RYBREVANT®
(amivantamab-vmjw)
Injection for IV Use | 350 mg/7 mL (50 mg/mL)

Testing and Treatment for *EGFR* Exon 20 Insertion Mutation+ mNSCLC

RYBREVANT® (amivantamab-vmjw) is indicated for the treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 20 insertion mutations, as detected by an FDA-approved test, whose disease has progressed on or after platinum-based chemotherapy.[1]

This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.[1]

IMPORTANT SAFETY INFORMATION

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.

Based on the safety population, 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. Monitor patients for any 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.

Please read Important Safety Information on page 4, and full Prescribing Information for RYBREVANT®.

Broad molecular profiling is recommended for identifying patients with *EGFR* exon 20 insertion mutation+ mNSCLC

NGS testing is preferred in identifying patients with *EGFR* exon 20 insertion mutation+ mNSCLC[2]*

Targeted PCR-based approaches for detection of EGFR variants may underdetect *EGFR* exon 20 insertion mutations[2]

According to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for NSCLC, **broad molecular profiling** is:

- **Strongly advised for identifying rare driver mutations** such as exon 20 insertion mutations[2†]
- **A key component in the improvement of care,** ensuring patients receive the most appropriate therapy option[2]

*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.
†It is recommended at this time that, when feasible, molecular testing be performed via a broad, panel-based approach, most typically performed by next-generation sequencing (NGS).

NGS, next-generation sequencing; PCR, polymerase chain reaction.

Biomarker testing is typically a covered benefit, but requirements and patient cost-sharing may vary by payer:

Payer Type	Prior Authorization Requirement	Lab: In-network Requirement	Patient Cost-Sharing	Verification of Benefits Recommended
Medicare ("Original")	No	Must participate in Medicare	20%‡	Yes
Medicare Advantage	Often	Yes	Yes§	Yes
Commercial	Often	Usually	Yes¶	Yes
Medicaid	Unknown	Must participate in Medicaid	Yes‖	Yes

‡Patient cost-sharing may be offset by Medicare Supplement (Medigap) insurance or other secondary payer.
§Up to 20% until patients reach their plan's annual out-of-pocket limit.
¶Varies by payer and plan.
‖Often nominal; varies by state program and patient income level.

Use an FDA-approved NGS test to accurately identify patients with *EGFR* exon 20 insertion mutations who may benefit from treatment with RYBREVANT®.[1]

IMPORTANT SAFETY INFORMATION (CONTINUED)

WARNINGS AND PRECAUTIONS (CONTINUED)

Interstitial Lung Disease/Pneumonitis

RYBREVANT® can cause interstitial lung disease (ILD)/pneumonitis. Based on the safety population, ILD/pneumonitis occurred in 3.3% of patients treated with RYBREVANT®, with 0.7% of patients experiencing Grade 3 ILD/pneumonitis. Three patients (1%) discontinued RYBREVANT® due to ILD/pneumonitis.

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In the efficacy population, *EGFR* exon 20 insertion mutation status was determined by prospective local testing using tissue (94%) and/or plasma (6%) samples[1]

Guardant360® CDx is an FDA-approved companion diagnostic liquid biopsy test, and Oncomine Dx Target Test is an FDA-approved companion diagnostic tissue biopsy test, for the identification of patients who may benefit from treatment with RYBREVANT®.[3,4]

For additional information about the Guardant360® CDx test for your patients, call **855-698-8887**.

The Oncomine Dx Target Test is currently available in the following commercial labs:

Reference Lab	Telephone Number	Website
Labcorp Oncology	800-447-5816	**oncology.labcorp.com**
Quest Laboratories, Inc.	866-697-8378	**questdiagnostics.com**
NeoGenomics Laboratories, Inc.	866-776-5907	**neogenomics.com**
PhenoPath, a Quest Diagnostics Company	888-927-4366	**phenopath.com**

When verifying benefits, you may be asked to identify the code for the requested test. The following codes and descriptors are provided for your reference[5]:

CPT® Code	Descriptor	Proprietary Name	Clinical Lab and/or Manufacturer
0022U	Targeted genomic sequence analysis panel, non-small cell lung neoplasia, DNA and RNA analysis, 23 genes, interrogation for sequence variants and rearrangements, reported as presence/absence of variants and associated therapy(ies) to consider	Oncomine™ Dx Target Test	Thermo Fisher Scientific/Life Technologies Corp.
0242U	Targeted genomic sequence analysis panel, solid organ neoplasm, cell-free circulating DNA analysis of 55-74 genes, interrogation for sequence variants, gene copy number amplifications, and gene rearrangements	Guardant 360® CDx	Guardant Health Inc. CPT

CPT®, Current Procedural Terminology. CPT® is a registered trademark of the American Medical Association, 2021.

Information on FDA-approved tests is available at http://www.fda.gov/CcompanionDiagnostics.

IMPORTANT SAFETY INFORMATION (CONTINUED)

WARNINGS AND PRECAUTIONS (CONTINUED)

Interstitial Lung Disease/Pneumonitis (continued)

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

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INDICATION

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Dermatologic Adverse Reactions

RYBREVANT® can cause rash (including dermatitis acneiform), pruritus and dry skin. Based on the safety population, rash occurred in 74% of patients treated with RYBREVANT®, 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®.

Instruct patients to limit sun exposure during and for 2 months after treatment with RYBREVANT®. Advise patients to wear protective clothing and use broad-spectrum UVA/UVB sunscreen. Alcohol-free emollient cream is recommended for dry skin.

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. Withhold, dose reduce or permanently discontinue RYBREVANT® based on severity.

Ocular Toxicity

RYBREVANT® can cause ocular toxicity including keratitis, dry eye symptoms, conjunctival redness, blurred vision, visual impairment, ocular itching, and uveitis. Based on the safety population, 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 presenting with eye symptoms to an ophthalmologist. Withhold, dose reduce or permanently discontinue RYBREVANT® based on severity.

Embryo-Fetal Toxicity

Based on its mechanism of action and findings from animal models, RYBREVANT® 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 final dose of RYBREVANT®.

Adverse Reactions

The most common adverse reactions (≥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 (≥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%).

Please read full Prescribing Information for RYBREVANT®.

cp-213274v2

REFERENCES: 1. RYBREVANT® [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. **2.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer V.3.2022. © National Comprehensive Cancer Network, Inc. 2022. All rights reserved. Accessed March 16, 2022. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **3.** FDA approves NGS-based companion diagnostic for EGFR Exon20 insertion mutant non-small cell lung cancer tumor tissue. News release. Thermo Fisher Scientific. December 9, 2021. Accessed May 3, 2022. https://corporate.thermofisher.com/content/tfcorpsite/us/en/index/newsroom/press-releases/2021/Dec/09-FDA-Approves-NGS-Based-Companion-Diagnostic-for-EGFR-Exon20-Insertion-Mutant-Non-Small-Cell-Lung-Cancer-Tumor-Tissue.html **4.** Guardant360® CDx Receives FDA Approval as Companion Diagnostic for Janssen's RYBREVANT™ (amivantamab-vmjw) for Use in Patients with Advanced Non-Small Cell Lung Cancer with EGFR Exon 20 Insertion Mutations. News Release. Guardant. May 21, 2021. Accessed May 3, 2022. https://investors.guardanthealth.com/press-releases/press-releases/2021/Guardant360-CDx-Receives-FDA-Approval-as-Companion-Diagnostic-for-Janssens-RYBREVANT-amivantamab-vmjw-for-Use-in-Patients-with-Advanced-Non-Small-Cell-Lung-Cancer-with-EGFR-Exon-20-Insertion-Mutations/default.aspx **5.** American Medical Association. Current Procedural Terminology: CPT® 2022: Professional Edition. AMA Press; 2021.

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