

PRODUCT MONOGRAPH
INCLUDING PATIENT MEDICATION INFORMATION

PrRybrevant®

amivantamab for injection

50 mg/mL Concentrate for Solution for Infusion

Antineoplastic, monoclonal antibody

PrRybrevant, indicated for:

- The treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with activating epidermal-growth factor receptor (EGFR) Exon 20 insertion mutations whose disease has progressed on or after platinum-based chemotherapy,

has been issued market authorization with conditions, pending the results of trials to verify its clinical benefit. Patients should be advised of the nature of the authorization. For further information for Rybrevant please refer to Health Canada's Notice of Compliance with conditions - drug products web site: <https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/notice-compliance/conditions.html>.

Janssen Inc.
19 Green Belt Drive
Toronto, Ontario
M3C 1L9
www.janssen.com/canada

Date of Authorization:
March 30, 2022

Submission Control Number: 254440

© 2022 Janssen Inc.

All trademarks used under license

What is a Notice of Compliance with Conditions (NOC/c)?

An NOC/c is a form of market approval granted to a product on the basis of promising evidence of clinical effectiveness following review of the submission by Health Canada.

Products authorized under Health Canada's NOC/c policy are intended for the treatment, prevention or diagnosis of a serious, life-threatening or severely debilitating illness. They have demonstrated promising benefit, are of high quality and possess an acceptable safety profile based on a benefit/risk assessment. In addition, they either respond to a serious unmet medical need in Canada or have demonstrated a significant improvement in the benefit/risk profile over existing therapies. Health Canada has provided access to this product on the condition that sponsors carry out additional clinical trials to verify the anticipated benefit within an agreed upon time frame.

TABLE OF CONTENTS

Sections or subsections that are not applicable at the time of authorization are not listed.

TABLE OF CONTENTS	3
PART I: HEALTH PROFESSIONAL INFORMATION	5
1 INDICATIONS	5
1.1 Pediatrics:	5
1.2 Geriatrics:.....	5
2 CONTRAINDICATIONS	5
4 DOSAGE AND ADMINISTRATION	5
4.1 Dosing Considerations	5
4.2 Recommended Dose and Dosage Adjustment.....	6
4.3 Reconstitution.....	9
4.4 Administration.....	10
4.5 Missed Dose	11
5 OVERDOSAGE	11
6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING	11
7 WARNINGS AND PRECAUTIONS	12
7.1 Special Populations.....	14
7.1.1 Pregnant Women.....	14
7.1.2 Breast-feeding.....	15
7.1.3 Pediatrics.....	15
7.1.4 Geriatrics	15
8 ADVERSE REACTIONS	15
8.1 Adverse Reaction Overview.....	15
8.2 Clinical Trial Adverse Reactions.....	16
8.3 Less Common Clinical Trial Adverse Reactions	18
8.4 Abnormal Laboratory Findings: Hematologic, Clinical Chemistry and Other Quantitative Data.....	19
9 DRUG INTERACTIONS	19
9.2 Drug Interactions Overview.....	19
9.3 Drug-Behavioural Interactions.....	19

9.4	Drug-Drug Interactions	20
9.5	Drug-Food Interactions	20
9.6	Drug-Herb Interactions	20
9.7	Drug-Laboratory Test Interactions	20
10	CLINICAL PHARMACOLOGY	20
10.1	Mechanism of Action.....	20
10.2	Pharmacodynamics	20
10.3	Pharmacokinetics.....	20
11	STORAGE, STABILITY AND DISPOSAL	21
12	SPECIAL HANDLING INSTRUCTIONS	21
PART II: SCIENTIFIC INFORMATION		22
13	PHARMACEUTICAL INFORMATION.....	22
14	CLINICAL TRIALS.....	22
14.1	Clinical Trials by Indication.....	22
14.3	Immunogenicity.....	24
15	MICROBIOLOGY	24
16	NON-CLINICAL TOXICOLOGY	24
PATIENT MEDICATION INFORMATION		26

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

Rybrevent (amivantamab for injection) is indicated for:

- The treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with activating epidermal-growth factor receptor (EGFR) Exon 20 insertion mutations whose disease has progressed on or after platinum-based chemotherapy.

Clinical effectiveness of Rybrevent is based on objective response rate (ORR) and duration of response (DOR) from a single-arm trial in patients with activating epidermal-growth factor receptor (EGFR) Exon 20 insertion mutations.

A validated test is required to identify EGFR Exon 20 insertions mutation-positive status prior to treatment (see [4.1 Dosing Considerations](#))

1.1 Pediatrics:

- Based on the data submitted and reviewed by Health Canada, the safety and efficacy of Rybrevent in pediatric patients (<18 years of age) has not been established; therefore, Health Canada has not authorized an indication for pediatric use.

1.2 Geriatrics:

- No clinically relevant differences in effectiveness were observed between elderly patients (≥65 years of age) and younger patients. Evidence from the clinical study (EDI1001) suggests that the use in the geriatric population is associated with differences in safety (see [7.1.4 Geriatrics](#)).

2 CONTRAINDICATIONS

Rybrevent (amivantamab for injection) is contraindicated in:

- Patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see [6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING](#).

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

- Rybrevent (amivantamab for injection) should be administered by a healthcare professional with appropriate medical support to manage infusion-related reactions (IRRs) if they occur (see [7 WARNINGS AND PRECAUTIONS](#)).
- When considering the use of Rybrevent, before treatment initiation the presence of an EGFR Exon 20 insertion mutation is required to be determined using a validated test (see [14 CLINICAL TRIALS](#)).

- Administer pre-infusion medications (see [4.2 Recommended Dose and Dosage Adjustment](#), [Table 3](#)).

4.2 Recommended Dose and Dosage Adjustment

The recommended dose of Rybrevant, based on baseline body weight is provided in [Table 1](#), and the dosing schedule is provided in [Table 2](#). It is recommended that patients are treated with Rybrevant until disease progression or unacceptable toxicity (see [4.4 Administration](#)). Pre-medications should be administered before each Rybrevant infusion as recommended (see [Pre-infusion medications](#) and [Table 3](#)).

Table 1: Recommended Dose of Rybrevant (amivantamab for injection)

Body Weight of Patient (at Baseline*)	Recommended Dose	Number of 350 mg/7 mL Rybrevant Vials
Less than 80 kg	1050 mg	3
Greater than or equal to 80 kg	1400 mg	4

* Dose adjustments not required for subsequent body weight changes

Table 2: Dosing Schedule for Rybrevant

Weeks	Schedule
Weeks 1 to 4	Weekly (total of 4 doses) (see Table 6 , 4.4 Administration) <ul style="list-style-type: none"> • Week 1 - split infusion on Day 1 and Day 2 • Weeks 2 to 4 - infusion on Day 1
Week 5 onwards	Every 2 weeks starting at Week 5

Pre-infusion medications

Prior to the initial infusion of Rybrevant (Week 1, Days 1 and 2), administer antihistamines, antipyretics, and glucocorticoids to reduce the risk of IRRs (see [Table 3](#)). For subsequent doses, administer antihistamines and antipyretics prior to all infusions, and glucocorticoids as necessary. Administer antiemetics as needed.

Table 3: Pre-Medications

Medication	Dose	Route of Administration	Dosing Window Prior to Rybrevant Administration
Antihistamine*	Diphenhydramine (25 to 50 mg) or equivalent	IV	15 to 30 minutes
		Oral	30 to 60 minutes

Medication	Dose	Route of Administration	Dosing Window Prior to Rybrevant Administration
Antipyretic*	Acetaminophen (650 to 1,000 mg)	IV	15 to 30 minutes
		Oral	30 to 60 minutes
Glucocorticoid [‡]	Dexamethasone (10 mg) or Methylprednisolone (40 mg) or equivalent	IV	45 to 60 minutes

* Required at all doses.

[‡] Required at initial dose (Week 1, Days 1 and 2); optional for subsequent doses

Dose Modifications

The recommended Rybrevant dose reductions for adverse reactions (see [Table 5](#)) are outlined in [Table 4](#).

Table 4: Rybrevant (amivantamab for injection) Dose Reductions for Adverse Reactions

Body Weight at Baseline	Initial Dose	1 st Dose Reduction	2 nd Dose Reduction	3 rd Dose Modification
Less than 80 kg	1050 mg	700 mg	350 mg	Discontinue Rybrevant
Greater than or equal to 80 kg	1400 mg	1050 mg	700 mg	

Table 5: Dose Modifications for Adverse Reactions

Adverse Reaction	Severity	Dose Modification
Infusion-Related Reactions (IRR) (see 7 WARNINGS AND PRECAUTIONS)	Grade 1 to 3	<ul style="list-style-type: none"> Interrupt Rybrevant infusion at the first sign of IRRs. Additional supportive medications (e.g., additional glucocorticoids, antihistamine, antipyretics and antiemetics) should be administered as clinically indicated. Upon resolution of symptoms, resume infusion at 50% of the previous rate. If there are no additional symptoms, the rate may be increased per the recommended infusion rate (see Table 6). Pre-medications should be administered prior to the next dose.

Adverse Reaction	Severity	Dose Modification
	Recurrent Grade 3 or any Grade 4	Permanently discontinue Rybrevant
Interstitial Lung Disease / Pneumonitis (see 7 WARNINGS AND PRECAUTIONS)	Suspected ILD/ pneumonitis (any Grade)	Withhold Rybrevant
	Confirmed ILD/ pneumonitis (any Grade)	Permanently discontinue Rybrevant
Skin and Nail Reactions (see 7 WARNINGS AND PRECAUTIONS)	Grade 2	<ul style="list-style-type: none"> • Supportive care should be initiated. • If there is no improvement after 2 weeks, consider reducing the dose (see Table 4).
	Grade 3	<ul style="list-style-type: none"> • Supportive care should be initiated. • Withhold Rybrevant until the adverse reaction improves. Upon recovery to ≤ Grade 2, resume Rybrevant at reduced dose (see Table 4). • If no improvement within 2 weeks, permanently discontinue treatment.
	Grade 4, and severe bullous, blistering or exfoliating skin conditions, including toxic epidermal necrolysis (TEN)	Permanently discontinue Rybrevant
Other Adverse Reactions (see 8 ADVERSE REACTIONS)	Grade 3	<ul style="list-style-type: none"> • Withhold Rybrevant until adverse reaction improves to ≤ Grade 1 or baseline. • Resume at same dose if recovery occurs within 1 week. • Resume Rybrevant at reduced dose (see Table 4) if recovery occurs after 1 week. • Permanently discontinue Rybrevant if recovery does not occur within 4 weeks.

Adverse Reaction	Severity	Dose Modification
	Grade 4	<ul style="list-style-type: none"> • Withhold Rybrevant until adverse reaction improves to \leq Grade 1 or baseline. • Resume at reduced dose (see Table 4) if recovery occurs within 4 weeks. • Permanently discontinue Rybrevant if recovery does not occur within 4 weeks. • Permanently discontinue Rybrevant for recurrent Grade 4 reactions.

Renal impairment

No formal studies of Rybrevant in patients with renal impairment have been conducted. Based on population pharmacokinetic (PK) analyses, no dosage adjustment is necessary for patients with mild ($60 \leq$ creatinine clearance [CrCl] < 90 mL/min) or moderate ($29 \leq$ CrCl < 60 mL/min) renal impairment. No data are available in patients with severe renal impairment ($15 \leq$ CrCl < 29 mL/min) (see [10.3 Pharmacokinetics](#)).

Hepatic impairment

No formal studies of Rybrevant in patients with hepatic impairment have been conducted. Based on population PK analyses, no dosage adjustment is necessary for patients with mild hepatic impairment [(total bilirubin \leq ULN and AST $>$ ULN) or (ULN $<$ total bilirubin $\leq 1.5 \times$ ULN)]. No data are available in patients with moderate (total bilirubin 1.5 to 3 times ULN) or severe (total bilirubin > 3 times ULN) hepatic impairment (see [10.3 Pharmacokinetics](#)).

Pediatrics (<18 years)

The safety and efficacy of Rybrevant have not been established in pediatric patients.

Geriatrics (≥ 65 years)

No formal studies have been conducted in elderly patients. Based on the safety, efficacy and pharmacokinetic data in study EDI1001, no adjustments to the initial dose were necessary based on age. There was a higher incidence of adverse events leading to dose interruptions in elderly patients (see [7.1.4 Geriatrics](#) and see [10.3 Pharmacokinetics](#)).

4.3 Reconstitution

Parenteral Products: Dilution

Rybrevant solution must be diluted and prepared for intravenous infusion by a healthcare professional using aseptic technique.

- Determine the dose required (either 1050 mg or 1400 mg) and number of Rybrevant vials needed based on patient's baseline weight (see [4.2 Recommended Dose and Dosage Adjustment](#)) Each vial of Rybrevant contains 350 mg of amivantamab.
- Check that the Rybrevant solution is colorless to pale yellow. Do not use if discoloration or visible particles are present.

- Withdraw and then discard a volume of either 5% dextrose [glucose] solution USP or 0.9% sodium chloride solution USP from the 250 mL infusion bag equal to the volume of Rybrevant to be added (i.e., discard 7 mL diluent from the infusion bag for each Rybrevant vial). Infusion bags must be made of polyvinylchloride (PVC), polypropylene (PP), polyethylene (PE), or polyolefin blend (PP+PE).
- Withdraw 7 mL of Rybrevant from each vial and add it to the infusion bag. The final volume in the infusion bag should be 250 mL. Each vial contains a 0.5 mL overfill to ensure sufficient extractable volume. Discard any unused portion left in the vial.
- Gently invert the bag to mix the solution. Do not shake.
- Visually inspect the diluted solution before administration. Do not use if discoloration or visible particles are observed.
- Diluted solutions should be administered within 10 hours (including infusion time of 2-5 hours, [Table 6](#)) at room temperature (15°C to 25°C) and in room light (see [11 STORAGE, STABILITY AND DISPOSAL](#)).

4.4 Administration

- Administer the diluted solution by intravenous infusion using an infusion set fitted with a flow regulator and with an in-line, sterile, non-pyrogenic, low protein-binding polyethersulfone (PES) filter (pore size 0.2 micrometer). Administration sets must be made of either polyurethane (PU), polybutadiene (PBD), PVC, PP, or PE.
- Do not infuse Rybrevant concomitantly in the same intravenous line with other agents.
- This medicinal product is for single use only. Any unused medicinal product should be disposed of in accordance with local requirements.
- Administer Rybrevant infusion intravenously according to the infusion rates in [Table 6](#). Due to the frequency of IRRs (see [7 WARNINGS AND PRECAUTIONS](#)) at the first dose, infusion via a peripheral vein at Week 1 and Week 2 should be considered to minimize drug exposure in the event of an IRR; infusion via central line may be administered for subsequent weeks. It is recommended for the first dose to be diluted as close to administration as possible to allow for maximal flexibility in IRR management.

Table 6: Infusion Rates for Rybrevant (amivantamab for injection) Administration

1050 mg Dose			
Week	Dose (per 250 mL bag)	Initial Infusion Rate	Subsequent Infusion Rate [†]
Week 1 (split dose infusion)			
Week 1 Cycle 1 Day 1	350 mg	50 mL/hr	75 mL/hr
Week 1 Cycle 1 Day 2	700 mg	50 mL/hr	75 mL/hr
Week 2 Cycle 1 Day 8	1050 mg	85 mL/hr	
Week 3 Cycle 1 Day 15	1050 mg	125 mL/hr	
Week 4 Cycle 1 Day 22	1050 mg	125 mL/hr	

Week 5 Cycle 2 Day 1 (and subsequent weeks/cycles)*	1050 mg	125 mL/hr	
1400 mg Dose			
Week	Dose (per 250 mL bag)	Initial Infusion Rate	Subsequent Infusion Rate[†]
Week 1 (split dose infusion)			
Week 1 Day 1 Cycle 1 Day 1	350 mg	50 mL/hr	75 mL/hr
Week 1 Day 2 Cycle 1 Day 2	1050 mg	35 mL/hr	50 mL/hr
Week 2 Cycle 1 Day 8	1400 mg	65 mL/hr	
Week 3 Cycle 1 Day 15	1400 mg	85 mL/hr	
Week 4 Cycle 1 Day 22	1400 mg	125 mL/hr	
Week 5 Cycle 2 Day 1 (and subsequent weeks/cycles)*	1400 mg	125 mL/hr	

* Starting at week 5 (start of Cycle 2), patients are dosed every 2 weeks.

† Increase the initial infusion rate to the subsequent infusion rate after 2 hours in the absence of infusion-related reactions.

4.5 Missed Dose

If a planned dose of Rybrevant is missed, the dose should be administered as soon as possible and the dosing schedule should be adjusted accordingly, maintaining the treatment interval.

5 OVERDOSAGE

There is no information on overdose with Rybrevant (amivantamab for injection). There is no known specific antidote for Rybrevant overdose. In the event of an overdose, stop Rybrevant, monitor patient for any signs or symptom of adverse reactions and undertake general supportive measures until clinical toxicity has diminished or resolved.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

To help ensure the traceability of biologic products, including biosimilars, health professionals should recognise the importance of recording both the brand name and the non-proprietary (active ingredient) name as well as other product-specific identifiers such as the Drug Identification Number (DIN) and the batch/lot number of the product supplied.

Table 7: Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Intravenous (IV) infusion	Liquid concentrate for IV infusion 350mg/7mL Vial	EDTA disodium salt dihydrate, L-Histidine, L-Histidine hydrochloride monohydrate, L-Methionine, Polysorbate 80, Sucrose, Water for Injection

Rybrevant (amivantamab for injection) is available as a colourless to pale yellow preservative-free liquid concentrate for intravenous infusion after dilution.

Each single-use vial contains 350 mg of amivantamab per 7 mL vial (or 50 mg of amivantamab per mL).

7 WARNINGS AND PRECAUTIONS

General

The safety data described in the **WARNINGS AND PRECAUTIONS** reflects exposure of 302 patients, with locally advanced or metastatic non-small cell lung cancer (NSCLC) to Rybrevant monotherapy in Study EDI1001. This includes 129 patients with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations whose disease has progressed on or after platinum-based chemotherapy. Patients were treated at a dose of 1050 mg (for patients <80 kg) or 1400 mg (for patients ≥80 kg) once weekly for 4 weeks, then every 2 weeks thereafter.

Carcinogenesis and Mutagenesis

No animal studies have been performed to evaluate the carcinogenic or mutagenic potential of amivantamab [see [16 NON-CLINICAL TOXICOLOGY](#)].

Driving and Operating Machinery

No studies on the effects on the ability to drive and use machines have been performed. Exercise caution when driving or operating a vehicle or potentially dangerous machinery.

If patients experience treatment-related symptoms affecting their ability to concentrate and react, it is recommended that they do not drive or use machines until the effect subsides.

Immune

Infusion-related reactions (IRR) occurred in 66% of patients treated with Rybrevant (amivantamab for injection). The most frequent signs and symptoms include chills, nausea, dyspnea, flushing, chest discomfort, hypotension and vomiting. 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 62.3% and 1.3% of patients permanently discontinued Rybrevant due to IRR.

Prior to initial infusion (Week 1) of Rybrevant, administer antihistamines, antipyretics, and glucocorticoids to reduce the risk of IRRs. For subsequent doses, administer antihistamines and antipyretics. Administer the initial infusion of Rybrevant in split doses on Week 1, Day 1 and Day 2. Administer Rybrevant via a peripheral line on Week 1 and Week 2 (see [4 DOSAGE AND ADMINISTRATION](#))

Treat patients with Rybrevant in a setting with appropriate medical support necessary to treat IRRs. Interrupt Rybrevant infusion at the first sign of IRRs and institute post-infusion medication as clinically indicated. Upon resolution of symptoms, resume the infusion at 50% of the previous rate. For recurrent Grade 3 or 4 IRRs, permanently discontinue Rybrevant (see [4 DOSAGE AND ADMINISTRATION](#)).

Ophthalmologic

Eye disorders, including keratitis (0.7%), occurred in 13.2% patients treated with Rybrevant. Other reported adverse reactions included dry eye, blurred vision, eye pruritus, lacrimation increased, visual impairment, ocular hyperemia, eyelid ptosis, aberrant eyelash growth, and uveitis. All events were Grade 1-2. Refer patients presenting with worsening eye symptoms promptly to an ophthalmologist and advise discontinuation of contact lenses until symptoms are evaluated. Withhold, dose reduce or permanently discontinue Rybrevant based on severity (see [4 DOSAGE AND ADMINISTRATION](#)).

Reproductive Health: Female and Male Potential

Due to the risk that Rybrevant can cause fetal harm when administered to pregnant women, advise female patients of reproductive potential to use effective contraception during treatment and for 3 months after the last dose of Rybrevant (see [7.1.1 Pregnant Women](#)). Male patients must use effective contraception (e.g., condom) and not donate or store semen during treatment and for 3 months after the last dose of Rybrevant.

- **Fertility**

No data are available to determine potential effects of Rybrevant on fertility in males or females (see [7.1.1 Pregnant Women](#)).

- **Teratogenic Risk**

Administration of other EGFR and MET inhibitor molecules to pregnant animals has resulted in an increased incidence of impairment of embryo-fetal development, embryoletality, and abortion. Therefore, based on its mechanism of action and findings in animal models, Rybrevant could cause fetal harm when administered to a pregnant woman (also see [7.1.1 Pregnant Women](#)).

Respiratory

Interstitial lung disease (ILD) or ILD-like adverse reactions (e.g. pneumonitis) occurred in 3.3% of patients treated with Rybrevant, with 0.7% of patients experiencing Grade 3 ILD. Three patients (1%) discontinued Rybrevant due to ILD/pneumonitis. Patients with a medical history

of ILD, drug-induced ILD, radiation pneumonitis that required steroid treatment, or any evidence of clinically active ILD were excluded from the clinical study.

Monitor patients for symptoms indicative of ILD/pneumonitis (e.g., dyspnea, cough, fever). If symptoms develop, interrupt treatment with Rybrevant pending investigation of these symptoms. Evaluate suspected ILD and initiate appropriate treatment as necessary. Discontinue Rybrevant in patients with confirmed ILD (see [4 DOSAGE AND ADMINISTRATION](#)).

Skin

Rash (including dermatitis acneiform) (73.5%), pruritis (17.9%) and dry skin (10.9%) occurred in patients treated with Rybrevant. Most cases were Grade 1 or 2, with Grade 3 events occurring in 3.6% of patients. Rash leading to dose reduction occurred in 5% of patients and Rybrevant discontinuation due to rash occurred in 0.7% of patients. Rash usually developed within the first 4 weeks of therapy, with a median time to onset of 14 days (range: 1 to 276 days). Paronychia occurred in patients treated with Rybrevant. Most events were Grade 1 or 2, with Grade 3 paronychia occurring in 1.4% of patients.

Toxic epidermal necrolysis (TEN) occurred in one patient (0.3%) treated with Rybrevant. Permanently discontinue Rybrevant if TEN is confirmed.

Instruct patients to limit sun exposure during and for 2 months after Rybrevant therapy. Protective clothing and use of sunscreen are advisable. Alcohol-free emollient cream is recommended for dry areas with the use of Rybrevant. If skin or nail reactions develop, start topical corticosteroids and topical and/or oral antibiotics. For Grade 3 or poorly-tolerated Grade 2 events, add systemic antibiotics and oral steroids and consider dermatologic consultation. For Grade 4 skin reactions, permanently discontinue Rybrevant. Promptly refer patients presenting with severe rash, atypical appearance or distribution, or lack of improvement within 2 weeks to a dermatologist. Interrupt Rybrevant based on severity (see [4 DOSAGE AND ADMINISTRATION](#)).

7.1 Special Populations

7.1.1 Pregnant Women

There are no human or animal data to assess the risk of Rybrevant in pregnancy. Administration of other EGFR and MET inhibitor molecules to pregnant animals has resulted in an increased incidence of impairment of embryo-fetal development, embryoletality, and abortion. Therefore, based on its mechanism of action and findings in animal models, Rybrevant could cause fetal harm when administered to a pregnant woman.

Rybrevant should not be used during pregnancy unless the benefit of treatment to the woman is considered to outweigh potential risks to the fetus. If the patient becomes pregnant while taking this drug, the patient should be informed of the potential risk to the fetus.

7.1.2 Breast-feeding

No studies have been conducted to determine if Rybrevant is excreted in human or animal milk or affects milk production. Rybrevant is a fully human, Immunoglobulin G1 (IgG1) based bispecific antibody. In general, human IgGs are known to be excreted in breast milk during the first few days after birth, which decreases to lower concentrations soon afterwards. Because of the potential for serious adverse reactions from Rybrevant in breast-fed infants, advise women not to breast-feed during treatment with Rybrevant and for 3 months following the last dose of Rybrevant.

7.1.3 Pediatrics

The efficacy and safety of Rybrevant in pediatric patients has not been established; therefore, Health Canada has not authorized an indication for pediatric use.

7.1.4 Geriatrics

Of the 302 patients treated with Rybrevant in EDI1001, 39.4% were 65 years of age or older, and 11.3% were 75 years of age or older. No clinically relevant differences in effectiveness were observed based on age. There was a higher incidence of serious adverse events observed in patients aged 65 years or older (39.5%) as compared to younger patients (25.1%). There was also a higher incidence of adverse events leading to dose interruptions observed in patients aged 65 years or older (44.5%) as compared to younger patients (28.4%).

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

The safety of Rybrevant (amivantamab for injection) described in the **ADVERSE REACTIONS** reflects the exposure of 129 patients with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations whose disease has progressed on or after platinum-based chemotherapy enrolled in Study EDI1001. Patients received Rybrevant 1050 mg (for patients < 80 kg) or 1400 mg (for patients ≥ 80 kg) by intravenous infusion once weekly for 4 weeks, then every 2 weeks thereafter, until disease progression or unacceptable toxicity. The median treatment duration was 5.6 months (range: 0.03 to 23.9 months), with 44.2% of patients for at least 6 months. The median age was 62 years (range: 36 to 84 years) with 41.1% of patients 65 years of age or older, and 8.5% of patients 75 years of age or older; 61.2% were female; 55.0% were Asian, 2.3% were Black, and 34.9% were White. Eighty-two percent of patients (n=106) had baseline body weight <80 kg and 18% (n=23) had baseline body weight ≥80 kg.

The most common adverse reactions ≥ 20% were dermatitis acneiform, rash, infusion-related reactions (IRR), nausea, paronychia, fatigue, hypoalbuminemia, constipation, stomatitis, and peripheral edema. Serious adverse reactions occurred in 30% of patients who received Rybrevant. Serious adverse reactions in ≥ 2% of patients included pulmonary embolism, pneumonitis, dyspnea, back pain, and muscular weakness. Adverse reactions resulting in

permanent discontinuation of Rybrevant in $\geq 1\%$ of patients were pneumonia, IRR, pneumonitis and pleural effusion.

Dose reductions due to an adverse reaction occurred in 15% of patients who received Rybrevant. Adverse reactions requiring dose reductions in $\geq 2\%$ of patients included dermatitis acneiform, and paronychia.

Grade 5 treatment-emergent adverse events, irrespective of relatedness to Rybrevant, were reported in 7.0% of patients. The most common events were pneumonia and dyspnea.

8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in the clinical trials; therefore, may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials may be useful in identifying and approximating rates of adverse drug reactions in real-world use.

[Table 8](#) presents adverse reactions reported in $\geq 5\%$ of patients treated with Rybrevant in Study EDI1001.

Table 8: Adverse reactions in Study EDI1001 Reported in $\geq 5\%$ of Patients

System Organ Class Adverse Reaction	Rybrevant	
	Exon 20 Ins Prior Chemotherapy(RP2D) (N=129)	
	All Grades(%)	Grade 3-4*(%)
Eye disorders		
Eye disorder ^a	9.3	0
Gastrointestinal disorders		
Stomatitis ^b	26.4	0.8
Nausea	24.0	0
Constipation	23.3	0
Diarrhoea	14.7	3.1
Vomiting	13.2	0
Abdominal pain ^c	9.3	0.8
General disorders and administration site conditions		
Fatigue ^d	32.6	2.3
Oedema ^e	26.4	0.8
Pyrexia	13.2	0
Infections and infestations		
Paronychia	49.6	3.1
Pneumonia	7.8	0.8
Injury, poisoning and procedural complications		
Infusion related reaction	64.3	3.1
Investigations		
Alanine aminotransferase increased	17.1	0.8

System Organ Class Adverse Reaction	Rybrevant Exon 20 Ins Prior Chemotherapy(RP2D) (N=129)	
	All Grades(%)	Grade 3-4*(%)
	Aspartate aminotransferase increased	13.2
Blood alkaline phosphatase increased	9.3	0.8
Gamma-glutamyltransferase increased	6.2	0.8
Metabolism and nutrition disorders		
Hypoalbuminemia ^f	32.6	3.1
Decreased appetite	14.7	0
Musculoskeletal and connective tissue disorders		
Musculoskeletal pain ^g	45.0	0
Nervous system disorders		
Dizziness ^h	10.1	0.8
Paraesthesia	8.5	0
Headache	6.2	0.8
Respiratory, thoracic and mediastinal disorders		
Dyspnea	19.4	0.8
Cough	13.2	0
Skin and subcutaneous tissue disorders		
Rash ⁱ	82.2	3.9
Pruritus	16.3	0
Dry skin ^j	15.5	0
Skin fissures	8.5	0

System Organ Class Adverse Reaction	Rybrevent	
	Exon 20 Ins Prior Chemotherapy(RP2D) (N=129)	
	All Grades(%)	Grade 3-4*(%)
<p>*No Grade 4 events observed RP2D (recommended phase 2 dose): 1050 mg if baseline weight <80 kg and 1400 mg if baseline weight >= 80 kg. Adverse events were coded using MedDRA version 23.0. Note: Patients are counted only once for any given event, regardless of the number of times they actually experienced the event. ^a includes Blepharitis, Conjunctival hyperaemia, Corneal irritation, Dry eye, Eye pruritus, Growth of eyelashes, Keratitis, Ocular hyperaemia, Uveitis, Vision blurred, Visual acuity reduced, Visual impairment ^b includes Aphthous ulcer, Cheilitis, Glossitis, Mouth ulceration, Mucosal inflammation, Stomatitis ^c includes Abdominal pain, Abdominal pain lower, Abdominal pain upper, Epigastric discomfort ^d includes Asthenia, Fatigue ^e includes Eyelid oedema, Face oedema, Generalised oedema, Oedema, Oedema peripheral, Periorbital oedema, Peripheral swelling ^f includes Blood albumin decreased, Hypoalbuminaemia ^g includes Arthralgia, Arthritis, Back pain, Bone pain, Musculoskeletal chest pain, Musculoskeletal discomfort, Musculoskeletal pain, Myalgia, Neck pain, Non-cardiac chest pain, Pain in extremity, Spinal pain. ^h includes Dizziness ⁱ includes Acne, Dermatitis, Dermatitis acneiform, Palmar-plantar erythrodysesthesia syndrome, Perineal rash, Rash, Rash erythematous, Rash maculo-papular, Rash papular, Rash vesicular, Skin exfoliation ^j includes Dry skin, Eczema, Eczema asteatotic</p>		

8.3 Less Common Clinical Trial Adverse Reactions

The following are clinically significant adverse reactions reported in <5% of patients receiving Rybrevent:

Respiratory, thoracic and mediastinal disorders: Interstitial lung disease (ILD) (see [7 WARNINGS AND PRECAUTIONS](#)).

Skin and subcutaneous tissue disorders: Toxic epidermal necrolysis (TEN) (see [7 WARNINGS AND PRECAUTIONS](#))

Interstitial lung disease or ILD-like adverse reactions have been reported with the use of Rybrevent as well as with other EGFR inhibitors.

8.4 Abnormal Laboratory Findings: Hematologic, Clinical Chemistry and Other Quantitative Data

Clinical Trial Findings

Table 9: Select Laboratory Abnormalities (≥10%) Worsening from Baseline in Patients Who Received Rybrevant in EDI1001

Laboratory Abnormality	Rybrevant (N=129)	
	Change from Baseline All Grades (%)	Change from Baseline Grade 3 or 4 (%)
Chemistry		
Albumin Decreased	79	8
Glucose Increased	56	4
Alkaline Phosphatase Increased	53	5
Creatinine Increased	46	0
Alanine Aminotransferase Increased	38	2
Phosphates Decreased	33	8
Aspartate Aminotransferase Increased	33	0
GGT Increased	27	4
Magnesium Decreased	27	0
Sodium Decreased	27	4
Potassium Decreased	26	6
Potassium Increased	14	1
Glucose Decreased	12	0
Hematology		
Lymphocyte Count Decreased	36	8
Hemoglobin Decreased	18	2
Neutrophil Count Decreased	18	3
Platelet Count Decreased	17	1
White Blood Cell Decreased	17	2
Note: Denominator used to calculate the rate is the number of patients with a baseline value and at least one post-treatment value for the specific lab test		

9 DRUG INTERACTIONS

9.2 Drug Interactions Overview

No formal drug interaction studies have been performed.

9.3 Drug-Behavioural Interactions

Drug-behavioural interactions have not been established.

9.4 Drug-Drug Interactions

Interactions with other drugs have not been established.

9.5 Drug-Food Interactions

Interactions with food have not been established.

9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Amivantamab is a bispecific antibody that binds to the extracellular domains of the EGFR and MET receptors, disrupting EGFR and MET signaling functions through blocking ligand binding and enhancing degradation of these receptors. The presence of EGFR and MET on the surface of tumor cells also allows for targeting of these cells for destruction by immune effector cells, such as natural killer cells and macrophages, through antibody-dependent cellular cytotoxicity (ADCC) and trogocytosis mechanisms, respectively.

10.2 Pharmacodynamics

Pharmacodynamic responses of amivantamab in NSCLC patients with EGFR exon 20 insertion mutations have not been fully characterized.

10.3 Pharmacokinetics

Amivantamab exposure, assessed by area under the concentration-time curve ($AUC_{1\text{week}}$) increases proportionally over a dose range from 350 to 1750 mg (0.33 to 1.67 times the recommended dose for patients < 80 kg and 0.25 to 1.25 times the recommended dose for patients \geq 80 kg).

Following administration of amivantamab at the recommended dosing regimen, steady state was achieved approximately 2 months into the every-2-week dosing period (by the ninth infusion). The mean \pm SD accumulation ratio at steady state was 2.44 ± 0.54 .

Distribution:

Amivantamab mean \pm SD volume of distribution estimated from population pharmacokinetic (PK) parameters was 5.13 ± 1.78 L.

Elimination

The mean \pm SD linear clearance was estimated to be 360 ± 144 mL/day and the terminal half-life was 11.3 ± 4.53 days, based on population PK modelling analysis.

Special Populations and Conditions

No clinically meaningful differences in the pharmacokinetics of amivantamab were observed based on age (32-87 years). The clearance of amivantamab was 24% higher in males than in females. The population PK analysis estimated that amivantamab exposure was 35% higher in women than in men at steady state; however, no clinically meaningful differences were observed based on gender.

- **Pediatrics (<18 years):** The pharmacokinetics of amivantamab in pediatric patients have not been investigated.
- **Hepatic Insufficiency:** No clinically meaningful difference in the pharmacokinetics of amivantamab was observed in patients with mild hepatic impairment [(total bilirubin \leq ULN and AST $>$ ULN) or (ULN $<$ total bilirubin \leq 1.5 x ULN)]. The pharmacokinetics of amivantamab have not been studied in patients with moderate (total bilirubin 1.5 to 3 times ULN) or severe (total bilirubin $>$ 3 times ULN) hepatic impairment.
- **Renal Insufficiency:** No clinically meaningful difference in the pharmacokinetics of amivantamab was observed in patients with mild ($60 \leq$ creatinine clearance [CrCl] $<$ 90 mL/min) or moderate ($29 \leq$ CrCl $<$ 60 mL/min) renal impairment. The pharmacokinetics of amivantamab have not been studied in patients with severe renal impairment ($15 \leq$ CrCl $<$ 29 mL/min).
- **Body Weight:** Amivantamab volume of distribution and clearance of increased with increasing body weight. Amivantamab exposures were 30-40% lower in patients who weighed \geq 80 kg compared to patients with a body weight $<$ 80 kg when given the same dose. At the recommended dose of amivantamab, 1050 mg for patients with a body weight $<$ 80 kg and 1400 mg for patients with a body weight \geq 80 kg, the amivantamab exposures were comparable.

11 STORAGE, STABILITY AND DISPOSAL

Unopened vial:

Store in a refrigerator at 2°C to 8°C. Do not freeze. Store in the original carton in order to protect from light.

After dilution:

Since amivantamab solutions do not contain a preservative, unless the method of opening/dilution precludes the risk of microbial contamination, the product should be used immediately. Administer diluted solutions within 10 hours (including infusion time) at room temperature (15°C to 25°C) and in room light.

12 SPECIAL HANDLING INSTRUCTIONS

Do not freeze. Protect from light. This product contains no preservative. Any unused medicinal product should be disposed of in accordance with local requirements.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: Amivantamab

Molecular mass: Approximately 148 kDa

Structure: Amivantamab is a low-fucose, fully human, bispecific Immunoglobulin G1 based bispecific antibody directed against the epidermal growth factor (EGF) and mesenchymal-epithelial transition (MET) receptors.

Physicochemical properties: Rybrevant is available as a colorless to pale yellow preservative-free liquid concentrate for intravenous infusion after dilution.

Product Characteristics: Amivantamab is produced by a mammalian cell line (Chinese Hamster Ovary [CHO]) using recombinant DNA technology (see [10.1 Mechanism of Action](#)).

14 CLINICAL TRIALS

14.1 Clinical Trials by Indication

Non-small cell lung cancer

Table 10: Summary of patient demographics for clinical trials in patients with NSCLC with Exon 20ins mutations

Study #	Study design	Dosage, route of administration and duration	Study subjects (n)	Median age (Range)	Sex
EDI1001 (CHRYSALIS)	Phase 1, open label, single arm, multi-cohort study	1050 mg, <80 kg body weight 1400 mg, >80 kg body weight IV, once weekly in cycle 1; bi-weekly thereafter	N=81 (efficacy population)	62 years (42-84)	Female: 48 Male: 33

EDI1001 (CHRYSALIS) was a multicenter, open-label, multi-cohort study conducted to assess the safety and efficacy of Rybrevant (amivantamab for injection) in patients with locally advanced or metastatic NSCLC. Efficacy was evaluated in 81 patients with locally advanced or metastatic NSCLC who had EGFR Exon 20 insertion mutation, with measurable disease, whose disease had progressed on or after platinum-based chemotherapy. For enrollment, EGFR exon

20 insertion mutation status was determined prospectively by local testing using tissue and/or plasma samples. Patients with untreated brain metastases and patients with a history of ILD requiring treatment with prolonged steroids or other immunosuppressive agents within the last 2 years were not eligible for the study. The median follow-up for the efficacy population was 9.7 months.

Rybrevent was administered intravenously at 1050 mg for patients < 80 kg or 1400 mg for patients ≥ 80 kg once weekly for 4 weeks, then every 2 weeks thereafter until disease progression or unacceptable toxicity. The major efficacy outcome measure was overall response rate (ORR) according to Response Evaluation Criteria in Solid Tumors (RECIST v1.1) as evaluated by Blinded Independent Central Review (BICR). Duration of response (DOR) by BICR was assessed as an additional measure of efficacy.

The median age was 62 (range: 42–84) years, with 9% of the patients ≥75 years of age; 59% were female; and 49% were Asian and 37% were White; 74% had baseline body weight <80 kg; 95% had adenocarcinoma; and 46% had received prior immunotherapy. The median number of prior therapies was 2 (range: 1 to 7 therapies). At baseline, 99% had Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1; 53% never smoked; 75% had Stage IV cancer; and 22% had previous treatment for brain metastases. Insertions in Exon 20 were observed at 8 different residues; the most common residues were A767 (24%), S768 (16%), D770 (11%), and N771 (11%).

Study Results

Efficacy results are summarized in [Table 11](#).

Table 11: Results from Study EDI1001 (CHRYSALIS): Patients with EGFR Exon 20 insertion mutations whose disease has progressed on or after platinum-based chemotherapy

	Prior Platinum Chemotherapy Treated (N=81)
Overall Response Rate ^{a,b} (95% CI)	40% (29%, 51%)
Complete response (%)	3.7%
Partial response (%)	35.8%
Duration of Response ^a (DOR)	
Median (95% CI), months ^c	11.1 (6.9, NE)
Patients with DOR ≥ 6 months	63%

^a Blinded Independent Central Review by RECIST v1.1

^b Confirmed response.

^c Based on Kaplan-Meier estimate.

NE=Not Estimable

14.3 Immunogenicity

As with all therapeutic proteins, there is the potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies in the studies described below with the incidence of antibodies in other studies or to other amivantamab products may be misleading.

In CHRYSALIS, 3 of the 286 (1%) patients who were treated with RYBREVANT and evaluable for the presence of anti-drug antibodies (ADA), tested positive for treatment emergent anti-amivantamab antibodies (one at 27 days, one at 59 days and one at 168 days after the first dose) with titers of 1:40 or less. Due to low immunogenicity observed with Rybrevant, no meaningful conclusions can be made regarding the impact of ADAs on PK, safety and efficacy.

15 MICROBIOLOGY

No microbiological information is required for this product.

16 NON-CLINICAL TOXICOLOGY

General Toxicology: In repeat-dose toxicity studies in cynomolgus monkeys, amivantamab was well-tolerated at weekly doses up to 120 mg/kg intravenously for 3 months and up to 125 mg/kg subcutaneously for 2 weeks. There were no effects on cardiovascular, respiratory, and nervous system function. Clinical pathology demonstrated non-adverse elevations in serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), and globulins, and non-adverse decreases in albumin when compared to the control group. All these values returned to normal ranges in recovery groups.

Carcinogenicity: No animal studies have been performed to establish the carcinogenic potential of amivantamab. Routine carcinogenicity studies are generally not applicable to biologic pharmaceuticals as large proteins cannot diffuse into cells and cannot interact with DNA or chromosomal material.

Genotoxicity: Routine genotoxicity studies are generally not applicable to biologic pharmaceuticals as large proteins cannot diffuse into cells and cannot interact with DNA or chromosomal material.

Reproductive and Developmental Toxicology: No long-term animal studies have been performed to evaluate whether Rybrevant affects fertility in males or females or reproduction.

Based on its mechanism of action, Rybrevant could cause fetal harm or developmental abnormalities when administered to a pregnant woman. Evidence from published literature showed that inhibition of EGFR and/or MET signaling pathways during pregnancy can cause impaired embryo-fetal development, embryo lethality and abortions in mice, rats and non-

human primates. Therefore, it is reasonable to expect that amivantamab may cause adverse effects on embryo-fetal and postnatal development in humans.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

Pr **Rybrevant**[®]

amivantamab for injection

50 mg/mL Concentrate for Solution for Infusion

Read this carefully before you start taking **Rybrevant**. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **Rybrevant**.

What is a Notice of Compliance with Conditions (NOC/c)?

A Notice of Compliance with Conditions (NOC/c) is a type of approval to sell a drug in Canada. Health Canada only gives an NOC/c to a drug that treats, prevents, or helps identify a serious or life-threatening illness. The drug must show promising proof that it works well, is of high quality, and is reasonably safe. Also, the drug must either respond to a serious medical need in Canada, or be much safer than existing treatments.

Drug makers must agree in writing to clearly state on the label that the drug was given an NOC/c, to complete more testing to make sure the drug works the way it should, to actively monitor the drug's performance after it has been sold, and to report their findings to Health Canada.

What is Rybrevant used for?

- See the following boxed text

Rybrevant is used in adults with a type of cancer called 'non-small cell lung cancer'. It is used when the cancer has spread in your body and has gone through certain genetic changes (Exon 20 insertion mutations) in a gene called 'epidermal growth factor receptor' (EGFR).

For this indication, Rybrevant has been approved with conditions (NOC/c). This means it has passed Health Canada's review and can be bought and sold in Canada, but the manufacturer has agreed to complete more studies to verify Rybrevant's clinical benefit. For more information, talk to your healthcare professional.

How does Rybrevant work?

Amivantamab is an antibody, that is a type of protein, that has been designed to recognise and attach to specific targets in the body. Amivantamab targets two proteins found on cancer cells:

- Epidermal growth factor receptor (EGFR), and
- Mesenchymal-epithelial transition factor (MET).

Rybrevant works by attaching to these proteins. This may help to slow or stop your lung cancer from growing. It may also help to reduce the size of the tumour.

What are the ingredients in Rybrevant?

Medicinal ingredients: Amivantamab

Non-medicinal ingredients: Ethylenediaminetetraacetic acid (EDTA), histidine, methionine, polysorbate 80, sucrose, and water for injection

Rybrevant comes in the following dosage forms:

Liquid concentrate for intravenous infusion, 350 mg / 7 mL vial

Do not use Rybrevant if:

- you are allergic to amivantamab or any other ingredients of Rybrevant (see “**What are the ingredients in Rybrevant?**”)

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Rybrevant. Talk about any health conditions or problems you may have, including if you:

- have a history of lung or breathing problems
- have suffered from inflammation of your lungs (a condition called “interstitial lung disease” or “pneumonitis”)

Other warnings you should know about:

Infusion-related reactions: Before each infusion of Rybrevant, you will be given medicines which help to lower the chance of infusion-related reactions. These may include:

- Medicines for an allergic reaction (antihistamines)
- Medicines for inflammation (corticosteroids)
- Medicines for fever (such as acetaminophen)

You may also be given additional medicines based on any symptoms you may experience. If you have any further questions on the use of this medicine, ask your doctor or nurse.

Tell your doctor or nurse straight away while taking Rybrevant if you get any of the following side effects:

- Any side effect during the intravenous infusion (drip into a vein) of Rybrevant.
- Sudden difficulty in breathing (shortness of breath), cough, or fever that may suggest inflammation of the lungs.
- Skin problems. To reduce the risk of skin problems, keep out of the sun, wear protective clothing, apply sunscreen, and use moisturisers regularly on your skin and nails while taking Rybrevant. You also need to do this for 2 months after you stop treatment.
- Eye problems. If you have vision problems or eye pain contact your doctor or nurse straight away. If you use contact lenses and have any new eye symptoms, stop using contact lenses and tell your doctor straight away.

Children and adolescents

Do not give Rybrevant to children or young people below 18 years of age. This is because it is not known how the medicine will affect them.

Contraception

If you or your partner could become pregnant, you must use effective contraception during and for 3 months after stopping treatment with Rybrevant.

Pregnancy and fertility – information for women

Tell your doctor or nurse before you are given Rybrevant if you are pregnant, think you might be pregnant or are planning to have a baby.

If you become pregnant while being treated with this medicine, tell your doctor or nurse straight away. You and your doctor will decide if the benefit of having the medicine is greater than the risk to your baby.

Pregnancy and fertility – information for men

If your partner becomes pregnant while you are taking this medicine, tell your doctor straight away.

Men should not donate or store semen during and for 3 months after stopping treatment with Rybrevant.

Breast-feeding

You should not breast-feed while taking this medicine and for 3 months after stopping treatment with Rybrevant.

Driving and using machines

If you feel tired or feel dizzy after taking Rybrevant, do not drive or use machines.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

Interactions with other drugs, vitamins, minerals, natural supplements or alternative medicines have not been established with Rybrevant.

How you are given Rybrevant:

- Rybrevant will be given to you by a healthcare professional in a healthcare setting
- A nurse or doctor will give you Rybrevant through a drip into a vein ('intravenous infusion') over several hours.
- Most people get Rybrevant once a week for the first 4 weeks; then once every 2 weeks after that as long as you are getting benefit from the treatment
- In the first week your doctor will give you the Rybrevant dose split over two days.

Usual dose:

Your doctor will determine your dose of Rybrevant. The dose of Rybrevant will depend on your body weight at the start of your therapy.

The usual dose of Rybrevant is:

- 1050 mg if you weigh less than 80 kg (175 lbs).
- 1400 mg if you weigh more than or equal to 80 kg (175 lbs).

Overdose:

This medicine will be given by your doctor or nurse. In the unlikely event that you are given too much (an overdose) your doctor will check you for side effects.

If you think you, or a person you are caring for, have taken too much Rybrevant, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

If you miss an appointment to get Rybrevant:

- If you miss an appointment, call your doctor and make another as soon as possible
- It is very important to go to all of your appointments

What are possible side effects from using Rybrevant?

These are not all the possible side effects you may have when taking Rybrevant. If you experience any side effects not listed here, tell your healthcare professional.

Very common side effects (may affect more than 1 in 10 people (>10%))

- Rash
- Infected skin around the nail
- Dry skin
- Itching
- Constipation or diarrhoea
- Sores in mouth
- Nausea or vomiting
- Feeling very tired
- Swollen hands, face, ankles or feet
- Decreased appetite
- Muscle aches and joint pain
- Dizziness

Rybrevant can cause abnormal blood tests. Your doctor will decide when to perform blood tests and will interpret the results. Rybrevant may cause:

- low level of 'albumin' in the blood
- increased level of the liver enzyme 'alanine aminotransferase' in the blood

Serious side effects and what to do about them		
Symptom / effect	Talk to your healthcare professional	
	Only if severe	In all cases
VERY COMMON (affecting more than 1 in 10 people)		
Infusion reactions: chills, nausea, feeling short of breath, flushing, chest discomfort, vomiting, or any side effect during an infusion. This can happen especially with the first dose.		x
Skin and Nail Problems: rash (including acne), infected skin around the nails, dry skin, itching, pain, blistering, and redness. Tell your doctor if your skin or nail problems get worse.		x
Eye Problems: dry eye, eye redness, itchy eyes, problems/changes with vision, growth of eyelashes, inflamed cornea (front part of the eye), excessive tearing		x
COMMON (affecting between 1 to 10 people out of every 100)		
Inflammation of the lungs: sudden difficulty in breathing, cough, or fever. This could lead to permanent damage ('interstitial lung disease')		x

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Rybrevant will be stored at a hospital or clinic.

Store in a refrigerator at 2°C to 8°C. Do not freeze. Protect from light.

If you want more information about Rybrevant:

- Talk to your healthcare professional
- For questions or concerns, please contact the manufacturer, Janssen Inc., at www.janssen.com/canada
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>); the manufacturer's website (<https://www.janssen.com/canada>), or by calling 1-800-567-3331 or 1-800-387-8781.

This leaflet was prepared by Janssen Inc.
Toronto, ON, M3C 1L9

Last Revised: March 30, 2022

© 2022 JANSSEN Inc

All trademarks used under license