

## Treatment algorithm for *EGFR* exon 20 insertion mutation–positive mNSCLC†

### First Line

Amivantamab-vmjw in combination with carboplatin + pemetrexed (nonsquamous)

Subsequent

Systemic Therapy

Amivantamab-vmjw (monotherapy) is also the only targeted second-line treatment option recommended for patients who progressed on or after platinum-based chemotherapy.

†For a complete listing of treatment options, see [NCCN.org](https://www.nccn.org).

*EGFR*, epidermal growth factor receptor; mNSCLC, metastatic non-small cell lung cancer; NCCN, National Comprehensive Cancer Network®.

Explore more at  
[RYBREVANTHCP.com](https://www.RYBREVANTHCP.com)



### INDICATIONS

RYBREVANT® (amivantamab-vmjw) is indicated in combination with carboplatin and pemetrexed for the first-line 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.

RYBREVANT® (amivantamab-vmjw) is indicated 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.

### SELECTED IMPORTANT SAFETY INFORMATION

Warnings and Precautions for RYBREVANT® include infusion-related reactions, interstitial lung disease/pneumonitis, dermatologic adverse reactions, ocular toxicity, and embryo-fetal toxicity.

The most common adverse reactions (≥20%) were rash, nail toxicity, stomatitis, infusion-related reaction, fatigue, edema, constipation, decreased appetite, nausea, COVID-19, diarrhea, and vomiting.

Please see Important Safety Information on the following pages.  
Please read full [Prescribing Information](#) for RYBREVANT®.

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## IMPORTANT SAFETY INFORMATION

### WARNINGS AND PRECAUTIONS

The safety population of RYBREVANT® with carboplatin and pemetrexed described in Warnings and Precautions was based on 151 patients in the PAPILLON study.

The safety population of RYBREVANT® as a single agent described in Warnings and Precautions was based on 129 patients in the CHRYSALIS study.

#### 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.

#### *RYBREVANT® with Carboplatin and Pemetrexed*

RYBREVANT® in combination with carboplatin and pemetrexed can cause infusion-related reactions. Based on the safety population, infusion-related reactions occurred in 42% of patients treated with RYBREVANT® in combination with carboplatin and pemetrexed, including Grade 3 (1.3%) adverse reactions. The incidence of infusion modifications due to IRR was 40%, and 0.7% of patients permanently discontinued RYBREVANT®.

#### *RYBREVANT® as a Single Agent*

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.

### Interstitial Lung Disease/Pneumonitis

RYBREVANT® can cause interstitial lung disease (ILD)/pneumonitis.

#### *RYBREVANT® with Carboplatin and Pemetrexed*

Based on the safety population, Grade 3 ILD/pneumonitis occurred in 2.6% of patients treated with RYBREVANT® in combination with carboplatin and pemetrexed. All patients required permanent discontinuation.

#### *RYBREVANT® as a Single Agent*

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.

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.

### Dermatologic Adverse Reactions

RYBREVANT® can cause rash (including dermatitis acneiform), pruritus, and dry skin.

#### *RYBREVANT® with Carboplatin and Pemetrexed*

RYBREVANT® in combination with carboplatin and pemetrexed can cause dermatologic adverse reactions. Based on the safety population, rash occurred in 89% of patients treated with RYBREVANT® in combination with carboplatin and pemetrexed, including Grade 3 (19%) adverse reactions. Rash leading to dose reductions occurred in 19% of patients; 2% permanently discontinued RYBREVANT®, and 1.3% discontinued pemetrexed.

#### *RYBREVANT® as a Single Agent*

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® as a single agent.

**Important Safety Information continues on the following page.**



## IMPORTANT SAFETY INFORMATION (CONT'D)

### WARNINGS AND PRECAUTIONS (CONT'D)

#### Dermatologic Adverse Reactions (cont'd)

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.

#### *RYBREVANT® with Carboplatin and Pemetrexed*

Based on the safety population, RYBREVANT® in combination with carboplatin and pemetrexed can cause ocular toxicity including blepharitis, dry eye, conjunctival redness, blurred vision, and eye pruritus. All events were Grade 1-2.

#### *RYBREVANT® as a Single Agent*

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 last dose of RYBREVANT®.

#### Adverse Reactions

#### *RYBREVANT® with Carboplatin and Pemetrexed*

For the 151 patients in the PAPILLON clinical trial who received RYBREVANT® in combination with carboplatin and pemetrexed, the most common adverse reactions ( $\geq 20\%$ ) 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 ( $\geq 2\%$ ) 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%).

Serious adverse reactions occurred in 37% of patients who received RYBREVANT® in combination with carboplatin and pemetrexed. Serious adverse reactions in  $\geq 2\%$  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.

#### *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.

**Please read full [Prescribing Information](#) for RYBREVANT®.**

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**Reference:** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer V2.2024. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed March 2, 2024. 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.

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