenary, signaling a potential paradigm shift for high-risk prostate cancer in patients receiving curative-intent surgical treatment*
- *Results from MajesTEC-9, the second positive Phase 3 study of TECVAYLI® (teclistamab-cqyv), reinforce TECVAYLI® regimens as potential new standard of care in multiple myeloma as early as second line*
- *Pivotal OrigAMI-4 results evaluating RYBREVANT FASPRO™ (amivantamab and hyaluronidase-lpuj) reinforce its potential to redefine treatment in advanced head and neck cancer*

RARITAN, N.J., April 29, 2026 – Johnson & Johnson (NYSE:JNJ) will present more than 20 abstracts at the [2026 American Society of Clinical Oncology \(ASCO\) Annual Meeting](#), highlighting the breadth of the Company's leadership in oncology research across solid tumors and hematologic malignancies. The data include late-breaking Phase 3 PROTEUS results for ERLEADA® (apalutamide) in curative-intent treatment of high-risk localized or locally advanced prostate cancer, to be featured in a plenary session, along with additional studies across multiple myeloma and prostate, head and neck, lung, colorectal, and bladder cancers.

Perspectives on Key Data Readouts at ASCO

“Our pivotal, practice-defining data at ASCO reflect the momentum of our oncology strategy and the depth of our scientific investment across solid tumors and hematologic malignancies,” said Yusri Elsayed, M.D., M.H.Sc., Ph.D., Global Therapeutic Area Head, Oncology, Johnson & Johnson. “With a portfolio built to intervene earlier, target smarter, and deliver more durable outcomes, we are advancing potential new standards of care for patients with high-risk localized prostate cancer, multiple myeloma, and recurrent head and neck cancer, and remain steadfast in our mission to one day eliminate cancer.”

Key Data Presentations

Prostate Cancer

- Final analysis from the Phase 3 PROTEUS study evaluating the safety and efficacy of perioperative **ERLEADA**[®] plus hormone therapy (androgen deprivation therapy) before and after prostate surgery in high-risk localized or locally advanced prostate cancer ([Plenary Session – Oral Abstract LBA#1](#))
- Trial-in-progress update from the Phase 3 KLK2-comPAS study of **pasritamig** (JNJ-78278343) in combination with best supportive care in metastatic castration-resistant prostate cancer ([Poster Abstract #TPS5136](#))
- Trial-in-progress update from the Phase 3 KLK2-PASenger study of **pasritamig** in combination with docetaxel compared with docetaxel alone in metastatic castration-resistant prostate cancer ([Poster Abstract #TPS5139](#))

Multiple Myeloma

- Results from the Phase 3 MajesTEC-9 study of **TECVAYLI**[®] (teclistamab-cqyv) versus standard of care therapies as early as second line in patients with multiple myeloma ([Oral Abstract #7507](#))
- Subgroup analysis from the Phase 3 PERSEUS study evaluating the benefit of **DARZALEX FASPRO**[®] (daratumumab and hyaluronidase-fihj) in transplant-eligible patients with high- and standard-risk multiple myeloma ([Oral Abstract #7505](#))
- Final subgroup analysis from the Phase 3 CEPHEUS study evaluating **DARZALEX FASPRO**[®] in combination with bortezomib, lenalidomide, and dexamethasone in transplant-ineligible newly diagnosed multiple myeloma ([Rapid Oral Abstract #7513](#))
- Results from the Phase 2 OPTec/OPTal study evaluating outpatient, step-up administration of **TECVAYLI**[®] or **TALVEY**[®] (talquetamab-tgvs) with prophylactic tocilizumab in patients with relapsed or refractory multiple myeloma (RRMM) ([Rapid Oral Abstract #7510](#))
- Cytogenetic subgroup analysis from the Phase 3 CARTITUDE-4 study evaluating **CARVYKTI**[®] (ciltacabtagene autoleucel; cilta-cel) in patients with lenalidomide-refractory multiple myeloma responding to bridging therapy ([Poster Abstract #7536](#))
- Results from the CARTITUDE clinical studies of **CARVYKTI**[®] evaluating incidence and characterization of Immune Effector Cell-Associated Enterocolitis (IEC-EC) in RRMM ([Poster Abstract #7533](#))

Head and Neck Cancer

- Pivotal Phase 1b/2 OrigAMI-4 results evaluating **RYBREVANT FASPRO**[™] (amivantamab and hyaluronidase-lpuj) in patients with recurrent or metastatic head and neck cancer following prior immunotherapy and chemotherapy ([Oral Abstract #6008](#))
- Trial-in-progress update from the Phase 3 OrigAMI-5 study of **RYBREVANT FASPRO**[™] in combination with immunotherapy and chemotherapy in the first-line recurrent or metastatic head and neck setting ([Abstract #TPS6127](#))

Lung Cancer

- Updated results from the CHRYSALIS-2 study, including overall survival, for **RYBREVANT**[®] (amivantamab-vmjw) and **LAZCLUZE**[®] (lazertinib) in the first-line treatment of patients with atypical *EGFR*-mutated non-small cell lung cancers ([Oral Abstract #8501](#))
- Early safety results from the Phase 2b COPERNICUS study evaluating a pragmatic approach to **RYBREVANT FASPRO**[™] plus **LAZCLUZE**[®] with proactive therapy management in the first-line treatment of patients with advanced *EGFR*-mutated non-small cell lung cancer ([Poster Abstract #8613](#))

- Interim efficacy and safety results from the Phase 2b COPERNICUS study of **RYBREVANT FASPRO™** plus chemotherapy with enhanced proactive management of potential dermatological effects in patients with previously treated advanced *EGFR*-mutated non-small cell lung cancer ([Poster Abstract #8614](#))

Colorectal Cancer

- Biomarker analyses from the Phase 1b/2 OrigAMI-1 study of **RYBREVANT®** across different tumor subtypes in RAS/BRAF wild-type metastatic colorectal cancer ([Poster Abstract #3548](#))

Bladder Cancer

- A real-world market research study exploring decision-making and regret after radical cystectomy ([Online Publication #e16605](#))

Information on abstracts sponsored by Johnson & Johnson is available on [JNJ.com](#).

About ERLEADA®

ERLEADA® (apalutamide) is an androgen receptor inhibitor indicated for the treatment of patients with non-metastatic castration-resistant prostate cancer (nmCRPC) and for the treatment of patients with metastatic castration-sensitive prostate cancer (mCSPC). ERLEADA® [received](#) U.S. Food and Administration (FDA) approval for nmCRPC in February 2018 and [received](#) U.S. FDA approval for mCSPC in September 2019. ERLEADA® is the first and only next-generation androgen receptor inhibitor offering a once-daily, single-tablet treatment option for patients. To date, more than 340,000 patients worldwide have been treated with ERLEADA®. Additional studies are ongoing to evaluate ERLEADA® in earlier stages of prostate cancer, including high-risk localized and locally advanced disease.¹

The legal manufacturer for ERLEADA® is Janssen Biotech, Inc. For more information, visit [www.ERLEADA.com](#).

About Pasritamig (JNJ-78278343)

Pasritamig (JNJ-78278343) is an investigational bispecific T-cell-engager antibody (bsAb) targeting human kallikrein 2 (KLK2), a novel and highly specific prostate cancer target, and CD3 receptor complexes on T cells, leveraging the body's immune system to selectively target and eliminate cancer cells. This innovative approach is being evaluated in patients with metastatic castration-resistant prostate cancer (mCRPC), who have limited treatment options.

About TECVAYLI®

TECVAYLI® (teclistamab-cqyv) 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. TECVAYLI® received accelerated [approval](#) from the U.S. Food and Drug Administration (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 received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 antibody.²

In February 2024, the U.S. FDA [approved](#) the supplemental Biologics License Application (sBLA) for TECVAYLI® for a reduced dosing frequency of 1.5 mg/kg every two weeks in patients with RRMM who achieved and maintained a complete response (CR) or better for a minimum of six months. In March 2026, the U.S. FDA [approved](#) TECVAYLI® in combination with DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj) for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least one prior line of therapy, including a proteasome inhibitor and an immunomodulatory agent. The supplemental Biologics License Application was proactively selected for the Commissioner's National Priority Voucher Pilot Program and also granted the application Breakthrough Therapy Designation and Real-Time Oncology Review. This approval expanded the use of TECVAYLI® into earlier lines of therapy and is the first bispecific antibody-based combination regimen in this setting, offering a potential new standard of care as early as second line.

To date, more than 26,000 patients have been treated worldwide with TECVAYLI®.

The European Commission (EC) granted TECVAYLI® [conditional marketing authorization](#) 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. In August 2023, the EC [approved](#) a Type II variation application for TECVAYLI®, providing the option for a reduced dosing frequency of 1.5 mg/kg every two weeks (Q2W) in patients who have achieved a complete response or better for a minimum of six months.

For more information, visit www.TECVAYLI.com.

About DARZALEX FASPRO® and DARZALEX®

DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj) [received](#) U.S. FDA approval in May 2020 and is approved for 11 indications in multiple myeloma, four of which are for frontline treatment in newly diagnosed patients who are transplant eligible or ineligible.³ It is the only subcutaneous CD38-directed antibody approved to treat patients with multiple myeloma. 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.⁴ In 2025, DARZALEX FASPRO® was approved by the U.S. FDA and EMA as the first and only treatment for patients with high-risk smoldering multiple myeloma.

DARZALEX® is the first CD38-directed antibody approved to treat multiple myeloma.² DARZALEX®-based regimens have been used in the treatment of more than 748,000 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 Janssen an exclusive license to develop, manufacture and commercialize daratumumab.

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 GPRC5D-targeting 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.⁵ Since FDA approval, 7,700 patients were treated with TALVEY®. The European Commission (EC) 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.⁶

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.

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.⁷

In April 2024, CARVYKTI® was approved in the U.S. for treatment of adult patients with relapsed or refractory multiple myeloma who have received at least one prior line of therapy including a proteasome inhibitor, an immunomodulatory agent, and who are refractory to lenalidomide, following a unanimous (11 to 0) FDA Oncologic Drugs Advisory Committee (ODAC) recommendation in support of this new indication. In April 2024, the European Medicines Agency (EMA) approved a Type II variation for CARVYKTI® for the treatment of adults with relapsed and refractory multiple myeloma who have received at least one prior therapy, including an immunomodulatory agent and a proteasome inhibitor, have demonstrated disease progression on the last therapy, and are refractory to lenalidomide. In September 2022, Japan's Ministry of Health, Labour and Welfare (MHLW) approved CARVYKTI® for the treatment of adults with relapsed or refractory multiple myeloma in patients that have no history of CAR-positive T cell infusion

therapy targeting BCMA and who have received three or more lines of therapies, including an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 monoclonal antibody, and in whom multiple myeloma has not responded to or has relapsed following the most recent therapy.

CARVYKTI® is a BCMA-directed, 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. CARVYKTI® is available in 17 markets worldwide and has been used to treat more than 11,000 patients globally.

In December 2017, Janssen Biotech, Inc., a Johnson & Johnson company, 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 RYBREVANT FASPRO™ and RYBREVANT®

In December 2025, the U.S. FDA [approved](#) RYBREVANT FASPRO™ (amivantamab and hyaluronidase-lpuj) across all indications of intravenous RYBREVANT® (amivantamab-vmjw). This subcutaneously administered therapy is also approved in Europe, Japan, China, and other markets.^{8,9}

RYBREVANT FASPRO™ is co-formulated with recombinant human hyaluronidase PH20 (rHuPH20), Halozyme's ENHANZE® drug delivery technology.

The effectiveness of RYBREVANT FASPRO™ has been established based on adequate and well controlled studies of RYBREVANT®. Data across multiple Phase 3 studies, including MARIPOSA, have demonstrated the clinical benefit of RYBREVANT® in improving progression-free survival (PFS) and overall survival (OS) in advanced EGFR-mutated non-small cell lung cancer (NSCLC).

RYBREVANT® is approved in the U.S., Europe and other markets across four indications in EGFR-mutated NSCLC, including two in the first-line setting and two in the second-line, for patients with either exon 19 deletions, exon 21 L858R mutations, or exon 20 insertion mutations, as monotherapy or in combination with LAZCLUZE® (lazertinib) or chemotherapy.

RYBREVANT® is a first-in-class, fully-human bispecific antibody targeting EGFR and MET with immune cell-directing activity.

The legal manufacturer for RYBREVANT® is Janssen Biotech, Inc. For more information, visit: <https://www.RYBREVANT.com>.

About LAZCLUZE®

In 2018, Janssen Biotech, Inc., entered into a license and collaboration agreement with Yuhan Corporation for the development of LAZCLUZE® (marketed as LECLAZA in South Korea). LAZCLUZE® is an oral, third-generation, brain-penetrant EGFR TKI that targets both the T790M mutation and activating EGFR mutations while sparing wild-type EGFR. An analysis of the efficacy and safety of LAZCLUZE® from the Phase 3 LASER301 study was published in [The Journal of Clinical Oncology](#) in 2023.^{10,11}

ERLEADA® INDICATIONS AND IMPORTANT SAFETY INFORMATION

INDICATIONS

ERLEADA® (apalutamide) is an androgen receptor inhibitor indicated for the treatment of patients with:

- Metastatic castration-sensitive prostate cancer (mCSPC)
- Non-metastatic castration-resistant prostate cancer (nmCRPC)

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Cerebrovascular and Ischemic Cardiovascular Events, including events leading to death, occurred in patients receiving ERLEADA. Monitor for signs and symptoms of ischemic heart disease and cerebrovascular disorders. Optimize management of cardiovascular risk factors, such as hypertension, diabetes, or dyslipidemia. Consider discontinuation of ERLEADA for Grade 3 and 4 events.

In a randomized study (SPARTAN) of patients with nmCRPC, ischemic cardiovascular events occurred in 3.7% of patients treated with ERLEADA and 2% of patients treated with placebo. In a randomized study (TITAN) in patients with mCSPC, ischemic cardiovascular events occurred in 4.4% of patients treated with ERLEADA and 1.5% of patients treated with placebo. Across the SPARTAN and TITAN studies, 4 patients (0.3%) treated with ERLEADA and 2 patients (0.2%) treated with placebo died from an ischemic cardiovascular event. Patients with history of unstable angina, myocardial infarction, congestive heart failure, stroke, or transient ischemic attack within 6 months of randomization were excluded from the SPARTAN and TITAN studies.

In the SPARTAN study, cerebrovascular events occurred in 2.5% of patients treated with ERLEADA and 1% of patients treated with placebo. In the TITAN study, cerebrovascular events occurred in 1.9% of patients treated with ERLEADA and 2.1% of patients treated with placebo. Across the SPARTAN and TITAN studies, 3 patients (0.2%) treated with ERLEADA and 2 patients (0.2%) treated with placebo died from a cerebrovascular event.

Fractures occurred in patients receiving ERLEADA. Evaluate patients for fracture risk. Monitor and manage patients at risk for fractures according to established treatment guidelines and consider use of bone-targeted agents.

In a randomized study (SPARTAN) of patients with nmCRPC, fractures occurred in 12% of patients treated with ERLEADA and in 7% of patients treated with placebo. In a randomized study (TITAN) of patients with mCSPC, fractures occurred in 9% of patients treated with ERLEADA and in 6% of patients treated with placebo.

Falls occurred in patients receiving ERLEADA with increased frequency in the elderly. Evaluate patients for fall risk.

In a randomized study (SPARTAN), falls occurred in 16% of patients treated with ERLEADA compared with 9% of patients treated with placebo. Falls were not associated with loss of consciousness or seizure.

Seizure occurred in patients receiving ERLEADA. Permanently discontinue ERLEADA in patients who develop a seizure during treatment. It is unknown whether anti-epileptic medications will prevent seizures with ERLEADA. Advise patients of the risk of developing a seizure while receiving ERLEADA and of engaging in any activity where sudden loss of consciousness could cause harm to themselves or others.

In two randomized studies (SPARTAN and TITAN), five patients (0.4%) treated with ERLEADA and one patient treated with placebo (0.1%) experienced a seizure. Seizure occurred from 159 to 650 days after initiation of ERLEADA. Patients with a history of seizure or, predisposing factors for seizure, or receiving drugs known to decrease the seizure threshold or to induce seizure were excluded. There is no clinical experience in re-administering ERLEADA to patients who experienced a seizure.

Severe Cutaneous Adverse Reactions — Fatal and life-threatening cases of severe cutaneous adverse reactions (SCARs), including Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN), and drug reaction with eosinophilia and systemic symptoms (DRESS) occurred in patients receiving ERLEADA.

Monitor patients for the development of SCARs. Advise patients of the signs and symptoms of SCARs (eg, a prodrome of fever, flu-like symptoms, mucosal lesions, progressive skin rash, or lymphadenopathy). If a SCAR is suspected, interrupt ERLEADA until the etiology of the reaction has been determined. Consultation with a dermatologist is recommended. If a SCAR is confirmed, or for other Grade 4 skin reactions, permanently discontinue ERLEADA [see *Dosage and Administration* (2.2)].

Interstitial Lung Disease (ILD)/Pneumonitis — Fatal and life-threatening interstitial lung disease (ILD) or pneumonitis can occur in patients treated with ERLEADA.

Post-marketing cases of ILD/pneumonitis, including fatal cases, occurred in patients treated with ERLEADA. Across clinical trials (TITAN and SPARTAN, n=1327), 0.8% of patients treated with ERLEADA experienced ILD/pneumonitis, including 0.2% who experienced Grade 3 events [see *Adverse Reactions* (6.1, 6.2)].

Monitor patients for new or worsening symptoms indicative of ILD/pneumonitis (eg, dyspnea, cough, fever). Immediately withhold ERLEADA if ILD/pneumonitis is suspected.

Permanently discontinue ERLEADA in patients with severe ILD/pneumonitis or if no other potential causes of ILD/pneumonitis are identified [see *Dosage and Administration* (2.2)].

Embryo-Fetal Toxicity — The safety and efficacy of ERLEADA have not been established in females. Based on findings from animals and its mechanism of action, ERLEADA can cause fetal harm and loss of pregnancy when administered to a pregnant

female. Advise males with female partners of reproductive potential to use effective contraception during treatment and for 3 months after the last dose of ERLEADA [see *Use in Specific Populations (8.1, 8.3)*].

ADVERSE REACTIONS

The most common adverse reactions ($\geq 10\%$) that occurred more frequently in the ERLEADA-treated patients ($\geq 2\%$ over placebo) from the randomized placebo-controlled clinical trials (TITAN and SPARTAN) were fatigue, arthralgia, rash, decreased appetite, fall, weight decreased, hypertension, hot flush, diarrhea, and fracture.

Laboratory Abnormalities — All Grades (Grade 3-4)

- **Hematology** — In the TITAN study: white blood cell decreased ERLEADA 27% (0.4%), placebo 19% (0.6%). In the SPARTAN study: anemia ERLEADA 70% (0.4%), placebo 64% (0.5%); leukopenia ERLEADA 47% (0.3%), placebo 29% (0%); lymphopenia ERLEADA 41% (1.8%), placebo 21% (1.6%)
- **Chemistry** — In the TITAN study: hypertriglyceridemia ERLEADA 17% (2.5%), placebo 12% (2.3%). In the SPARTAN study: hypercholesterolemia ERLEADA 76% (0.1%), placebo 46% (0%); hyperglycemia ERLEADA 70% (2%), placebo 59% (1.0%); hypertriglyceridemia ERLEADA 67% (1.6%), placebo 49% (0.8%); hyperkalemia ERLEADA 32% (1.9%), placebo 22% (0.5%)

Rash — In 2 randomized studies (SPARTAN and TITAN), rash was most commonly described as macular or maculopapular. Adverse reactions of rash were 26% with ERLEADA vs 8% with placebo. Grade 3 rashes (defined as covering $>30\%$ body surface area [BSA]) were reported with ERLEADA treatment (6%) vs placebo (0.5%).

The onset of rash occurred at a median of 83 days. Rash resolved in 78% of patients within a median of 78 days from onset of rash. Rash was commonly managed with oral antihistamines and topical corticosteroids, and 19% of patients received systemic corticosteroids. Dose reduction or dose interruption occurred in 14% and 28% of patients, respectively. Of the patients who had dose interruption, 59% experienced recurrence of rash upon reintroduction of ERLEADA.

Hypothyroidism — In 2 randomized studies (SPARTAN and TITAN), hypothyroidism was reported for 8% of patients treated with ERLEADA and 1.5% of patients treated with placebo based on assessments of thyroid-stimulating hormone (TSH) every 4 months. Elevated TSH occurred in 25% of patients treated with ERLEADA and 7% of patients treated with placebo. The median onset was at the first scheduled assessment. There were no Grade 3 or 4 adverse reactions. Thyroid replacement therapy, when clinically indicated, should be initiated or dose adjusted.

DRUG INTERACTIONS

Effect of Other Drugs on ERLEADA

ERLEADA Strong CYP2C8 or CYP3A4 Inhibitors

Reduce the ERLEADA dose as recommended for adverse reactions [see *Dosage and Administration (2.2)*]. Co-administration of a strong CYP2C8 or CYP3A4 inhibitor is predicted to increase the steady-state exposure of the active moieties (sum of unbound apalutamide plus the potency-adjusted unbound N-desmethyl-apalutamide).

Effect of ERLEADA on Other Drugs

Substrates of CYP3A4, CYP2C9, CYP2C19, P-gp, BCRP, or OATP1B1

Refer to the Prescribing Information for these substrates. Consider alternative agents when possible or evaluate for loss of activity of the substrate if concomitant use cannot be avoided.

- Apalutamide is a strong inducer of CYP3A4 and CYP2C19, a weak inducer of CYP2C9, and an inducer of P-gp, BCRP, and OATP1B1. Apalutamide decreases exposure of substrates of CYP3A4, CYP2C19, CYP2C9, P-gp, BCRP, or OATP1B [see *Clinical Pharmacology (12.3)*], which may decrease the effectiveness of these substrates.

USE IN SPECIFIC POPULATIONS

The recommended ERLEADA dosage in patients with (Child-Pugh C) is lower than the recommended dosage in patients with normal hepatic function. No dosage modification is recommended for patients with mild (Child-Pugh A) or moderate (Child-Pugh B) hepatic impairment.

Please see full [Prescribing Information](#) for ERLEADA.

TECVAYLI® INDICATIONS AND IMPORTANT SAFETY INFORMATION

INDICATIONS AND USAGE

TECVAYLI® (teclistamab-cqyv) is a bispecific B-cell maturation antigen (BCMA)-directed CD3 T-cell engager indicated for the treatment of adult patients with relapsed or refractory multiple myeloma:

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

IMPORTANT SAFETY INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGIC TOXICITY including IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME

Cytokine release syndrome (CRS), including life-threatening or fatal reactions, can occur in patients receiving TECVAYLI. Initiate treatment with TECVAYLI step-up dosing schedule to reduce risk of CRS. Withhold TECVAYLI until CRS resolves or permanently discontinue based on severity.

Neurologic toxicity, including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) and serious, life-threatening, or fatal reactions, can occur in patients receiving TECVAYLI. Monitor patients for signs or symptoms of neurologic toxicity, including ICANS, during treatment. Withhold TECVAYLI until neurologic toxicity resolves or permanently discontinue based on severity.

TECVAYLI is available only through a restricted program called the TECVAYLI and TALVEY® Risk Evaluation and Mitigation Strategy (REMS).

WARNINGS AND PRECAUTIONS

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

In the clinical trials (monotherapy and combination therapy; N=448), CRS occurred in 64% of patients who received TECVAYLI at the recommended dose, with Grade 1 CRS occurring in 46% of patients, Grade 2 in 18%, and Grade 3 in 0.2%. Recurrent CRS occurred in 27% of patients. Most patients experienced CRS during the initial step-up dosing schedule (step-up dose 1 [37%], step-up dose 2 [32%], or the initial treatment dose [20%]). CRS first occurred following subsequent doses of TECVAYLI in 2.5% of patients. The median time to onset of CRS was 2 (range: 1 to 9) days after the most recent dose and the median duration of CRS was 2 (range: 1 to 22) days.

Clinical signs and symptoms of CRS included, but were not limited to, fever, hypoxia, chills, hypotension, sinus tachycardia, headache, and elevated liver enzymes (aspartate aminotransferase and alanine aminotransferase elevation).

Initiate therapy according to TECVAYLI step-up dosing schedule to reduce risk of CRS. Administer pretreatment medications to reduce risk of CRS and monitor patients following administration of TECVAYLI accordingly.

At the first sign of CRS, immediately evaluate patient for hospitalization. Administer supportive care based on severity and consider further management per current practice guidelines. Withhold until CRS resolves or permanently discontinue TECVAYLI based on severity.

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

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

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

In MajesTEC-1, ICANS was reported in 6% of patients who received TECVAYLI as monotherapy at the recommended dosage. Recurrent ICANS occurred in 1.8% of patients. Most patients experienced ICANS following step-up dose 1 (1.2%), step-up dose 2 (0.6%), or the initial treatment dose (1.8%). Less than 3% of patients developed first occurrence of ICANS following subsequent TECVAYLI doses. The median time to onset of ICANS was 4 (range: 2 to 8) days after the most recent dose with a median duration of 3 (range: 1 to 20) days. The most frequent clinical manifestations of ICANS reported were confusional state and dysgraphia.

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

The onset of ICANS can be concurrent with CRS, following resolution of CRS, or in the absence of CRS.

Monitor patients for signs and symptoms of neurologic toxicity, including ICANS during TECVAYLI treatment. At the first sign of neurologic toxicity, including ICANS, immediately evaluate patient and provide supportive therapy based on severity. Withhold until neurologic toxicity resolves or permanently discontinue TECVAYLI based on severity per recommendations and consider further management per current practice guidelines.

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

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

TECVAYLI and TALVEY REMS - TECVAYLI is available only through a restricted program under a REMS called the TECVAYLI and TALVEY REMS because of the risks of CRS and neurologic toxicity, including ICANS.

Hepatotoxicity - TECVAYLI can cause hepatotoxicity, including fatalities. There was one fatal case of hepatic failure in MajesTEC-1. In patients who received TECVAYLI at the recommended dose in the clinical trials (monotherapy and combination therapy trials; N=448) elevated aspartate aminotransferase (AST) occurred in 47% of patients, with Grade 3 or 4 elevations in 2.9%. Elevated alanine aminotransferase (ALT) occurred in 48% of patients, with Grade 3 or 4 elevations in 3.8%. Elevated total bilirubin occurred in 10% of patients with Grade 3 or 4 elevations in 0.7%. Liver enzyme elevation can occur with or without concurrent CRS.

Monitor liver enzymes and bilirubin at baseline and during treatment as clinically indicated. Withhold TECVAYLI or consider permanent discontinuation of TECVAYLI based on severity.

Infections - TECVAYLI can cause severe, life-threatening, or fatal infections.

In MajesTEC-1 (N=165), in patients who received the recommended TECVAYLI dosage, serious infections, including opportunistic infections, occurred in 30% of patients, Grade 3 or 4 infections in 35% of patients, and fatal infections in 4.2% of patients.

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

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

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

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

Neutropenia - TECVAYLI can cause neutropenia and febrile neutropenia. In patients who received TECVAYLI at the recommended dose in the clinical trials (monotherapy and combination therapy trials; N=448), decreased neutrophils occurred in 88% of patients, with Grade 3 or 4 decreased neutrophils in 70%. Febrile neutropenia occurred in 6% of patients.

Monitor complete blood cell counts at baseline and periodically during treatment and provide supportive care per local institutional guidelines.

Monitor patients with neutropenia for signs of infection.

Withhold TECVAYLI based on severity.

Hypersensitivity and Other Administration Reactions - TECVAYLI can cause both systemic administration-related and local injection-site reactions.

Systemic Reactions - In patients who received the recommended TECVAYLI dosage in the clinical trials (monotherapy and combination therapy trials; N=448), 2.5% of patients experienced systemic-administration reactions, which included recurrent pyrexia and rash.

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

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

Embryo-Fetal Toxicity - Based on its mechanism of action, TECVAYLI may cause fetal harm when administered to a pregnant patient. Advise pregnant patients of the potential risk to the fetus. Advise females of reproductive potential to use effective contraception during treatment with TECVAYLI and for 5 months after the last dose.

ADVERSE REACTIONS

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

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

Please read full [Prescribing Information](#), including **Boxed WARNING**, for TECVAYLI.

DARZALEX FASPRO® INDICATIONS AND 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, lenalidomide, and dexamethasone for induction and consolidation in newly diagnosed patients who are eligible for autologous stem cell transplant
- 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 (PI)
- 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 PI and an immunomodulatory agent or who are double refractory to a PI and an immunomodulatory agent

DARZALEX FASPRO® as monotherapy is indicated for the treatment of adult patients with high-risk smoldering multiple myeloma.

IMPORTANT SAFETY INFORMATION

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 1446 patients with multiple myeloma (N=1235) or light chain (AL) amyloidosis (N=193) who received DARZALEX FASPRO® as monotherapy or in combination, 7% of patients experienced a systemic administration-related reaction (Grade 2: 3%, Grade 3: 0.8%, Grade 4: 0.1%). In patients with high-risk smoldering multiple myeloma (N=193), systemic administration-related reactions occurred in 17% of patients in AQUILA (Grade 2: 7%, Grade 3: 1%).

In all patients (N=1639), systemic administration-related reactions occurred in 7% of patients with the first injection, 0.5% 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 283 systemic administration-related reactions that occurred in 135 patients, 240 (85%) 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 of 1446 patients with multiple myeloma (N=1253) or light chain amyloidosis (N=193), injection-site reactions occurred in 8% of patients, including Grade 2 reactions in 1.1%. The most frequent (>1%) injection-site reactions were injection site erythema and injection site rash. In patients with high-risk smoldering multiple myeloma (N=193), injection-site reactions occurred in 28% of patients, including Grade 2 reactions in 3%. These local reactions occurred a median of 6 minutes (range: 0 minutes to 6.5 days) after starting administration of DARZALEX FASPRO®. Monitor for local reactions and consider symptomatic management.

Infections

DARZALEX FASPRO® can cause serious, life-threatening, or fatal infections. In patients who received DARZALEX FASPRO® in a pooled safety population including patients with smoldering multiple myeloma and light chain (AL) amyloidosis (N=1639), serious infections, including opportunistic infections, occurred in 24% of patients, Grade 3 or 4 infections occurred in 22%, and fatal infections occurred in 2.5%. The most common type of serious infection reported was pneumonia (8.5%).

Monitor patients for signs and symptoms of infection prior to and during treatment with DARZALEX FASPRO® and treat appropriately. Administer prophylactic antimicrobials according to guidelines.

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 ($\geq 20\%$) with DARZALEX FASPRO[®] monotherapy is upper respiratory tract infection. The most common adverse reactions with combination therapy ($\geq 20\%$ for any combination) include fatigue, nausea, diarrhea, dyspnea, insomnia, headache, rash, pyrexia, cough, muscle spasms, back pain, vomiting, hypertension, musculoskeletal pain, upper respiratory tract infection, peripheral neuropathy, peripheral sensory neuropathy, constipation, pneumonia, edema, peripheral edema, and anemia.

The most common adverse reactions ($\geq 20\%$) in patients with high-risk smoldering multiple myeloma who received DARZALEX FASPRO[®] monotherapy are upper respiratory tract infection, musculoskeletal pain, fatigue, diarrhea, rash, sleep disorder, sensory neuropathy, and injection site reactions.

The most common hematology laboratory abnormalities ($\geq 40\%$) with DARZALEX FASPRO[®] are decreased leukocytes, decreased lymphocytes, decreased neutrophils, decreased platelets, and decreased hemoglobin.

Please [click here](#) to read the full Prescribing Information for DARZALEX FASPRO[®].

DARZALEX[®] INDICATIONS AND IMPORTANT SAFETY INFORMATION

INDICATIONS

DARZALEX[®] (daratumumab) 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[®] 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 $\geq 20\%$) 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 ($\geq 40\%$) with DARZALEX[®] are: neutropenia, lymphopenia, thrombocytopenia, leukopenia, and anemia.

Please [click here](#) to read the full Prescribing Information for DARZALEX[®].

TALVEY[®] IMPORTANT SAFETY INFORMATION

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).

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 and treat promptly. Withhold or permanently 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 TECVAYL[®] and TALVEY[®] Risk Evaluation and Mitigation Strategy (REMS).

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. Most events occurred following step-up dose 1 (29%) or step-up dose 2(44%) at the recommended dosages. 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, or life-threatening neurologic toxicity 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 and treat promptly. 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, regardless of having an oral toxicity, including 29% 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 consider permanent discontinuation of 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. Withhold TALVEY® as recommended based on severity.

Hepatotoxicity: TALVEY® can cause hepatotoxicity. 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®.

CARVYKI® IMPORTANT SAFETY INFORMATION

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

Cytokine Release Syndrome (CRS), including fatal or life-threatening reactions, occurred in patients following treatment with CARVYKI®. Do not administer CARVYKI® 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 CARVYKI®, including before CRS onset, concurrently with CRS, after CRS resolution, or in the absence of CRS. Monitor for neurologic events after treatment with CARVYKI®. Provide supportive care and/or corticosteroids as needed.

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

Hemophagocytic Lymphohistiocytosis/Macrophage Activation Syndrome (HLH/MAS), including fatal and life-threatening reactions, occurred in patients following treatment with CARVYKI®. 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 CARVYKI®.

Immune Effector Cell-associated Enterocolitis (IEC-EC), including fatal or life-threatening reactions, occurred following treatment with CARVYKI®.

Secondary hematological malignancies, including myelodysplastic syndrome and acute myeloid leukemia, have occurred in patients following treatment with CARVYKI®. T-cell malignancies have occurred following treatment of hematologic malignancies with BCMA- and CD19-directed genetically modified autologous T-cell immunotherapies, including CARVYKI®.

WARNINGS AND PRECAUTIONS

INCREASED EARLY MORTALITY - In CARTITUDE-4, a (1:1) randomized controlled trial, there was a numerically higher percentage of early deaths in patients randomized to the CARVYKI® treatment arm compared to the control arm. Among patients with deaths occurring within the first 10 months from randomization, a greater proportion (29/208; 14%) occurred in the CARVYKI® arm compared to (25/211; 12%) in the control arm. Of the 29 deaths that occurred in the CARVYKI® arm within the first 10 months of randomization, 10 deaths occurred prior to CARVYKI® infusion, and 19 deaths occurred after CARVYKI® infusion. Of the 10 deaths that occurred prior to CARVYKI® infusion, all occurred due to disease progression, and none occurred due to adverse events. Of the 19 deaths that occurred after CARVYKI® infusion, 3 occurred due to disease progression, and 16 occurred due to adverse events. The most common adverse events were due to infection (n=12).

CYTOKINE RELEASE SYNDROME (CRS), including fatal or life-threatening reactions, occurred following treatment with CARVYKI®. Among patients receiving CARVYKI® for RRMM in the CARTITUDE-1 & -4 studies (N=285), CRS occurred in 84% (238/285), including ≥ Grade 3 CRS (ASTCT 2019) in 4% (11/285) of patients. Median time to onset of CRS, any grade, was 7 days (range: 1 to 23 days). CRS resolved in 82% with a median duration of 4 days (range: 1 to 97 days). The most common manifestations of CRS in all patients combined (≥10%) included fever (84%), hypotension (29%) and aspartate aminotransferase increased (11%). Serious events that may be associated with CRS include pyrexia, hemophagocytic lymphohistiocytosis, respiratory failure, disseminated intravascular coagulation, capillary leak syndrome, and supraventricular and ventricular tachycardia. CRS occurred in 78% of patients in CARTITUDE-4 (3% Grade 3 to 4) and in 95% of patients in CARTITUDE-1 (4% Grade 3 to 4).

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.

Confirm that a minimum of 2 doses of tocilizumab are available prior to infusion of CARVYKTI®.

Of the 285 patients who received CARVYKTI® in clinical trials, 53% (150/285) patients received tocilizumab; 35% (100/285) received a single dose, while 18% (50/285) received more than 1 dose of tocilizumab. Overall, 14% (39/285) of patients received at least 1 dose of corticosteroids for treatment of CRS.

Monitor patients at least daily for 7 days following CARVYKTI® infusion for signs and symptoms of CRS. Monitor patients for signs or symptoms of CRS for at least 2 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, GBS, 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.

Among patients receiving CARVYKTI® in the CARTITUDE-1 & 4 studies for RRMM, one or more neurologic toxicities occurred in 24% (69/285), including ≥ Grade 3 cases in 7% (19/285) of patients. Median time to onset was 10 days (range: 1 to 101) with 63/69 (91%) of cases developing by 30 days. Neurologic toxicities resolved in 72% (50/69) of patients with a median duration to resolution of 23 days (range: 1 to 544). Of patients developing neurotoxicity, 96% (66/69) also developed CRS. Subtypes of neurologic toxicities included ICANS in 13%, peripheral neuropathy in 7%, cranial nerve palsy in 7%, parkinsonism in 3%, and immune mediated myelitis in 0.4% of the patients.

Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS): Patients receiving CARVYKTI® 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.

Among patients receiving CARVYKTI® in the CARTITUDE-1 & -4 studies, ICANS occurred in 13% (36/285), including Grade ≥3 in 2% (6/285) of the patients. Median time to onset of ICANS was 8 days (range: 1 to 28 days). ICANS resolved in 30 of 36 (83%) of patients, with a median time to resolution of 3 days (range: 1 to 143 days). Median duration of ICANS was 6 days (range: 1 to 1229 days) in all patients, including those with ongoing neurologic events at the time of death or data cutoff. Of patients with ICANS, 97% (35/36) had CRS. The onset of ICANS occurred during CRS in 69% of patients, before and after the onset of CRS in 14% of patients, respectively.

Immune Effector Cell-associated Neurotoxicity Syndrome occurred in 7% of patients in CARTITUDE-4 (0.5% Grade 3) and in 23% of patients in CARTITUDE-1 (3% Grade 3). The most frequent (≥2%) manifestations of ICANS included encephalopathy (12%), aphasia (4%), headache (3%), motor dysfunction (3%), ataxia (2%), and sleep disorder (2%).

Monitor patients at least daily for 7 days following CARVYKTI® infusion for signs and symptoms of ICANS. Rule out other causes of ICANS symptoms. Monitor patients for signs or symptoms of ICANS for at least 2 weeks after infusion and treat promptly. Neurologic toxicity should be managed with supportive care and/or corticosteroids as needed. Advise patients to avoid driving for at least 2 weeks following infusion.

Parkinsonism: Neurologic toxicity with parkinsonism has been reported in clinical trials of CARVYKTI®. Among patients receiving CARVYKTI® in the CARTITUDE-1 & -4 studies, parkinsonism occurred in 3% (8/285), including Grade ≥3 in 2% (5/285) of the patients. Median time to onset of parkinsonism was 56 days (range: 14 to 914 days). Parkinsonism resolved in 1 of 8 (13%) of patients with a median time to resolution of 523 days. Median duration of parkinsonism was 243.5 days (range: 62 to 720 days) in all patients, including those with ongoing neurologic events at the time of death or data cutoff. The onset of parkinsonism occurred after CRS for all patients and after ICANS for 6 patients.

Parkinsonism occurred in 1% of patients in CARTITUDE-4 (no Grade 3 to 4) and in 6% of patients in CARTITUDE-1 (4% Grade 3 to 4).

Manifestations of parkinsonism included movement disorders, cognitive impairment, and personality changes. 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 GBS occurred following treatment with CARVYKTI® despite treatment with intravenous immunoglobulins. 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 immunoglobulins and plasma exchange, depending on severity of GBS.

Immune Mediated Myelitis: Grade 3 myelitis occurred 25 days following treatment with CARVYKTI® in CARTITUDE-4 in a patient who received CARVYKTI® as subsequent therapy. 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 immune globulin. Myelitis was ongoing at the time of death from other cause.

Peripheral Neuropathy occurred following treatment with CARVYKTI®. Among patients receiving CARVYKTI® in the CARTITUDE-1 & -4 studies, peripheral neuropathy occurred in 7% (21/285), including Grade ≥ 3 in 1% (3/285) of the patients. Median time to onset of peripheral neuropathy was 57 days (range: 1 to 914 days). Peripheral neuropathy resolved in 11 of 21 (52%) of patients with a median time to resolution of 58 days (range: 1 to 215 days). Median duration of peripheral neuropathy was 149.5 days (range: 1 to 692 days) in all patients, including those with ongoing neurologic events at the time of death or data cutoff.

Peripheral neuropathies occurred in 7% of patients in CARTITUDE-4 (0.5% Grade 3 to 4) and in 7% of patients in CARTITUDE-1 (2% Grade 3 to 4). Monitor patients for signs and symptoms of peripheral neuropathies. Patients who experience peripheral neuropathy may also experience cranial nerve palsies or GBS.

Cranial Nerve Palsies occurred following treatment with CARVYKTI®. Among patients receiving CARVYKTI® in the CARTITUDE-1 & -4 studies, cranial nerve palsies occurred in 7% (19/285), including Grade ≥ 3 in 1% (1/285) of the patients. Median time to onset of cranial nerve palsies was 21 days (range: 17 to 101 days). Cranial nerve palsies resolved in 17 of 19 (89%) of patients with a median time to resolution of 66 days (range: 1 to 209 days). Median duration of cranial nerve palsies was 70 days (range: 1 to 262 days) in all patients, including those with ongoing neurologic events at the time of death or data cutoff. Cranial nerve palsies occurred in 9% of patients in CARTITUDE-4 (1% Grade 3 to 4) and in 3% of patients in CARTITUDE-1 (1% Grade 3 to 4).

The most frequent cranial nerve affected was the 7th cranial nerve. Additionally, cranial nerves III, V, and VI have been reported to be affected.

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): Among patients receiving CARVYKTI® in the CARTITUDE-1 & -4 studies, HLH/MAS occurred in 1% (3/285) of patients. All events of HLH/MAS had onset within 99 days of receiving CARVYKTI®, with a median onset of 10 days (range: 8 to 99 days), and all occurred in the setting of ongoing or worsening CRS. The manifestations of HLH/MAS included hyperferritinemia, hypotension, hypoxia with diffuse alveolar damage, coagulopathy and hemorrhage, cytopenia, and multi-organ dysfunction, including renal dysfunction and respiratory failure.

Patients who develop HLH/MAS have an increased risk of severe bleeding. Monitor hematologic parameters in patients with HLH/MAS and transfuse per institutional guidelines. Fatal cases of HLH/MAS occurred following treatment with CARVYKTI®.

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.

PROLONGED AND RECURRENT CYTOPENIAS: Patients may exhibit prolonged and recurrent cytopenias following lymphodepleting chemotherapy and CARVYKTI® infusion.

Among patients receiving CARVYKTI® in the CARTITUDE-1 & -4 studies, Grade 3 or higher cytopenias not resolved by Day 30 following CARVYKTI® infusion occurred in 62% (176/285) of the patients and included thrombocytopenia 33% (94/285), neutropenia 27% (76/285), lymphopenia 24% (67/285), and anemia 2% (6/285). After Day 60 following CARVYKTI® infusion, 22%, 20%, 5%, and 6% of patients had a recurrence of Grade 3 or 4 lymphopenia, neutropenia, thrombocytopenia, and anemia, respectively, after initial recovery of their Grade 3 or 4 cytopenia. Seventy-seven percent (219/285) 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. Sixteen and 25 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.

Among patients receiving CARVYKTI® in the CARTITUDE-1 & -4 studies, infections occurred in 57% (163/285), including Grade ≥3 in 24% (69/285) of patients. Grade 3 or 4 infections with an unspecified pathogen occurred in 12%, viral infections in 6%, bacterial infections in 5%, and fungal infections in 1% of patients. Overall, 5% (13/285) of patients had Grade 5 infections, 2.5% of which were due to COVID-19. Patients treated with CARVYKTI® had an increased rate of fatal COVID-19 infections compared to the standard therapy arm.

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 5% of patients after CARVYKTI® 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. 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.

Reactivation of John Cunningham (JC) virus, leading to progressive multifocal leukoencephalopathy (PML), including cases with fatal outcomes, have been reported following treatment. Perform appropriate diagnostic evaluations in patients with neurological adverse events.

HYPOGAMMAGLOBULINEMIA: can occur in patients receiving treatment with CARVYKTI®. Among patients receiving CARVYKTI® in the CARTITUDE-1 & -4 studies, hypogammaglobulinemia adverse event was reported in 36% (102/285) of patients; laboratory IgG levels fell below 500 mg/dL after infusion in 93% (265/285) of patients. Hypogammaglobulinemia either as an adverse reaction or laboratory IgG level below 500 mg/dL after infusion occurred in 94% (267/285) of patients treated. Fifty-six percent (161/285) of patients received intravenous immunoglobulin (IVIG) post CARVYKTI® for either an adverse reaction or prophylaxis.

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 occurred following treatment with CARVYKTI®. Among patients receiving CARVYKTI® in the CARTITUDE-1 & -4 studies, hypersensitivity reactions occurred in 5% (13/285), all of which were ≤2 Grade. Manifestations of hypersensitivity reactions included flushing, chest discomfort, tachycardia, wheezing, tremor, burning sensation, non-cardiac chest pain, and pyrexia.

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 patients appropriately according to the severity of the hypersensitivity reaction.

IMMUNE EFFECTOR CELL-ASSOCIATED ENTERCOLITIS (IEC-EC) has occurred in patients treated with CARVYKTI®. Manifestations include severe or prolonged diarrhea, abdominal pain, and weight loss requiring parenteral nutrition. IEC-EC has been associated with fatal outcome from perforation or sepsis. Manage according to institutional guidelines, including referral to gastroenterology and infectious disease specialists.

In cases of refractory IEC-EC, consider additional workup to exclude alternative etiologies, including T-cell lymphoma of the GI tract, which has been reported in the post marketing setting.

SECONDARY MALIGNANCIES: Patients treated with CARVYKTI® may develop secondary malignancies. Among patients receiving CARVYKTI® in the CARTITUDE-1 & -4 studies, myeloid neoplasms occurred in 5% (13/285) of patients (9 cases of myelodysplastic syndrome, 3 cases of acute myeloid leukemia, and 1 case of myelodysplastic syndrome followed by acute myeloid leukemia). The median time to onset of myeloid neoplasms was 447 days (range: 56 to 870 days) after treatment with CARVYKTI®. Ten of these 13 patients died following the development of myeloid neoplasms; 2 of the 13 cases of myeloid neoplasm occurred after initiation of subsequent antimyeloma therapy. Cases of myelodysplastic syndrome and acute myeloid leukemia have also been reported in the post marketing setting. T-cell malignancies have occurred following treatment of hematologic malignancies with BCMA- and CD19-directed genetically modified autologous T-cell immunotherapies, including CARVYKTI®. Mature T-cell malignancies, including CAR-positive tumors, may present as soon as weeks following infusions, and may include fatal outcomes.

Monitor lifelong 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.

ADVERSE REACTIONS

The most common nonlaboratory adverse reactions (incidence greater than 20%) are pyrexia, cytokine release syndrome, hypogammaglobulinemia, hypotension, musculoskeletal pain, fatigue, infections-pathogen unspecified, 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 Grade 3 or 4 laboratory adverse reactions (incidence greater than or equal to 50%) include lymphopenia, neutropenia, white blood cell decreased, thrombocytopenia, and anemia.

Please read full [Prescribing Information](#), including Boxed Warning, for CARVYKTI®.

RYBREVANT FASPRO™ AND RYBREVANT® INDICATIONS AND IMPORTANT SAFETY INFORMATION

INDICATIONS

RYBREVANT FASPRO™ (amivantamab and hyaluronidase-lpuj) and RYBREVANT® (amivantamab-vmjw) are indicated:

- in combination with LAZCLUZE® (lazertinib) for the first-line treatment of adult patients with locally advanced or metastatic NSCLC with *EGFR* exon 19 deletions or exon 21 L858R substitution mutations, as detected by an FDA-approved test.
- in combination with carboplatin and pemetrexed for the treatment of adult patients with locally advanced or metastatic NSCLC with *EGFR* exon 19 deletions or exon 21 L858R substitution mutations, whose disease has progressed on or after treatment with an *EGFR* tyrosine kinase inhibitor.
- in combination with carboplatin and pemetrexed for the first-line treatment of adult patients with locally advanced or metastatic NSCLC with *EGFR* exon 20 insertion mutations, as detected by an FDA-approved test.
- as a single agent for the treatment of adult patients with locally advanced or metastatic NSCLC with *EGFR* exon 20 insertion mutations, as detected by an FDA approved test, whose disease has progressed on or after platinum-based chemotherapy.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

RYBREVANT FASPRO™ is contraindicated in patients with known hypersensitivity to hyaluronidase or to any of its excipients.

WARNINGS AND PRECAUTIONS

Hypersensitivity and Administration-Related Reactions with RYBREVANT FASPRO™

RYBREVANT FASPRO™ can cause hypersensitivity and administration-related reactions (ARRs); signs and symptoms of ARR include dyspnea, flushing, fever, chills, chest discomfort, hypotension, and vomiting. The median time to ARR onset is approximately 2 hours.

RYBREVANT FASPRO™ with LAZCLUZE®

In PALOMA-3 (n=206), all Grade ARR occurred in 13% of patients, including 0.5% Grade 3. Of the patients who experienced ARRs, 89% occurred with the initial dose (Week 1, Day 1).

Premedicate with antihistamines, antipyretics, and glucocorticoids and administer RYBREVANT *FASPRO*[™] as recommended. Monitor patients for any signs and symptoms of administration-related reactions during injection in a setting where cardiopulmonary resuscitation medication and equipment are available. Interrupt RYBREVANT *FASPRO*[™] injection if ARR is suspected. Resume treatment upon resolution of symptoms or permanently discontinue RYBREVANT *FASPRO*[™] based on severity.

Infusion-Related Reactions with RYBREVANT[®]

RYBREVANT[®] can cause infusion-related reactions (IRR) including anaphylaxis; signs and symptoms of IRR include dyspnea, flushing, fever, chills, nausea, chest discomfort, hypotension, and vomiting. The median time to IRR onset is approximately 1 hour.

RYBREVANT[®] with LAZCLUZE[®]

In MARIPOSA (n=421), IRRs occurred in 63% of patients, including Grade 3 in 5% and Grade 4 in 1% of patients. IRR-related infusion modifications occurred in 54%, dose reduction in 0.7%, and permanent discontinuation of RYBREVANT[®] in 4.5% of patients.

RYBREVANT[®] with Carboplatin and Pemetrexed

Based on the pooled safety population (n=281), IRRs occurred in 50% of patients including Grade 3 (3.2%) adverse reactions. IRR-related infusion modifications occurred in 46%, and permanent discontinuation of RYBREVANT[®] in 2.8% of patients.

RYBREVANT[®] as a Single Agent

In CHRYSALIS (n=302), IRRs occurred in 66% of patients. IRRs occurred in 65% of patients on Week 1 Day 1, 3.4% on Day 2 infusion, 0.4% with Week 2 infusion, and were cumulatively 1.1% with subsequent infusions. 97% were Grade 1-2, 2.2% were Grade 3, and 0.4% were Grade 4. The median time to onset was 1 hour (range: 0.1 to 18 hours) after start of infusion. IRR-related infusion modifications occurred in 62%, and permanent discontinuation of RYBREVANT[®] in 1.3% of patients.

Premedicate with antihistamines, antipyretics, and glucocorticoids and infuse RYBREVANT[®] as recommended. Administer RYBREVANT[®] via a peripheral line on Week 1 and Week 2 to reduce the risk of IRRs. Monitor patients for signs and symptoms of IRRs in a setting where cardiopulmonary resuscitation medication and equipment are available. Interrupt infusion if IRR is suspected. Reduce the infusion rate or permanently discontinue RYBREVANT[®] based on severity. If an anaphylactic reaction occurs, permanently discontinue RYBREVANT[®].

Interstitial Lung Disease/Pneumonitis

RYBREVANT *FASPRO*[™] and RYBREVANT[®] can cause severe and fatal interstitial lung disease (ILD)/pneumonitis.

*RYBREVANT *FASPRO*[™] with LAZCLUZE[®]*

In PALOMA-3, ILD/pneumonitis occurred in 6% of patients, including Grade 3 in 1%, Grade 4 in 1.5%, and fatal cases in 1.9% of patients. 5% of patients permanently discontinued RYBREVANT *FASPRO*[™] and LAZCLUZE[®] due to ILD/pneumonitis.

RYBREVANT[®] with LAZCLUZE[®]

In MARIPOSA, ILD/pneumonitis occurred in 3.1% of patients, including Grade 3 in 1.0% and Grade 4 in 0.2% of patients. There was one fatal case of ILD/pneumonitis and 2.9% of patients permanently discontinued RYBREVANT[®] and LAZCLUZE[®] due to ILD/pneumonitis.

RYBREVANT[®] with Carboplatin and Pemetrexed

Based on the pooled safety population, ILD/pneumonitis occurred in 2.1% of patients with 1.8% of patients experiencing Grade 3 ILD/pneumonitis. 2.1% discontinued RYBREVANT® due to ILD/pneumonitis.

RYBREVANT® as a Single Agent

In CHRYSALIS, ILD/pneumonitis occurred in 3.3% of patients, with 0.7% of patients experiencing Grade 3 ILD/pneumonitis. Three patients (1%) permanently discontinued RYBREVANT® due to ILD/pneumonitis.

Monitor patients for new or worsening symptoms indicative of ILD/pneumonitis (e.g., dyspnea, cough, fever). Immediately withhold RYBREVANT FASPRO™ or RYBREVANT® and LAZCLUZE® (when applicable) in patients with suspected ILD/pneumonitis and permanently discontinue if ILD/pneumonitis is confirmed.

Venous Thromboembolic (VTE) Events with Concomitant Use with LAZCLUZE®

RYBREVANT FASPRO™ and RYBREVANT® in combination with LAZCLUZE® can cause serious and fatal venous thromboembolic (VTE) events, including deep vein thrombosis and pulmonary embolism. Without prophylactic anticoagulation, the majority of these events occurred during the first four months of treatment.

RYBREVANT FASPRO™ with LAZCLUZE®

In PALOMA-3 (n=206), all Grade VTE occurred in 11% of patients and 1.5% were Grade 3. 80% (n=164) of patients received prophylactic anticoagulation at study entry, with an all Grade VTE incidence of 7%. In patients who did not receive prophylactic anticoagulation (n=42), all Grade VTE occurred in 17% of patients. In total, 0.5% of patients had VTE leading to dose reductions of RYBREVANT FASPRO™ and no patients required permanent discontinuation. The median time to onset of VTEs was 95 days (range: 17 to 390).

RYBREVANT® with LAZCLUZE®

In MARIPOSA, VTEs occurred in 36% of patients including Grade 3 in 10% and Grade 4 in 0.5% of patients. On-study VTEs occurred in 1.2% of patients (n=5) while receiving anticoagulation therapy. There were two fatal cases of VTE (0.5%), 9% of patients had VTE leading to dose interruptions of RYBREVANT®, and 7% of patients had VTE leading to dose interruptions of LAZCLUZE®; 1% of patients had VTE leading to dose reductions of RYBREVANT®, and 0.5% of patients had VTE leading to dose reductions of LAZCLUZE®; 3.1% of patients had VTE leading to permanent discontinuation of RYBREVANT®, and 1.9% of patients had VTE leading to permanent discontinuation of LAZCLUZE®. The median time to onset of VTEs was 84 days (range: 6 to 777).

Administer prophylactic anticoagulation for the first four months of treatment. The use of Vitamin K antagonists is not recommended.

Monitor for signs and symptoms of VTE events and treat as medically appropriate. Withhold RYBREVANT FASPRO™ or RYBREVANT® and LAZCLUZE® based on severity. Once anticoagulant treatment has been initiated, resume RYBREVANT FASPRO™ or RYBREVANT® and LAZCLUZE® at the same dose level at the discretion of the healthcare provider. In the event of VTE recurrence despite therapeutic anticoagulation, permanently discontinue RYBREVANT FASPRO™ or RYBREVANT®. Treatment can continue with LAZCLUZE® at the same dose level at the discretion of the healthcare provider. Refer to the LAZCLUZE® Prescribing Information for recommended LAZCLUZE® dosage modification.

Dermatologic Adverse Reactions

RYBREVANT FASPRO™ and RYBREVANT® can cause severe rash including toxic epidermal necrolysis (TEN), dermatitis acneiform, pruritus and dry skin.

RYBREVANT FASPRO™ with LAZCLUZE®

In PALOMA-3, rash occurred in 80% of patients, including Grade 3 in 17% and Grade 4 in 0.5% of patients. Rash leading to dose reduction occurred in 11% of patients, and RYBREVANT FASPRO™ was permanently discontinued due to rash in 1.5% of patients.

RYBREVANT® with LAZCLUZE®

In MARIPOSA, rash occurred in 86% of patients, including Grade 3 in 26% of patients. The median time to onset of rash was 14 days (range: 1 to 556 days). Rash leading to dose interruptions occurred in 37% of patients for RYBREVANT® and 30% for LAZCLUZE®, rash leading to dose reductions occurred in 23% of patients for RYBREVANT® and 19% for LAZCLUZE®, and rash leading to permanent discontinuation occurred in 5% of patients for RYBREVANT® and 1.7% for LAZCLUZE®.

RYBREVANT® with Carboplatin and Pemetrexed

Based on the pooled safety population, rash occurred in 82% of patients, including Grade 3 (15%) adverse reactions. Rash leading to dose reductions occurred in 14% of patients, and 2.5% permanently discontinued RYBREVANT® and 3.1% discontinued pemetrexed.

RYBREVANT® as a Single Agent

In CHRYSALIS, rash occurred in 74% of patients, including Grade 3 in 3.3% of patients. The median time to onset of rash was 14 days (range: 1 to 276 days). Rash leading to dose reduction occurred in 5% and permanent discontinuation due to rash occurred in 0.7% of patients. Toxic epidermal necrolysis occurred in one patient (0.3%).

When initiating treatment with RYBREVANT FASPRO™ or RYBREVANT®, prophylactic and concomitant medications are recommended to reduce the risk and severity of dermatologic adverse reactions. Instruct patients to limit sun exposure during and for 2 months after treatment. Advise patients to wear protective clothing and use broad spectrum UVA/UVB sunscreen.

If skin reactions develop, administer supportive care including topical corticosteroids and topical and/or oral antibiotics. For Grade 3 reactions, add oral steroids and consider dermatologic consultation. Promptly refer patients presenting with severe rash, atypical appearance or distribution, or lack of improvement within 2 weeks to a dermatologist. For patients receiving RYBREVANT FASPRO™ or RYBREVANT® in combination with LAZCLUZE®, withhold, reduce the dose, or permanently discontinue both drugs based on severity. For patients receiving RYBREVANT FASPRO™ or RYBREVANT® as a single agent or in combination with carboplatin and pemetrexed, withhold, dose reduce or permanently discontinue RYBREVANT FASPRO™ or RYBREVANT® based on severity.

Ocular Toxicity

RYBREVANT FASPRO™ and RYBREVANT® can cause ocular toxicity including keratitis, blepharitis, dry eye symptoms, conjunctival redness, blurred vision, visual impairment, ocular itching, eye pruritus and uveitis.

RYBREVANT FASPRO™ with LAZCLUZE®

In PALOMA-3, all Grade ocular toxicity occurred in 13% of patients, including 0.5% Grade 3.

RYBREVANT® with LAZCLUZE®

In MARIPOSA, ocular toxicity occurred in 16%, including Grade 3 or 4 ocular toxicity in 0.7% of patients. Withhold, reduce the dose, or permanently discontinue RYBREVANT® and continue LAZCLUZE® based on severity.

RYBREVANT® with Carboplatin and Pemetrexed

Based on the pooled safety population, ocular toxicity occurred in 16% of patients. All events were Grade 1 or 2.

RYBREVANT® as a Single Agent

In CHRYSALIS, keratitis occurred in 0.7% and uveitis occurred in 0.3% of patients. All events were Grade 1-2.

Promptly refer patients presenting with new or worsening eye symptoms to an ophthalmologist. Withhold, dose reduce or permanently discontinue RYBREVANT FASPRO™ or RYBREVANT® based on severity.

Embryo-Fetal Toxicity

Based on animal models, RYBREVANT FASPRO™, RYBREVANT® and LAZCLUZE® can cause fetal harm when administered to a pregnant woman. Verify pregnancy status of females of reproductive potential prior to initiating RYBREVANT FASPRO™ and RYBREVANT®. Advise pregnant women and females of reproductive potential of the potential risk to the fetus. Advise patients of reproductive potential to use effective contraception during treatment and for 3 months after the last dose of RYBREVANT FASPRO™ or RYBREVANT®, and for 3 weeks after the last dose of LAZCLUZE®.

ADVERSE REACTIONS

RYBREVANT FASPRO™ with LAZCLUZE®

In PALOMA-3 (n=206), the most common adverse reactions (≥20%) were rash (80%), nail toxicity (58%), musculoskeletal pain (50%), fatigue (37%), stomatitis (36%), edema (34%), nausea (30%), diarrhea (22%), vomiting (22%), constipation (22%), decreased appetite (22%), and headache (21%). The most common Grade 3 or 4 laboratory abnormalities (≥2%) were decreased lymphocyte count (6%), decreased sodium (5%), decreased potassium (5%), decreased albumin (4.9%), increased alanine aminotransferase (3.4%), decreased platelet count (2.4%), increased aspartate aminotransferase (2%), increased gamma-glutamyl transferase (2%), and decreased hemoglobin (2%).

Serious adverse reactions occurred in 33% of patients, with those occurring in ≥2% of patients including ILD/pneumonitis (6%); and pneumonia, VTE and fatigue (2.4% each). Death due to adverse reactions occurred in 5% of patients treated with RYBREVANT FASPRO™, including ILD/pneumonitis (1.9%), pneumonia (1.5%), and respiratory failure and sudden death (1% each).

RYBREVANT® with LAZCLUZE®

In MARIPOSA (n=421), the most common adverse reactions (ARs) (≥20%) were rash (86%), nail toxicity (71%), infusion-related reactions (IRRs) (RYBREVANT®) (63%), musculoskeletal pain (47%), stomatitis (43%), edema (43%), VTE (36%), paresthesia (35%), fatigue (32%), diarrhea (31%), constipation (29%), COVID-19 (26%), hemorrhage (25%), dry skin (25%), decreased appetite (24%), pruritus (24%), and nausea (21%). The most common Grade 3 or 4 laboratory abnormalities (≥2%) were decreased albumin (8%), decreased sodium (7%), increased ALT (7%), decreased potassium (5%), decreased hemoglobin (3.8%), increased AST (3.8%), increased GGT (2.6%), and increased magnesium (2.6%).

Serious ARs occurred in 49% of patients, with those occurring in ≥2% of patients including VTE (11%), pneumonia (4%), ILD/pneumonitis and rash (2.9% each), COVID-19 (2.4%), and pleural effusion and IRRs (RYBREVANT®) (2.1% each). Fatal ARs occurred in 7% of patients due to death not otherwise specified (1.2%); sepsis and respiratory failure (1% each); pneumonia, myocardial infarction, and sudden death (0.7% each); cerebral infarction, pulmonary embolism (PE), and COVID-19 infection (0.5% each); and ILD/pneumonitis, acute respiratory distress syndrome (ARDS), and cardiopulmonary arrest (0.2% each).

RYBREVANT® with Carboplatin and Pemetrexed

In MARIPOSA-2 (n=130), the most common ARs (≥20%) were rash (72%), IRRs (59%), fatigue (51%), nail toxicity (45%), nausea (45%), constipation (39%), edema (36%), stomatitis (35%), decreased appetite (31%), musculoskeletal pain (30%), vomiting (25%), and COVID-19 (21%). The most common Grade 3 to 4 laboratory abnormalities (≥2%) were decreased neutrophils (49%), decreased white blood cells (42%), decreased lymphocytes (28%), decreased platelets (17%), decreased hemoglobin (12%), decreased potassium (11%), decreased sodium (11%), increased alanine aminotransferase (3.9%), decreased albumin (3.8%), and increased gamma-glutamyl transferase (3.1%).

In MARIPOSA-2, serious ARs occurred in 32% of patients, with those occurring in >2% of patients including dyspnea (3.1%), thrombocytopenia (3.1%), sepsis (2.3%), and PE (2.3%). Fatal ARs occurred in 2.3% of patients; these included respiratory failure, sepsis, and ventricular fibrillation (0.8% each).

In PAPILLON (n=151), the most common ARs (≥20%) were rash (90%), nail toxicity (62%), stomatitis (43%), IRRs (42%), fatigue (42%), edema (40%), constipation (40%), decreased appetite (36%), nausea (36%), COVID-19 (24%), diarrhea (21%), and vomiting (21%). The most common Grade 3 to 4 laboratory abnormalities (≥2%) were decreased albumin (7%), increased alanine aminotransferase (4%), increased gamma-glutamyl transferase (4%), decreased sodium (7%), decreased potassium (11%), decreased magnesium (2%), and decreases in white blood cells (17%), hemoglobin (11%), neutrophils (36%), platelets (10%), and lymphocytes (11%).

In PAPILLON, serious ARs occurred in 37% of patients, with those occurring in $\geq 2\%$ of patients including rash, pneumonia, ILD, PE, vomiting, and COVID-19. Fatal adverse reactions occurred in 7 patients (4.6%) due to pneumonia, cerebrovascular accident, cardio-respiratory arrest, COVID-19, sepsis, and death not otherwise specified.

RYBREVANT[®] as a Single Agent

In CHRYSALIS (n=129), the most common ARs ($\geq 20\%$) were rash (84%), IRR (64%), paronychia (50%), musculoskeletal pain (47%), dyspnea (37%), nausea (36%), fatigue (33%), edema (27%), stomatitis (26%), cough (25%), constipation (23%), and vomiting (22%). The most common Grade 3 to 4 laboratory abnormalities ($\geq 2\%$) were decreased lymphocytes (8%), decreased albumin (8%), decreased phosphate (8%), decreased potassium (6%), increased alkaline phosphatase (4.8%), increased glucose (4%), increased gamma-glutamyl transferase (4%), and decreased sodium (4%).

Serious ARs occurred in 30% of patients, with those occurring in $\geq 2\%$ of patients including PE, pneumonitis/ILD, dyspnea, musculoskeletal pain, pneumonia, and muscular weakness. Fatal adverse reactions occurred in 2 patients (1.5%) due to pneumonia and 1 patient (0.8%) due to sudden death.

LAZCLUZE[®] DRUG INTERACTIONS

Avoid concomitant use of LAZCLUZE[®] with strong and moderate CYP3A4 inducers. Consider an alternate concomitant medication with no potential to induce CYP3A4.

Monitor for adverse reactions associated with a CYP3A4 or BCRP substrate where minimal concentration changes may lead to serious adverse reactions, as recommended in the approved product labeling for the CYP3A4 or BCRP substrate.

Please see full Prescribing Information for [RYBREVANT FASPRO[™]](#), [RYBREVANT[®]](#) and [LAZCLUZE[®]](#).

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.innovativemedicine.jnj.com.

Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 related to ERLEADA[®] (apalutamide), pasritamig (JNJ-78278343), TECVAYL[®] (teclistamab-cqyv), DARZALEX[®] (daratumumab), TALVEY[®] (talquetamab-tgvs), CARVYKT[®] (cilta-cel), RYBREVANT FASPRO[™] (amivantamab and hyaluronidase-lpuj), RYBREVANT[®] (amivantamab-vmjw) and LAZCLUZE[®] (lazertinib). The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties materialize, actual results could vary materially from the expectations and projections of 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 most recent Annual Report on Form 10-K, 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, www.investor.jnj.com or on request from Johnson & Johnson. Johnson & Johnson does not undertake to update any forward-looking statement as a result of new information or future events or developments.

¹ ERLEADA[®] U.S. Prescribing Information. Horsham, PA: Janssen Biotech, Inc.

² U.S. FDA Approves TECVAYLI® (teclistamab-cqyv), the First Bispecific T-cell Engager Antibody for the Treatment of Patients with Relapsed or Refractory Multiple Myeloma. <https://www.jnj.com/u-s-fda-approves-tecvayli-teclistamab-cqyv-the-first-bispecific-t-cell-engager-antibody-for-the-treatment-of-patients-with-relapsed-or-refractory-multiple-myeloma>. Accessed April 2026.

³ DARZALEX FASPRO® U.S. Prescribing Information. Horsham, PA: Janssen Biotech, Inc.

⁴ DARZALEX® U.S. Prescribing Information. Horsham, PA: Janssen Biotech, Inc.

⁵ TALVEY® U.S. Prescribing Information, August 2023.

⁶ European Medicines Agency. TALVEY® Summary of Product Characteristics. August 2023.

⁷ CARVYKTI® U.S. Prescribing Information. Horsham, PA: Janssen Biotech, Inc.

⁸ RYBREVANT FASPRO® Prescribing Information. Horsham, PA: Janssen Biotech, Inc.

⁹ RYBREVANT® Prescribing Information. Horsham, PA: Janssen Biotech, Inc.

¹⁰ Cho BC, et al. Lazertinib versus gefitinib as first-line treatment in patients with EGFR-mutated advanced non-small-cell lung cancer: Results From LASER301. *J Clin Oncol*. 2023;41(26):4208-4217.

¹¹ LAZCLUZE® Prescribing Information. Horsham, PA: Janssen Biotech, Inc.