

For Immediate Release

RYBREVANT® (amivantamab-vmjw) plus standard of care approved in the U.S. as first and only targeted regimen to cut risk of disease progression by more than half in second-line EGFR-mutated advanced lung cancer

Approval based on compelling safety and efficacy from the Phase 3 MARIPOSA-2 study, marking the third new indication for RYBREVANT® this year, with four indications overall

RARITAN, New Jersey (September 19, 2024) – Johnson & Johnson (NYSE: JNJ) announced today that the U.S. Food and Drug Administration (FDA) approved RYBREVANT® (amivantamab-vmjw) in combination with standard of care chemotherapy (carboplatin and pemetrexed) for the treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletions (ex19del) or L858R substitution mutations, whose disease has progressed on or after treatment with an EGFR tyrosine kinase inhibitor (TKI).¹

“RYBREVANT plus chemotherapy may address the most common mechanisms of treatment resistance to third generation EGFR TKIs, such as osimertinib, in the first line,” said Martin Dietrich*, M.D., Ph.D., Oncologist, Cancer Care Centers of Brevard. “This multitargeted combination extended progression-free survival and improved overall response compared to chemotherapy alone, offering an important and effective new second-line option for patients.”

The five-year survival rate is less than 20 percent for all people with advanced EGFR-mutated NSCLC.^{2,3} Acquired resistance mechanisms after TKI monotherapy are diverse and polyclonal, making targeted therapy at progression more difficult, thus limiting the efficacy of targeted therapies at progression.^{4,5} Adding immunotherapy to chemotherapy has also failed to demonstrate clinically meaningful improvements.^{6,7}

“The progression-free survival benefits seen in the MARIPOSA-2 study are exciting,” said Andrea Ferris**, President and CEO, LUNGEvity Foundation. “It is good to see new therapeutic options like the combination of RYBREVANT and chemotherapy helping to address unmet needs impacting individuals with EGFR-mutated lung cancer, with the potential for positive change, which gives hope to more patients and their families.”

The FDA approval is based on results from the Phase 3 MARIPOSA-2 (NCT04988295) study evaluating the efficacy and safety of RYBREVANT® in combination with chemotherapy for the treatment of adult patients with locally advanced or metastatic NSCLC with EGFR ex19del or L858R substitution mutations after disease progression on or after osimertinib.¹ Results showed RYBREVANT® plus chemotherapy reduced the risk of disease progression or death (progression-free survival [PFS]) by 52 percent vs. chemotherapy alone, the study’s primary endpoint.¹ The median PFS for patients receiving RYBREVANT® plus chemotherapy was 6.3 months, compared to 4.2 months for chemotherapy alone.¹ Additionally, RYBREVANT® plus chemotherapy showed a confirmed overall response rate (ORR) of 53 percent compared to 29 percent with chemotherapy alone.¹

Amivantamab-vmjw (RYBREVANT®) in combination with chemotherapy is the only National Comprehensive Cancer Network® (NCCN®) Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Category 1 treatment option for patients with EGFR-mutated NSCLC progressing on osimertinib who are symptomatic with multiple lesions.^{8 ††}

“This milestone reinforces RYBREVANT as an important treatment option for patients with EGFR-mutated NSCLC who continue to face high unmet needs after disease progression on or after TKI therapy,” said Kiran Patel, M.D., Vice President, Clinical Development, Solid Tumors, Johnson & Johnson Innovative Medicine. “Patients need and deserve effective, targeted approaches across all lines of therapy. With RYBREVANT-based regimens, we are bringing potential new standards of care to the nearly 30,000 patients diagnosed with EGFR-mutated NSCLC in the United States each year.”

The safety profile of RYBREVANT® in combination with chemotherapy was consistent with the established profiles of the individual treatments. Permanent discontinuation of RYBREVANT® due to adverse reactions occurred in 11 percent of patients.¹

MARIPOSA-2 Publications & Presentations

Results from MARIPOSA-2 were first [presented](#) in a Presidential Symposium at the European Society of Medical Oncology (ESMO) 2023 Congress ([Abstract #LBA15](#)) and simultaneously published in the [Annals of Oncology](#).⁹

Regulatory Milestones

This approval marks the third new indication for RYBREVANT® this year, following the August 20, 2024, U.S. FDA [approval](#) announcement of RYBREVANT® 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 L858R substitution mutations, based on the Phase 3 MARIPOSA study, and the March 1, 2024, U.S. FDA [approval](#) announcement of RYBREVANT® in combination with chemotherapy (carboplatin-pemetrexed) for the first-line treatment of patients with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations, based on the Phase 3 PAPHILLON study.¹

On June 17, 2024, Johnson & Johnson also announced the [submission](#) of a Biologics License Application to the U.S. FDA for a fixed combination of amivantamab and recombinant human hyaluronidase for subcutaneous administration (SC amivantamab) for all currently approved or submitted indications of intravenous (IV) RYBREVANT®. This application is based on the Phase 3 PALOMA-3 study, with preliminary results which showed a five-fold reduction in infusion-related reactions (IRR) with a five-minute administration of SC amivantamab.¹⁰ Longer overall survival (OS), PFS and duration of response (DOR) were also observed with SC amivantamab.¹⁰ On August 14, 2024, the U.S. FDA designated this application for Priority Review.

About the MARIPOSA-2 Study

MARIPOSA-2 ([NCT04988295](#)), which enrolled 657 patients, is a randomized, open-label Phase 3 study evaluating the efficacy and safety of two combination regimens of RYBREVANT® (with and without LAZCLUZE™) and chemotherapy.¹¹ Patients with locally advanced or metastatic EGFR ex19del or L858R substitution NSCLC who had disease progression on or after treatment with osimertinib were randomized to treatment with RYBREVANT® plus chemotherapy, RYBREVANT® plus chemotherapy with LAZCLUZE™ or chemotherapy alone.¹¹ The dual primary endpoint was used to compare the PFS (using RECIST v1.1 guidelines⁸) as assessed by blinded independent central review (BICR) for each experimental arm to chemotherapy alone.¹¹ Secondary endpoints included objective response as assessed by BICR, OS, DOR, time to subsequent therapy, PFS2 and intracranial PFS.¹¹

About RYBREVANT®

RYBREVANT® (amivantamab-vmjw), a fully-human bispecific antibody targeting EGFR and MET with immune cell-directing activity, is approved in the [U.S.](#), [Europe](#), and in other markets around the world as monotherapy 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.¹ In the subcutaneous formulation, amivantamab is co-formulated with recombinant human hyaluronidase PH20 (rHuPH20), Halozyme's ENHANZE® drug delivery technology.

RYBREVANT® is approved in the [U.S.](#), [Europe](#), and in other markets around the world in combination with chemotherapy (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.

RYBREVANT® is approved in the [U.S.](#) 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 L858R substitution mutations, as detected by an FDA-approved test. A marketing authorization application (MAA) and type II extension of indication application were [submitted](#) to the EMA seeking approval of LAZCLUZE™ in combination with RYBREVANT® based on the MARIPOSA study.

In November 2023, Johnson & Johnson [submitted](#) a supplemental Biologics License Application (sBLA) to the U.S. FDA for RYBREVANT® in combination with chemotherapy for the treatment of patients with EGFR-mutated NSCLC who progressed on or after osimertinib based on the MARIPOSA-2 study. This indication was approved in [Europe](#) in August 2024.

In June 2024, Johnson & Johnson [submitted](#) a BLA to the U.S. FDA for the subcutaneous formulation of RYBREVANT® in combination with LAZCLUZE™ for all currently approved or submitted indications of IV RYBREVANT® in certain patients with NSCLC. In August 2024, the U.S. FDA designated this application for Priority Review.

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for NSCLC¹ prefer next-generation sequencing–based strategies over polymerase chain reaction–based approaches for the detection of EGFR exon 20 insertion variants. The NCCN Guidelines include:

- Amivantamab-vmjw (RYBREVANT®) plus lazertinib (LAZCLUZE™) as a Category 1 recommendation for first-line therapy in patients with locally advanced or metastatic NSCLC with EGFR exon 19 deletions or exon 21 L858R mutations.^{8††}

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- Amivantamab-vmjw (RYBREVANT[®]) plus chemotherapy as a Category 1 recommendation for patients with locally advanced or metastatic NSCLC with EGFR exon 19 deletions or exon 21 L858R mutations who experienced disease progression after treatment with osimertinib.^{8††}
- Amivantamab-vmjw (RYBREVANT[®]) plus carboplatin and pemetrexed as a Category 1 recommendation for first-line therapy in treatment-naive patients with newly diagnosed advanced or metastatic EGFR exon 20 insertion mutation-positive advanced NSCLC, or as a Category 2A recommendation for patients that have progressed on or after platinum-based chemotherapy with or without immunotherapy and have EGFR exon 20 insertion mutation-positive advanced NSCLC.^{8††}
- Amivantamab-vmjw (RYBREVANT[®]) as a Category 2A recommendation for patients that have progressed on or after platinum-based chemotherapy with or without an immunotherapy and have EGFR exon 20 insertion mutation-positive NSCLC.^{8††}

In addition to MARIPOSA-2, RYBREVANT[®] is being studied in multiple clinical trials in NSCLC, including:

- The Phase 3 MARIPOSA (NCT04487080) study assessing RYBREVANT[®] in combination with LAZCLUZE™ versus osimertinib and versus LAZCLUZE™ alone in the first-line treatment of patients with locally advanced or metastatic NSCLC with EGFR ex19del or substitution mutations.¹²
- The Phase 3 PAPILLON (NCT04538664) study assessing RYBREVANT[®] in combination with carboplatin-pemetrexed versus chemotherapy alone in the first-line treatment of patients with advanced or metastatic NSCLC with EGFR exon 20 insertion mutations.¹³
- The Phase 3 PALOMA-3 (NCT05388669) study assessing LAZCLUZE™ with subcutaneous amivantamab compared to intravenous amivantamab in patients with EGFR-mutated advanced or metastatic NSCLC.¹⁰
- The Phase 1 CHRYSALIS (NCT02609776) study evaluating RYBREVANT[®] in patients with advanced NSCLC.¹⁴
- The Phase 1/1b CHRYSALIS-2 (NCT04077463) study evaluating RYBREVANT[®] in combination with LAZCLUZE™ and LAZCLUZE™ as a monotherapy in patients with advanced NSCLC with EGFR mutations.¹⁵
- The Phase 1 PALOMA (NCT04606381) study assessing the feasibility of subcutaneous administration of amivantamab based on safety and pharmacokinetics and to determine a dose, dose regimen and formulation for amivantamab subcutaneous delivery.¹⁶
- The Phase 2 PALOMA-2 (NCT05498428) study assessing subcutaneous amivantamab in patients with advanced or metastatic solid tumors including EGFR-mutated NSCLC.¹⁷
- The Phase 1/2 METalmark (NCT05488314) study assessing RYBREVANT[®] and capmatinib combination therapy in locally advanced or metastatic NSCLC.¹⁸
- The Phase 1/2 PolyDamas (NCT05908734) study assessing RYBREVANT[®] and cetrelimab combination therapy in locally advanced or metastatic NSCLC.¹⁹
- The Phase 2 SKIPPirr study (NCT05663866) exploring how to decrease the incidence and/or severity of first-dose infusion-related reactions with RYBREVANT[®] in combination with LAZCLUZE™ in relapsed or refractory EGFR-mutated advanced or metastatic NSCLC.²⁰

For more information, visit: <https://www.RYBREVANT.com>.

Access to RYBREVANT[®]

J&J offers comprehensive access and support information and resources to assist patients in gaining access to RYBREVANT[®]. Our patient support program, J&J withMe, is available to provide personalized support to help patients start and stay on their J&J medicines. J&J withMe offers providers help supporting their patients by verifying patients' insurance coverage, providing information on Prior Authorization and Appeals processes and educating on reimbursement processes. Patients can connect to RYBREVANT withMe to receive cost support, regardless of insurance type, free, personalized one-on-one support from a Care Navigator, and resources and community connections. Learn more at RYBREVANTwithMe.com or by calling 833-JNJ-wMe1 (833-565-9631).*

About Non-Small Cell Lung Cancer (NSCLC)

Worldwide, lung cancer is one of the most common cancers, with NSCLC making up 80 to 85 percent of all lung cancer cases.^{21,22} The main subtypes of NSCLC are adenocarcinoma, squamous cell carcinoma and large cell carcinoma.²³ Among the most common driver mutations in NSCLC are alterations in EGFR, which is a receptor tyrosine kinase controlling cell growth and division.²⁴ EGFR mutations are present in 10 to 15 percent of Western patients with NSCLC with adenocarcinoma histology and occur in 40 to 50 percent of Asian patients.^{23,24,25,26,27,28} EGFR ex19del or EGFR L858R mutations are the most common EGFR mutations.²⁹ The five-year survival rate for all people with advanced NSCLC and EGFR mutations treated with EGFR tyrosine kinase inhibitors (TKIs) is less than 20 percent.^{2,3} EGFR exon 20 insertion mutations are the third most prevalent activating EGFR mutation.³⁰ Patients with EGFR exon 20 insertion mutations have a real-world five-year OS of eight percent in the frontline setting, which is worse than patients with EGFR ex19del or L858R mutations, who have a real-world five-year OS of 19 percent.³¹

IMPORTANT SAFETY INFORMATION^{1,32}

WARNINGS AND PRECAUTIONS

Infusion-Related Reactions

RYBREVANT[®] can cause infusion-related reactions (IRR); 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™

RYBREVANT[®] in combination with LAZCLUZE™ can cause infusion-related reactions. In MARIPOSA (n=421), IRRs occurred in 63% of patients treated with RYBREVANT[®] in combination with LAZCLUZE™, including Grade 3 in 5% and Grade 4 in 1% of patients. The incidence of infusion modifications due to IRR was 54% of patients, and IRRs leading to dose reduction of RYBREVANT[®] occurred in 0.7% of patients. Infusion-related

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reactions leading to permanent discontinuation of RYBREVANT[®] occurred in 4.5% of patients receiving RYBREVANT[®] in combination with LAZCLUZE[™].

RYBREVANT[®] with Carboplatin and Pemetrexed

Based on the pooled safety population (n=281), IRR occurred in 50% of patients treated with RYBREVANT[®] in combination with carboplatin and pemetrexed, including Grade 3 (3.2%) adverse reactions. The incidence of infusion modifications due to IRR was 46%, and 2.8% of patients permanently discontinued RYBREVANT[®] due to IRR.

RYBREVANT[®] as a Single Agent

In CHRYSALIS (n=302), IRR occurred in 66% of patients treated with RYBREVANT[®]. Among patients receiving treatment on Week 1 Day 1, 65% experienced an IRR, while the incidence of IRR was 3.4% with the Day 2 infusion, 0.4% with the Week 2 infusion, and cumulatively 1.1% with subsequent infusions. Of the reported IRRs, 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. The incidence of infusion modifications due to IRR was 62% and 1.3% of patients permanently discontinued RYBREVANT[®] due to IRR.

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 infusion-related reactions. Monitor patients for signs and symptoms of infusion reactions during RYBREVANT[®] infusion 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.

Interstitial Lung Disease/Pneumonitis

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

RYBREVANT[®] with LAZCLUZE[™]

In MARIPOSA, ILD/pneumonitis occurred in 3.1% of patients treated with RYBREVANT[®] in combination with LAZCLUZE[™], including Grade 3 in 1.0% and Grade 4 in 0.2% of patients. There was one fatal case (0.2%) 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% treated with RYBREVANT[®] in combination with carboplatin and pemetrexed 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 treated with RYBREVANT[®], 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). For patients receiving RYBREVANT[®] in combination with LAZCLUZE[™], immediately withhold both drugs in patients with suspected ILD/pneumonitis and permanently discontinue if ILD/pneumonitis is confirmed. For patients receiving RYBREVANT[®] as a single agent or in combination with carboplatin and pemetrexed, immediately withhold RYBREVANT[®] in patients with suspected ILD/pneumonitis and permanently discontinue if ILD/pneumonitis is confirmed.

Venous Thromboembolic (VTE) Events with Concomitant Use of RYBREVANT[®] and LAZCLUZE[™]

RYBREVANT[®] in combination with LAZCLUZE[™] can cause serious and fatal venous thromboembolic (VTE) events, including deep vein thrombosis and pulmonary embolism. The majority of these events occurred during the first four months of therapy.

In MARIPOSA, VTEs occurred in 36% of patients receiving RYBREVANT[®] in combination with LAZCLUZE[™], 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).

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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[®] and LAZCLUZE[™] based on severity. Once anticoagulant treatment has been initiated, resume 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[®] and continue treatment with LAZCLUZE[™] at the same dose level at the discretion of the healthcare provider.

Dermatologic Adverse Reactions

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

RYBREVANT[®] with LAZCLUZE[™]

In MARIPOSA, rash occurred in 86% of patients treated with RYBREVANT[®] in combination with LAZCLUZE[™], 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 treated with RYBREVANT[®] in combination with carboplatin and pemetrexed, 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 treated with RYBREVANT[®] as a single agent, including Grade 3 rash 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% of patients, and RYBREVANT[®] was permanently discontinued due to rash in 0.7% of patients.

Toxic epidermal necrolysis occurred in one patient (0.3%) treated with RYBREVANT[®] as a single agent.

Instruct patients to limit sun exposure during and for 2 months after treatment with RYBREVANT[®] or LAZCLUZE[™] in combination with RYBREVANT[®]. Advise patients to wear protective clothing and use broad-spectrum UVA/UVB sunscreen. Alcohol-free (e.g., isopropanol-free, ethanol-free) emollient cream is recommended for dry skin.

When initiating RYBREVANT[®] treatment with or without LAZCLUZE[™], administer alcohol-free emollient cream to reduce the risk of dermatologic adverse reactions. Consider prophylactic measures (e.g. use of oral antibiotics) to reduce the risk of dermatologic reactions. If skin reactions develop, start 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[®] in combination with LAZCLUZE[™], withhold, reduce the dose, or permanently discontinue both drugs based on severity. For patients receiving RYBREVANT[®] as a single agent or in combination with carboplatin and pemetrexed, withhold, dose reduce or permanently discontinue RYBREVANT[®] based on severity.

Ocular Toxicity

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

RYBREVANT[®] with LAZCLUZE[™]

In MARIPOSA, ocular toxicity occurred in 16% of patients treated with RYBREVANT[®] in combination with LAZCLUZE[™], 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 treated with RYBREVANT[®] in combination with carboplatin and pemetrexed. All events were Grade 1 or 2.

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RYBREVANT® as a Single Agent

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

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

Embryo-Fetal Toxicity

Based on its mechanism of action and findings from animal models, RYBREVANT® and LAZCLUZE™ can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential of the potential risk to the fetus.

Advise female patients of reproductive potential to use effective contraception during treatment and for 3 months after the last dose of RYBREVANT®.

Advise females of reproductive potential to use effective contraception during treatment with LAZCLUZE™ and for 3 weeks after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with LAZCLUZE™ and for 3 weeks after the last dose.

Adverse Reactions

RYBREVANT® with LAZCLUZE™

For the 421 patients in the MARIPOSA clinical trial who received RYBREVANT® in combination with LAZCLUZE™, the most common adverse reactions (≥20%) were rash (86%), nail toxicity (71%), infusion-related reactions (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%), nausea (21%), and ocular toxicity (16%). 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 adverse reactions occurred in 49% of patients who received RYBREVANT® in combination with LAZCLUZE™. Serious adverse reactions occurring in ≥2% of patients included VTE (11%), pneumonia (4%), ILD/pneumonitis and rash (2.9% each), COVID-19 (2.4%), and pleural effusion and infusion-related reaction (RYBREVANT®) (2.1% each). Fatal adverse reactions occurred in 7% of patients who received RYBREVANT® in combination with LAZCLUZE™ 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

For the 130 patients in the MARIPOSA-2 clinical trial who received RYBREVANT® in combination with carboplatin and pemetrexed, the most common adverse reactions (≥20%) were rash (72%), infusion-related reactions (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 adverse reactions occurred in 32% of patients who received RYBREVANT® in combination with carboplatin and pemetrexed. Serious adverse reactions in >2% of patients included dyspnea (3.1%), thrombocytopenia (3.1%), sepsis (2.3%), and pulmonary embolism (2.3%). Fatal adverse reactions occurred in 2.3% of patients who received RYBREVANT® in combination with carboplatin and pemetrexed; these included respiratory failure, sepsis, and ventricular fibrillation (0.8% each).

For the 151 patients in the PAPILLON clinical trial who received RYBREVANT® in combination with carboplatin and pemetrexed, the most common adverse reactions (≥20%) were rash (90%), nail toxicity (62%), stomatitis (43%), infusion-related reaction (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 adverse reactions occurred in 37% of patients who received RYBREVANT® in combination with carboplatin and pemetrexed. Serious adverse reactions in ≥2% of patients included rash, pneumonia, ILD, pulmonary embolism, 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.

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RYBREVANT[®] as a Single Agent

For the 129 patients in the CHRYSALIS clinical trial who received RYBREVANT[®] as a single agent, the most common adverse reactions ($\geq 20\%$) 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 adverse reactions occurred in 30% of patients who received RYBREVANT[®]. Serious adverse reactions in $\geq 2\%$ of patients included pulmonary embolism, 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 read full [Prescribing Information](#) for RYBREVANT[®].

Please read full [Prescribing Information](#) for LAZCLUZE[™].

About Johnson & Johnson

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Cautions Concerning Forward-Looking Statements

This press release contains “forward-looking statements” as defined in the Private Securities Litigation Reform Act of 1995 regarding product development and the potential benefits and treatment impact of RYBREVANT[®] (amivantamab-vmjw) and chemotherapy. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties materialize, actual results could vary materially from the expectations and projections of Janssen Research & Development, LLC, Janssen Biotech, Inc. and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; manufacturing difficulties and delays; competition, including technological advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; changes in behavior and spending patterns of purchasers of health care products and services; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and descriptions of these risks, uncertainties and other factors can be found in Johnson & Johnson’s Annual Report on Form 10-K for the fiscal year ended December 31, 2023, including in the sections captioned “Cautionary Note Regarding Forward-Looking Statements” and “Item 1A. Risk Factors,” and in Johnson & Johnson’s subsequent Quarterly Reports on Form 10-Q and other filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov, www.jnj.com or on request from Johnson & Johnson. None of Janssen Research & Development, LLC, Janssen Biotech, Inc. nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

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* Dr. Martin Dietrich has provided consulting, advisory, and speaking services to Johnson & Johnson; he has not been paid for any media work.

** Andrea Ferris has not been paid for any media work.

† See the NCCN Guidelines for detailed recommendations, including other treatment options.

‡ The NCCN Guidelines for NSCLC provide recommendations for certain individual biomarkers that should be tested and recommend testing techniques but do not endorse any specific commercially available biomarker assays or commercial laboratories.

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[§] RECIST (v1.1) refers to Response Evaluation Criteria in Solid Tumors, which is a standard way to measure how well solid tumors respond to treatment and is based on whether tumors shrink, stay the same or get bigger.

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* The patient support and resources provided by J&J withMe are not intended to provide medical advice, replace a treatment plan from the patient's doctor or nurse, provide case management services, or serve as a reason to prescribe a J&J medicine.

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