Product Monograph

Including Patient Medication Information

Pr **RYSTIGGO®**

rozanolixizumab injection

Solution by subcutaneous use from vial

140 mg/mL of rozanolixizumab

Neonatal Fc Receptor Blocker

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Recent Major Label Changes

4 Dosage and Administration	2026-03 2026-10

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Certain sections or subsections that are not applicable at the time of the preparation of the most recent authorized product monograph are not listed.

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Part 1: Healthcare Professional Information

1. Indications

RYSTIGGO (rozanolixizumab injection) is indicated for the treatment of adult patients with generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) or anti-muscle-specific tyrosine kinase (MuSK) antibody positive.

1.1. Pediatrics

Pediatrics (<18 years of age): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

1.2. Geriatrics

Geriatrics (≥65 years of age): Limited safety and efficacy data are available in patients ≥65 years of age treated with RYSTIGGO at the recommended dose in the gMG placebo-controlled study (n=17). The number of patients aged 65 years or older is not sufficient to determine whether they respond differently from younger adult patients (see 14 Clinical Trials).

2. Contraindications

RYSTIGGO 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

RYSTIGGO is intended for use under the guidance of a healthcare professional.

Subcutaneous administration of RYSTIGGO can be performed by:

1. a healthcare professional using an infusion pump (also known as syringe pump) or using a syringe manual push. OR
2. the patient (self-administration) or a caregiver using syringe manual push, after proper training by a healthcare professional on how to administer RYSTIGGO.

Monitor for clinical signs and symptoms of hypersensitivity reactions for at least 15 minutes after administration. If a hypersensitivity reaction occurs, the patient should seek medical attention and the healthcare professional should institute appropriate measures, if needed (see 7 Warnings and Precautions, Hypersensitivity and infusion related reactions).

4.2. Recommended Dose and Dosage Adjustment

The recommended dosage is administered as a subcutaneous infusion once weekly for 6 weeks (defined as one treatment cycle).

Table 1 indicates the recommended total weekly dose of RYSTIGGO according to the patient's body weight. One mL of solution for injection contains 140 mg of rozanolixizumab. One or more vials might be needed to meet the appropriate volume to be administered, depending on vial size availability.

Table 1: Recommended Dose Based on Body Weight

Body weight	**≥ 35 to <50 kg**	**≥ 50 to < 70 kg**	**≥ 70 to < 100 kg**	**≥ 100 kg**
Weekly dose (mg)	280 mg	420 mg	560 mg	840 mg
Weekly dose (mL)	2 mL*	3 mL*	4 mL*	6 mL*

*Each vial contains excess volume for priming of the infusion line. For detailed preparation and administration instructions using an infusion pump, see Section 4.4 Administration below. For detailed preparation and administration instructions using a syringe manual push, see Instructions for Use – Self-administration via Syringe Manual Push.

Administer subsequent treatment cycles according to clinical evaluation. The frequency of treatment cycles may vary by patient. The safety of initiating subsequent cycles sooner than 4 weeks from the last infusion of the previous treatment cycle has not been established.

Pediatrics (<18 years of age): The safety and efficacy of RYSTIGGO in children and adolescents aged below the age of 18 years have not been established. RYSTIGGO is not indicated for use in pediatric patients.

Geriatrics (≥65 years of age): No dose adjustment is required (see 10 Clinical Pharmacology, Pharmacokinetics, Special Populations and Conditions, Geriatrics).

Renal Impairment: No dose adjustment is required. There is limited safety and efficacy data in patients with moderate renal impairment (eGFR 30-59mL/min/1.73 m^2) and no safety and efficacy data in patients with severe renal impairment (eGFR <30 mL/min/1.73 m^2) (see 10 Clinical Pharmacology, Pharmacokinetics, Special Populations and Conditions, Renal Insufficiency).

4.4. Administration

Infusion with an Infusion Pump (by a Healthcare Professional)

Infusion pumps, syringes and infusion sets appropriate for subcutaneous administration of medicinal products should be used. Refer to the infusion pump manufacturer's instructions for full preparation and administration information. It is recommended to use pumps where the administered volume can be pre-set as each vial contains excess volume for priming of the infusion line.

The following criteria are recommended for administration of RYSTIGGO using an infusion pump:

- Syringe pump occlusion alarm limits should be at the maximum setting.
- Administration tubing length should be 61 cm (24 in) or shorter.
- Infusion set with a needle of 26 gauge or with a larger diameter should be used.

Read the Instructions for Use (Infusion Pump) below before preparing and administering RYSTIGGO solution.

- Use aseptic technique when preparing and administering RYSTIGGO.
- Prior to use, allow vials to reach room temperature. This will take between 30 minutes and 120 minutes. Do not use heating devices. Keep the vial in the original carton to protect from light until ready to use. Do not shake.

- Vials may be stored at room temperature up to 25°C (77°F) for a single period of up to 20 days in the original carton (see 11 Storage, Stability, and Disposal).

- Infuse RYSTIGGO within 4 hours of puncturing the vial. RYSTIGGO should be administered immediately after priming the infusion set.
- RYSTIGGO vials should be inspected visually for particulate matter and discolouration prior to administration. The solution should be colourless to pale brownish-yellow, clear to slightly opalescent. Do not use the vial if the liquid looks cloudy, contains foreign particles, or has changed colour.
- Use transfer needle to fill the syringe.
- Remove the needle from the syringe and attach the infusion set to the syringe.
- RYSTIGGO should not be mixed with other medications upon administration.
- Follow the device manufacturer's instructions to prepare the pump and prime the tubing.
- Each vial contains excess volume (to allow priming of the infusion line); therefore, pre-set the pump to deliver the prescribed volume. If not using a programmable pump, the volume in the syringe should be adjusted to the prescribed dose prior to administration.
- Choose an infusion site in the lower right or lower left part of the abdomen below the navel and clean with an alcohol wipe. Other infusion sites have not been studied in the clinical development program. Do not infuse where the skin is tender, bruised, red, or hard. Avoid infusing into tattoos, scars, or stretch marks. Rotate infusion sites for subsequent administrations.
- Insert the infusion set needle into the infusion site and secure the needle to the skin with sterile gauze and tape or a transparent dressing.
- Infuse RYSTIGGO at a constant flow rate up to 20 mL/hour.
- When the infusion is complete, **do not flush** the infusion line as the volume of infusion has been adjusted taking into account the losses in the line.
- Remove needle from the infusion site.
- Each RYSTIGGO vial is for one-time use only. RYSTIGGO does not contain preservatives. **Discard any remaining solution** (see 11 Storage, Stability, and Disposal).

Infusion by Syringe Manual Push (by Healthcare Professional or by Patient/Caregiver)

Syringes and infusion sets appropriate for subcutaneous administration of medicinal products should be used.

The following criteria are recommended for administration of RYSTIGGO using a syringe manual push:

- The volume in the syringe should be adjusted to the prescribed dose prior to administration.
- RYSTIGGO administration using a syringe should be performed at a flow rate that is comfortable for the patient. In clinical trials, infusion times by syringe manual push ranged from 1 to 30 minutes with a median infusion time of 5 minutes per patient. This range of infusion times may serve as a guide when training the patient or caregiver.
- Administration tubing length of 61cm or shorter is recommended
- An infusion set with a needle of 26 gauge or with a larger diameter should be used

Read the Instructions for Use – Self-administration via Syringe Manual Push included in the Patient Medication Information section of this Product Monograph before preparing and administering RYSTIGGO.

4.5. Missed Dose

If a scheduled infusion is missed, RYSTIGGO may be administered up to 4 days after the scheduled time point. Thereafter, resume the original dosing schedule until the treatment cycle is completed.

5. Overdose

There is no data on symptoms associated with an overdose.

Single subcutaneous dose of up to 20 mg/kg (2162 mg) and weekly subcutaneous doses of around 10 mg/kg (1120 mg) for up to 52 weeks have been administered per protocol in clinical studies without dose limiting toxicity.

In case of overdose, it is recommended that patients are monitored closely for any adverse effects, and appropriate supportive measures should be instituted immediately.

For the most recent information in the management of a suspected drug overdose, contact your regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669).

6. Dosage Forms, Strengths, Composition, and Packaging

To help ensure the traceability of biologic products, healthcare professionals should record 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 2: Dosage Forms, Strengths, and Composition

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Subcutaneous use	Solution / 140 mg/mL / single-use vials (2 mL, 3 mL, 4 mL, 6 mL)	L-histidine, L-histidine hydrochloride monohydrate, L-proline, polysorbate 80, water for injection

Description

RYSTIGGO is available in the following formats:

- Carton containing one 280 mg / 2 mL single-use glass vial.
- Carton containing one 420 mg / 3 mL single-use glass vial.
- Carton containing one 560 mg / 4 mL single-use glass vial.
- Carton containing one 840 mg / 6 mL single-use glass vial.

7. Warnings and Precautions

General

Clinical monitoring

A limited number of patients received RYSTIGGO repeated cyclic treatment at the recommended dose. RYSTIGGO is a symptom driven cyclic treatment. Considering individual variability in clinical response and expected fluctuations in disease manifestations, patients should be closely monitored. In the clinical development program, despite treatment with RYSTIGGO (i.e., ≈7mg/kg or ≈10mg/kg), 13.8% of patients reported worsening of symptoms up to myasthenia crisis (2.1%).

Body weight <50 kg

In the clinical study program, only a very limited number of patients with a body weight below 50 kg were examined. In addition, the efficacy of repeated cyclic treatment with RYSTIGGO was more variable in this population (see 14 Clinical Trials).

Excipients

This medicinal product contains 29 mg of proline in each mL.

The use in patients suffering from hyperprolinaemia should be restricted to cases where no alternative treatment is available.

Myasthenic crisis

Treatment with RYSTIGGO in patients with impending, or who manifest myasthenic crisis has not been studied. The sequence of therapy initiation between established therapies for MG crisis and RYSTIGGO, and their potential interactions, should be considered (see 9 Drug Interactions).

Immune

Infections

Based on its mechanism of action, rozanolixizumab may increase the risk of infection (see 8 Adverse Reactions).

Treatment with RYSTIGGO should not be initiated in patients with a clinically important active infection until the infection resolves or is adequately treated. During treatment with RYSTIGGO, monitor for clinical signs and symptoms of infections. If a clinically important active infection occurs, consider withholding RYSTIGGO until the infection has resolved.

Immunization

Immunization with vaccines during RYSTIGGO treatment has not been studied. The safety of immunization with live or live-attenuated vaccines and the response to immunization with any vaccine are unknown. Because RYSTIGGO causes a reduction in IgG levels, vaccination with live-attenuated or live vaccines is not recommended during treatment with RYSTIGGO. Evaluate the need to administer age-appropriate vaccines according to immunization guidelines and administer at least 4 weeks before initiation of treatment with RYSTIGGO. For all other vaccines, vaccination should take place at least 2 weeks after the last infusion of a treatment cycle and 4 weeks before initiating the next cycle with RYSTIGGO.

Neurologic

Aseptic Meningitis

Serious adverse reactions of drug induced aseptic meningitis have been reported following treatment with RYSTIGGO (see 8 Adverse Reactions). If symptoms consistent with aseptic meningitis develop, diagnostic workup and treatment should be initiated according to the standard of care.

Reproductive Health

- **Fertility**

  The effect of RYSTIGGO on human fertility is unknown.

Sensitivity/Resistance

Hypersensitivity and infusion related reactions

Hypersensitivity reactions, including angioedema and rash, were observed in patients treated with RYSTIGGO (see 8 Adverse Reactions). Patients should be monitored during treatment with RYSTIGGO and for 15 minutes after the administration is completed for clinical signs and symptoms of hypersensitivity reactions. If a hypersensitivity reaction occurs during administration, discontinue the infusion and institute appropriate supportive measures, if needed. Once resolved, and based on the severity of the reaction, administration may be cautiously resumed based on clinical evaluation.

Patients should be informed of the signs and symptoms of hypersensitivity reactions and advised to contact their healthcare provider should they occur.

7.1. Special Populations

7.1.1. Pregnancy

Limited data does not allow conclusions to be drawn on the use of RYSTIGGO in pregnant women. Based on animal data, RYSTIGGO may cause fetal harm. Administration of rozanolixizumab to pregnant cynomolgus monkeys resulted in an increase in early pregnancy losses. As expected by the pharmacological mode of action, pregnant animals had reduced levels of plasma total IgG concentrations. Neonatal offspring also had very low levels of IgG at birth, indicating inhibition of maternal IgG transfer across the placenta to the fetus. Low concentrations of rozanolixizumab were occasionally detected in neonatal plasma at birth, indicating possible drug transfer across the placental barrier (see 16 Non-Clinical Toxicology). As precautionary measure, avoid the use of RYSTIGGO during pregnancy.

As RYSTIGGO is expected to reduce maternal IgG antibody levels, and is also expected to inhibit the transfer of maternal antibodies to the fetus, reduction in passive protection to the newborn is anticipated. Risk and benefits should be considered prior to administering live or live-attenuated vaccines to infants from pregnant women treated with RYSTIGGO.

7.1.2. Breastfeeding

There is no information regarding the presence of RYSTIGGO in human milk, the effects on the breastfed infant, or the effects on milk production. Maternal IgG is known to be excreted in human milk. A risk to the breastfed newborn/infant cannot be excluded. The developmental and health

benefits of breastfeeding should be considered along with the mother's clinical need for RYSTIGGO and any potential adverse effects on the breastfed child from RYSTIGGO.

7.1.3. Pediatrics

No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

7.1.4. Geriatrics

Geriatrics (≥65 years of age): Limited safety and efficacy data are available in patients ≥65 years of age treated with RYSTIGGO at the recommended dose in the gMG placebo-controlled study (n=17). The number of patients aged 65 years or older is not sufficient to determine whether they respond differently from younger adult patients (see 14 Clinical Trials).

8. Adverse Reactions

8.1. Adverse Reaction Overview

In the placebo-controlled study (Study 1) and an extension study in patients with gMG, (where the median time in study was 24.20 months and the median number of treatment cycles received was 6), out of 188 patients treated with RYSTIGGO, 29.3% serious adverse events, 33.0% severe adverse events and 17.6% adverse events leading to treatment discontinuation were reported. The most commonly reported adverse events (≥ 10%) in patients with Myasthenia Gravis were headache (50.0 %), diarrhea (33.5 %), COVID-19 (21.8%), pyrexia (20.7 %), nausea (17.6%), myasthenia gravis worsening (13.8%), arthralgia (12.2%), nasopharyngitis (12.2%), IgG decreased (11.2%), abdominal pain (10.1%), and upper respiratory tract infection (10.1%).

8.2. Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. Therefore, the frequencies of adverse reactions observed in the clinical trials may not reflect frequencies observed in clinical practice and should not be compared to frequencies reported in clinical trials of another drug.

In a placebo-controlled study (Study 1) in patients with gMG, 133 patients received 1 treatment cycle of RYSTIGGO. One treatment cycle consisted of one weight-tiered dose of RYSTIGGO per week for a period of 6 weeks followed by an 8-week observation period. The weight-tiered doses of RYSTIGGO were equivalent to approximately (≈) 7 mg/kg (corresponding to the recommended dose, see 4 Dosage and Administration) or a higher dose.

In an extension study, the minimum time for initiating subsequent treatment cycles, specified by study protocol, was 4 weeks from the last infusion of the previous treatment cycle. The safety of initiating subsequent cycles sooner than 4 weeks from the last infusion of the previous treatment cycle has not been established.

Table 3 describes adverse reactions that occurred at a frequency of 5% or more and at greater frequency than placebo among adult patients with gMG treated with RYSTIGGO.

Table 3: Adverse Reactions Reported in ≥5% and at Greater Frequency than Placebo in RYSTIGGO (rozanolixizumab)-treated patients with gMG in Study 1

Adverse reaction	rozanolixizumab N=133 n (%)	Placebo N=67 n (%)
Nervous system disorders		
Headache[1]	58 (43.6)	13 (19.4)
Gastrointestinal disorders		
Diarrhea	27 (20.3)	9 (13.4)
Nausea	13 (9.8)	5 (7.5)
Abdominal pain[2]	10 (7.5)	4 (6.0)
Infections and Infestations		
Upper respiratory tract infections[3]	11 (8.3)	4 (6.0)
Skin and subcutaneous tissue disorders		
Rash[4]	9 (6.8)	2 (3.0)
Musculoskeletal and connective tissue disorders		
Arthralgia	9 (6.8)	2 (3.0)
General disorders and administration site conditions		
Pyrexia	22 (16.5)	1 (1.5)
Injection site reactions[5]	7 (5.3)	1 (1.5)

[1] Includes headache and migraine
[2] Includes abdominal pain, abdominal pain upper and abdominal discomfort
[3] Includes nasopharyngitis, upper respiratory tract infection, rhinitis and sinusitis
[4] Includes rash, rash papular and rash erythematous
[5] Includes injection site rash, injection site reaction, injection site erythema, injection site inflammation, injection site discomfort, infusion site erythema, infusion site pain, and injection site urticaria.

Infections

In Study 1 and an extension study, out of 188 patients treated with RYSTIGGO, 109 (58.0%) patients reported infections. Common infections (at least 5% frequency) were upper respiratory tract infections which includes nasopharyngitis, upper respiratory tract infection, rhinitis, and sinusitis (23.4%), COVID-19 (21.8%), urinary tract infection (6.9%), and herpes viral infections which includes herpes simplex, oral herpes and herpes zoster (8.5%). Serious infections were reported in 6.4% of patients treated with RYSTIGGO and 4.8% cases of infections led to discontinuation of RYSTIGGO. Three fatal cases of pneumonia identified were caused by COVID-19 infection in two patients and an unknown pathogen in one patient. See 7 Warnings and Precautions, Infections.

Headache

In Study 1, seven (5.3%) cases of severe headache were reported in patients treated with RYSTIGGO. None of the patients who received placebo reported severe headache. One patient was hospitalized due to severe headache and one patient discontinued treatment due to severe headache associated with fever, photophobia, phonophobia, nausea, and vertigo. Headache occurred most frequently after the first infusion of RYSTIGGO and within 1 to 4 days after infusion.

Aseptic Meningitis

In clinical trials, one patient with gMG and two patients with another neurological disease experienced a serious adverse reaction of drug-induced aseptic meningitis, which led to hospitalization for 2 participants and discontinuation for all with full recovery.

8.3. Less Common Clinical Trial Adverse Reactions

The following adverse reactions were reported in the double-blind placebo-controlled trial at an incidence of <5% in RYSTIGGO-treated patients, in more than one patient at a higher frequency (%) than placebo:

Gastrointestinal disorders: vomiting

Musculoskeletal and connective tissue disorders: myalgia

9. Drug Interactions

9.2. Drug Interactions Overview

Clinical drug interactions studies have not been performed with RYSTIGGO. Interactions with highly-protein bound medications or medications that are substrates, inducers or inhibitors of cytochrome P450 enzymes or transporters are unlikely. Rozanolixizumab interferes with the neonatal Fc receptor (FcRn) recycling mechanism of immunoglobulin G (IgG) (see 9.4 Drug-Drug Interactions).

9.3. Drug-Behaviour Interactions

The interaction of RYSTIGGO with individual behavioural risks (e.g. cigarette smoking, cannabis use, and/or alcohol consumption) has not been studied.

9.4. Drug-Drug Interactions

Rozanolixizumab is expected to decrease the serum concentration of IgG-based drugs (e.g. monoclonal antibodies and IVIg) and Fc–peptide fusion proteins if administered concomitantly or within 2 weeks after administration of rozanolixizumab. It is recommended to initiate these drugs 2 weeks after a rozanolixizumab infusion and closely monitor for attenuated effectiveness of these medications when administered concomitantly with rozanolixizumab.

Treatment with IV or SC immunoglobulins, PLEX/plasmapheresis and immunoadsorption may reduce circulating levels of rozanolixizumab.

9.5. Drug-Food Interactions

Interactions with food have not been studied.

9.6. Drug-Herb Interactions

Interactions with herbal products have not been studied.

9.7. Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been studied.

10. Clinical Pharmacology

10.1. Mechanism of Action

Rozanolixizumab is a humanized immunoglobulin (Ig) G4 monoclonal antibody that binds to neonatal Fc receptor (FcRn), and decreases serum concentrations of IgG and pathogenic IgG autoantibodies by inhibiting the binding of IgG to FcRn, a receptor that normally protects IgG from intracellular degradation and recycles IgG back to the cell surface.

10.2. Pharmacodynamics

Weekly subcutaneous administration of rozanolixizumab at the recommended dose (see 4.2 Recommended Dose and Dosage Adjustment) resulted in a rapid and sustained reduction in total IgG serum concentrations, with lowering of IgG of 45% compared to baseline within 1 week, and a maximum decrease of 73% at about 3 weeks. After stopping administration, IgG concentrations recovered towards baseline levels within approximately 8 weeks.

10.3. Pharmacokinetics

Rozanolixizumab exhibited nonlinear pharmacokinetics. Rozanolixizumab exposure increased in a greater than dose-proportional manner over a dose range from 1 mg/kg to 20 mg/kg (over two times the maximum recommended dose of approximately 7 mg/kg) following subcutaneous administration.

Absorption

Following subcutaneous administration of rozanolixizumab, peak plasma levels are achieved after approximately 2 days in healthy subjects. The absolute bioavailability of rozanolixizumab after SC administration was about 70% as estimated by population pharmacokinetic analysis.

Distribution:

The apparent volume of distribution of rozanolixizumab is approximately 7 L estimated by population pharmacokinetic analysis.

Metabolism:

Rozanolixizumab is expected to be degraded into small peptides and amino acids via catabolic pathways in a manner similar to endogenous IgG.

Elimination:

The apparent linear clearance for the free drug is approximately 0.9 L/day. The half-life of rozanolixizumab is concentration-dependent and cannot be calculated. Rozanolixizumab plasma concentrations are undetectable within one week after dosing.

Special populations and conditions

- **Pediatrics:** Pharmacokinetics of rozanolixizumab have not been established in pediatric patients.
- **Geriatrics:** A population pharmacokinetic analysis did not reveal a clinically significant impact of age on the pharmacokinetics of rozanolixizumab.
- **Sex:** A population pharmacokinetic analysis did not reveal a clinically significant impact of sex on the pharmacokinetics of rozanolixizumab.
- **Ethnic Origin:** A population pharmacokinetic analysis did not reveal a clinically significant impact of race on the pharmacokinetics of rozanolixizumab.
- **Hepatic Insufficiency:** No dedicated studies have been conducted in patients with hepatic impairment. Based on a population pharmacokinetic analysis, hepatic biochemical and function test results (ALT, AST, alkaline phosphatase and bilirubin) had no clinically significant effect on rozanolixizumab apparent linear clearance. The pharmacokinetics of rozanolixizumab are unlikely to be affected by hepatic impairment.
- **Renal Insufficiency:** No dedicated studies have been conducted in patients with renal impairment. Based on a population pharmacokinetic analysis involving study participants with mild to moderate renal impairment, renal function (estimated glomerular filtration rate [eGFR] 38-161 ml/min/1.73m^2) had no clinically significant effect on rozanolixizumab apparent linear clearance. The pharmacokinetics of rozanolixizumab are unlikely to be affected by renal impairment.
- **Body Weight:** Population PK modelling indicated that rozanolixizumab exposure decreased as body weight increased. Doses are adjusted based on body weight categories (see 4 Dosage and Administration).

10.4. Immunogenicity

As with all therapeutic proteins, there is a potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay.

In the pooled cyclic treatment data from the phase 3 program, after one treatment cycle of 6 rozanolixizumab weekly doses, 26.9 % (42/156) of patients developed antidrug antibodies and 10.3 % (16/156) had antibodies that were classified as neutralising. Upon reinitiating therapy, the proportion of patients who developed antidrug antibodies and neutralising antibodies increased to 61.4 % (35/57) and 43.9 % (25/57) respectively, after 5 treatment cycles. Development of neutralising antibodies was associated with a 24% decrease in overall plasma exposure of rozanolixizumab. While the data were limited, there was no apparent impact of immunogenicity on efficacy. The rate for certain events (dyslipidemia, upper respiratory tract infections, and dyspnea) was at least two times higher in patients with anti-drug antibodies (ADAs) than in patients without ADAs.

11. Storage, Stability, and Disposal

Store in a refrigerator (2°C to 8°C or 36°F to 46°F).

Do not freeze. Do not shake.

Keep the vial in the outer carton to protect from light.

RYSTIGGO may be stored at room temperature (up to 25°C/77°F) for a single period of maximum 20 days with protection from light. Once removed from the refrigerator and stored under these conditions, discard after 20 days or by the expiry date, whichever occurs first.

RYSTIGGO vial is for single-use only. RYSTIGGO does not contain preservatives.

Any unused medicinal product remaining in the vial or waste material should not be used and should be disposed of in accordance with local requirements.

Part 2: Scientific Information

13. Pharmaceutical Information

Drug Substance

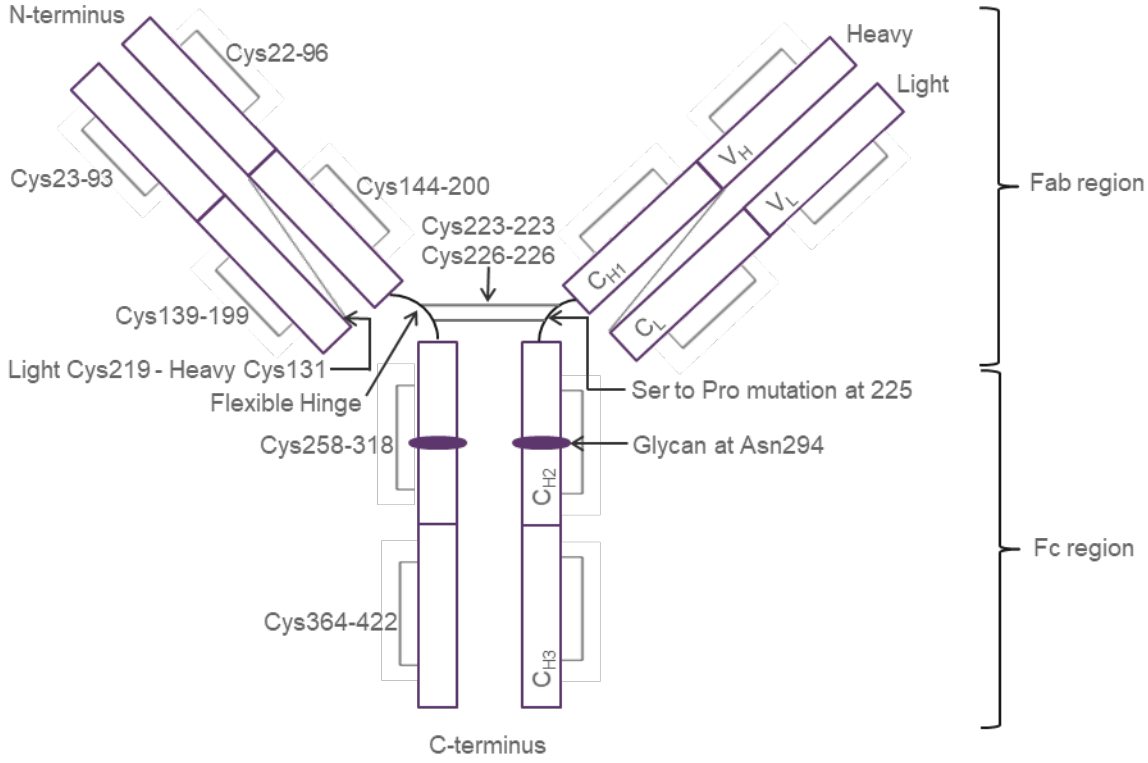
Non-proprietary name of the drug substance(s): rozanolixizumab

Chemical name: Immunoglobulin G4P, anti-FcRn

Molecular formula and molecular mass: $C_{6462}H_{9984}N_{1704}O_{2016}S_{44}$

147846 Da

Structure:



Physicochemical properties:

Product characteristics: Rozanolixizumab is a recombinant, humanized anti-neonatal Fc receptor (FcRn) IgG4P monoclonal antibody produced from a genetically engineered Chinese Hamster Ovary cell line. The light chain is composed of 219 amino acid residues and the heavy chain is composed of 444 amino acid residues.

14. Clinical Trials

14.1. Clinical Trials by Indication

Generalized Myasthenia Gravis (gMG)

The efficacy of RYSTIGGO (rozanolixizumab injection) for the treatment of generalized myasthenia gravis (gMG) in adults was established in a multicenter, randomized, double-blind, placebo-controlled study (Study 1).

Study 1 enrolled patients who met the following criteria:

- At least 18 years of age, had a body weight of at least 35 kg
- Presence of autoantibodies against AChR or MuSK
- Myasthenia Gravis Foundation of America (MGFA) Clinical Classification Class II to IVa
- Myasthenia Gravis-Activities of Daily Living (MG-ADL) total score of at least 3 (with at least 3 points from non-ocular symptoms)
- A Quantitative Myasthenia Gravis (QMG) score of at least 11
- On stable dose of MG therapy prior to screening that included acetylcholinesterase (AChE) inhibitors, steroids, or non-steroidal immunosuppressive therapies (NSISTs), either in combination or alone
- Considered for additional treatment such as intravenous immunoglobulin (IVIg) and/or plasma exchange (PLEX)
- Serum IgG levels of at least 5.5 g/L

Patients were excluded from the study if they had an absolute neutrophil count < 1 500 cells/mm3, clinically relevant active infection or serious infections, mycobacterial infections, hepatitis B, hepatitis C, HIV infections, or have been treated with PLEX, IVIg 1 month and monoclonal antibodies 3 to 6 months prior to starting treatment.

Table 4: Summary of trial design and study demographics for Study 1 in generalized Myasthenia Gravis

Study #	Study design	Dosage, route of administration and duration	Study subjects (n)	Mean age (range)	Sex
Study 1	Phase III, randomized, double-blind, placebo-controlled	RYSTIGGO ≈ 7 mg/kg, SC infusion, once per week for 6 weeks followed by an observation period of up to 8 weeks RYSTIGGO ≈ 10 mg/kg, SC infusion, once per week for 6 weeks followed by an observation period of up to 8 weeks PBO: SC infusion, once per week for 6 weeks followed by an observation period of up to 8 weeks	Adult patients with generalized myasthenia gravis TOTAL: 200 RYSTIGGO (≈ 7 mg/kg): 66 RYSTIGGO (≈ 10 mg/kg): 67 PBO: 67	51.8 (18-89)	Male: 39.5% Female: 60.5%

PBO = Placebo; SC = subcutaneous;

In Study 1, a total of 200 patients were randomized 1:1:1 to receive weight-tiered doses of RYSTIGGO (n=133), equivalent to ≈ 7 mg/kg (n=66) or ≈ 10 mg/kg (n=67), or placebo (n=67). Treatment consisted of 1 dose per week for a period of 6 weeks (defined as one treatment cycle) followed by an 8-week observation period.

Baseline characteristics were similar between treatment groups, including median age at screening (52 years), and median duration of disease (6 years). Sixty-one percent of patients were female, 68% were White, 11% were Asian, 3% were Black or African American, 1% were American Indian or Alaska Native, and 7% were of Hispanic or Latino ethnicity. The study population was representative of a gMG patient population with moderate to severe disease at baseline. The majority of study participants were MGFA Disease Class ≥ III (39% were Class II, 57% were Class III, and 4% were Class IV).

Baseline median MG-ADL total score was 8, and the baseline median Quantitative Myasthenia Gravis (QMG) total score was 15. The majority of patients, 89.5% (n=179), were positive for AChR antibodies and 10.5% (n=21) were positive for MuSK antibodies.

At baseline in each group, over 83% of patients received AChE inhibitors, over 56% of patients received steroids, and approximately 50% received NSISTs, at stable doses.

Study Results

The primary efficacy endpoint was the change from baseline in MG-ADL total score at day 43 (one week after completing the initial treatment cycle with RYSTIGGO). MG-ADL scale assesses the impact of gMG on daily functions of 8 signs or symptoms that are typically affected in gMG. Each item is assessed on a 4-point scale where a score of 0 represents normal function and a score of 3 represents loss of ability to perform that function. A total score ranges from 0 to 24, with the higher scores indicating more impairment.

Secondary efficacy endpoints included change from Baseline to Day 43 in MGC score and QMG score. MGC total score measures symptoms and signs of gMG based on physician examination and patient history. The overall score ranges from 0 to 50, with a higher score indicating more severe disease. The QMG total score is a 13-item categorical grading system that assesses muscle weakness. Each item is assessed on a 4-point scale where a score of 0 represents no weakness and a score of 3 represents severe weakness. A total possible score ranges from 0 to 39, where higher scores indicate more severe impairment.

Results from Study 1 for the primary and secondary efficacy endpoints are provided in Table 5 below.

Table 5: Efficacy outcomes change from Baseline to Day 43

Efficacy endpoints	**Placebo (N=67)**	**RYSTIGGO ≈7 mg/kg (N=66)**
Primary endpoint		
MG-ADL		
LS Mean (SE)	-0.784 (0.488)	-3.370 (0.486)
Difference vs Placebo	NA	-2.586
95% CI for difference	NA	-4.091, -1.249
P-value for difference	NA	<0.001

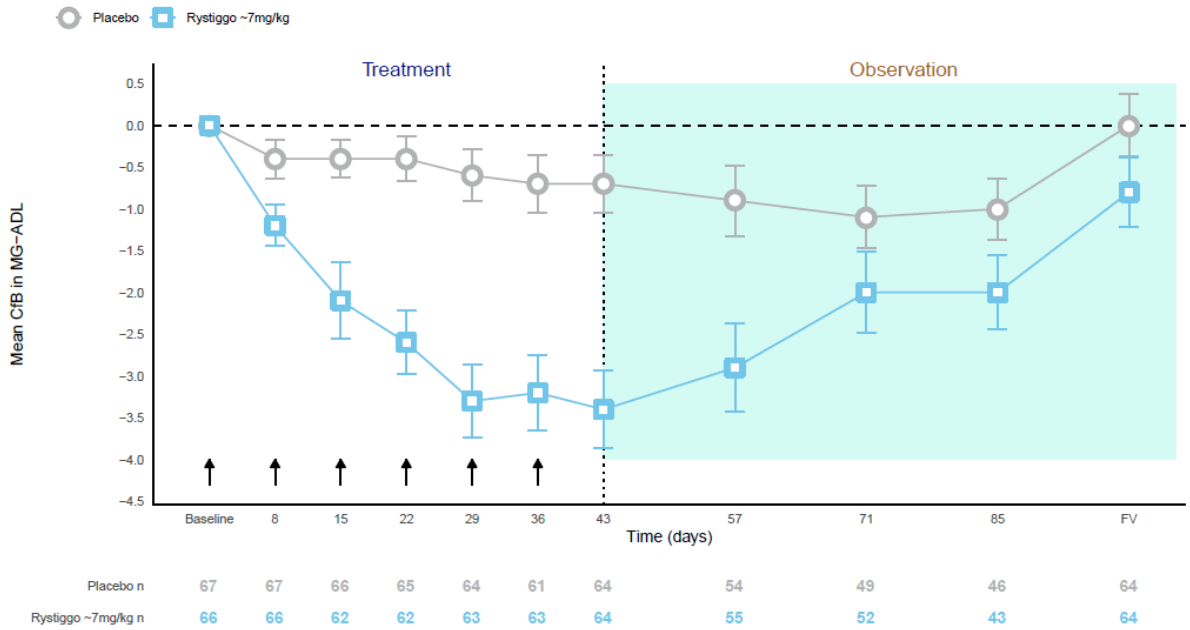
Efficacy endpoints	Placebo (N=67)	RYSTIGGO ≈7 mg/kg (N=66)
Key secondary endpoints		
MGC		
LS Mean (SE)	-2.029 (0.917)	-5.930 (0.916)
Difference vs Placebo	NA	-3.901
95% CI for difference	NA	-6.634, -1.245
P-value for difference	NA	<0.001
QMG		
LS Mean (SE)	-1.915 (0.682)	-5.398 (0.679)
Difference vs Placebo	NA	-3.483
95% CI for difference	NA	-5.614, -1.584
P-value for difference	NA	<0.001

≈=approximate dose; CI= confidence interval; N=total number of patients in treatment group; n=number of patients; LS=least square; SE=standard error.

The proportion of MG-ADL clinical responders with at least 2 point improvement from Baseline at Day 43 was 68.2% (n=45) in the RYSTIGGO group and 28.4% (n=19) in the placebo group.

Figure 1 shows the mean change from baseline in MG-ADL in Study 1.

Figure 1: Observed mean change from Baseline in MG-ADL score



CfB=Change from Baseline; FV=Final Visit; MG−ADL=Myasthenia Gravis Activities of Daily Living
NOTE: Arrows indicate timepoints at which treatment was administered.
NOTE: Error bars represent +/− standard error

Long-term response – cyclic treatment

Patients who enrolled in the open label extension study were allowed to receive repeated cycles of RYSTIGGO treatment. Each treatment consisted of 6 weeks of treatment followed by an observation period. Initiation of additional treatment cycles was based on clinical evaluation of individual MG symptom worsening. MG symptom worsening was defined as, for example, an increase of 2.0 points on the MG-ADL scale or 3.0 points on the QMG scale. Twenty-six patients were exclusively treated with RYSTIGGO 7 mg/kg and received more than 3 treatment cycles. Based upon the first 3 treatment cycles, patients who originally responded to RYSTIGGO 7 mg/kg showed a consistent treatment response following administration of subsequent treatment cycles of RYSTIGGO. Patients treated with RYSTIGGO on average initiated 4 cycles in one year.

Body weight ≥ 35 to <50 kg

In the clinical study program only a limited number of patients with a body weight <50 kg were examined. In Study 1, lower efficacy was observed in study participants with body weight <50 kg (n=7). The number of study participants with a body weight <50kg who received repeated RYSTIGGO 7 mg/kg in the open label extension study was small (n=4). The efficacy of repeated cyclic treatment with RYSTIGGO was more variable in this population.

16. Non-Clinical Toxicology

General toxicology

13-week toxicity study with 8-week recovery

Rozanolixizumab was administered to cynomolgus monkeys every 3 days at 50 or 150 mg/kg subcutaneously or at 150 mg/kg intravenously for 13 weeks. Based on AUC, these doses resulted in margins of exposure of 7-, 64-, and 91-fold, respectively, at the maximum recommended human dose [MRHD] (840 mg subcutaneously once weekly in a 100 kg patient). Intermittent dosing was also evaluated in an additional group (2 consecutive subcutaneous doses of 150 mg/kg 3 days apart on Weeks 1, 6, and 10). No adverse effects attributable to rozanolixizumab were observed during the dosing phase or the recovery phase. In line with the mechanism of action, rozanolixizumab induced sustained reductions in plasma total IgG concentrations (typically 80% from the baseline) during the dosing phase (leading to decreases in total serum protein and serum globulin levels), with a return to baseline approximately 40 days after cessation of dosing. Upon intermittent dosing, a loss of pharmacodynamic response was observed in some animals, likely as a consequence of immunogenicity. Upon T cell-dependent antibody response (TDAR) assessment with keyhole limpet haemocyanin (KLH) challenge (immunotoxicity assessment), rozanolixizumab administration resulted in decreased anti-KLH IgG titers in all animals as a consequence of IgG accelerated degradation but did not impact anti-KLH IgM titers. The No Observed Adverse Effect Level (NOAEL) was the highest dose tested of 150 mg/kg every 3 days, by the subcutaneous or intravenous route of administration.

26-week toxicity study with 8-week recovery

Rozanolixizumab was administered to sexually mature cynomolgus monkeys every 3 days at 150 mg/kg subcutaneously for 26 weeks. Based on AUC, this dosing regimen resulted in a margin of exposure of 92-fold at the MRHD (840 mg subcutaneously once weekly in a 100 kg patient).

In line with the mechanism of action of rozanolixizumab, a sustained decrease in plasma levels of total IgG (up to 90% from baseline levels), proteins, and globulins was observed in most animals throughout the dosing period. These changes were reversed after cessation of dosing. A TDAR assay with KLH challenges during the dosing phase resulted in a marked reduction of anti-KLH-specific IgG response in all animals administered rozanolixizumab. A KLH challenge during the recovery period demonstrated an anti-KLH IgG response comparable to control animals.

No adverse effects were generally associated to rozanolixizumab administration, including effects on reproductive organs. Two treated females (out of 14 treated animals) showed evidence of immune complex disease at histopathological evaluation, in the absence of clinical signs. The first one was ADA-negative but was euthanized before scheduled termination due to the loss of pharmacodynamic effect. The second animal maintained the desired pharmacodynamic effect but developed high titers of ADA. The severity of some histopathological lesions in the first animal did not allow the setting of an overall NOAEL. Immune complex disease may occur in nonclinical species administered high doses of humanized therapeutic antibodies in case of emergent anti-drug antibodies and does not translate to humans.

Genotoxicity: Genotoxicity studies have not been conducted with rozanolixizumab.

Carcinogenicity: Carcinogenicity studies have not been conducted with rozanolixizumab.

Reproductive and developmental toxicology

In an enhanced pre/postnatal development (ePPND) study, pregnant cynomolgus monkeys were administered rozanolixizumab subcutaneously at doses of 50 or 150 mg/kg every 3 days from gestation day (GD)20 to parturition. Based on AUC, these doses resulted in margins of exposure of 4- and 54-fold, respectively, at the MRHD (840 mg subcutaneously once weekly in a 100 kg patient). A higher incidence of early pregnancy loss (between GD20 and GD50) was seen in in both rozanolixizumab groups, and therefore, an effect of rozanolixizumab administration on early pregnancy maintenance cannot be excluded. Infant mortality was higher in the control group compared to the rozanolixizumab groups, but the number of live infants on postnatal (PND) 8 and 180 were comparable across all groups (10 to 12 infants). Mean body weights in female infants were decreased in both dose groups compared to the control group due to excess perinatal mortality in the control group and overall less weight gain in some smaller infants at birth compared to the control group.

In line with the mechanism of action of rozanolixizumab, decreased circulating IgG concentrations were observed in maternal animals administered rozanolixizumab. Infants from rozanolixizumab-administered mothers also had very low circulating IgG concentrations at birth, especially in the high dose group, indicating inhibition of maternal IgG transfer across the placenta. IgG levels in infants subsequently increased during the post-natal period and no adverse effects on immune function were observed (TDAR assay with KLH challenges initiated at 4 months of age led to an IgM and IgG response within the variability of the control group). Rozanolixizumab was generally undetectable in infants at birth, except in some individuals from the high dose group. Exposure in these infants was limited, but indicated some drug transfer across the placental barrier. No exposure was seen in infants and most mothers past PND1.

Based on the increase in prenatal losses in both dose groups, a NOAEL for effects of rozanolixizumab on development cannot be established.

Fertility

In the 26-week repeat dose toxicology study of rozanolixizumab in monkeys, no rozanolixizumab - related changes were noted in the male and female reproductive organs of sexually mature animals. An assessment of menstrual cycling in females and male reproductive endpoints (ejaculate weight, sperm count, sperm motility, and morphology) demonstrated no rozanolixizumab-related changes.

Patient Medication Information

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

[Pr]RYSTIGGO®

rozanolixizumab injection

This Patient Medication Information is written for the person who will be taking **RYSTIGGO**. This may be you or a person you are caring for. Read this information carefully. Keep it as you may need to read it again.

This Patient Medication Information is a summary. It will not tell you everything about this medication. If you have more questions about this medication or want more information about **RYSTIGGO**, talk to a healthcare professional.

What RYSTIGGO is used for:

RYSTIGGO is used to treat adult patients with generalized Myasthenia Gravis (gMG), a certain type of disease affecting the muscles.

Generalized MG causes weakness of muscles involved in movement and/or breathing. This is an "autoimmune disorder" which means that it is caused by your antibodies. These antibodies target and destroy proteins that are responsible for communication between nerves and muscles. This then results in muscle weakness.

How RYSTIGGO works:

RYSTIGGO belongs to a group of medicines called monoclonal antibodies. This medicine works by reducing the level of immunoglobulin G (IgG) antibodies, including IgG autoantibodies (antibodies against your own body) that attack healthy tissue in autoimmune diseases such as generalised myasthenia gravis.

RYSTIGGO contains the active substance rozanolixizumab. Rozanolixizumab is a monoclonal antibody (a type of protein) designed to recognize and attach to FcRn, a protein that keeps the IgG antibodies in the body for a longer period of time.

The ingredients in RYSTIGGO are:

Medicinal ingredient: rozanolixizumab

Non-medicinal ingredients: L-histidine, L-histidine hydrochloride monohydrate, L-proline, polysorbate 80, and water for injection

RYSTIGGO comes in the following dosage forms:

Solution for subcutaneous infusion: 140 mg/mL

- 280 mg rozanolixizumab in 2 mL vial
- 420 mg rozanolixizumab in 3 mL vial
- 560 mg rozanolixizumab in 4 mL vial
- 840 mg rozanolixizumab in 6 mL vial

Do not use RYSTIGGO if:

- You are allergic to rozanolixizumab or any of the other ingredients of this medicine. **See "The ingredients in RYSTIGGO are".**

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

- have a condition called hyperprolinaemia, a rare genetic disorder in which an excess of the amino acid, proline, builds up in the body
- have had a recent vaccination or are scheduled to receive any vaccinations. You should receive any required vaccines at least 4 weeks before you start treatment with RYSTIGGO.
- have a history of infection or think you have an infection. Before starting or during treatment with this medicine, inform your healthcare professional if you have any infections.
- are pregnant, think you may be pregnant or are planning to have a baby, ask your healthcare professional for advice before using this medicine. The effects of RYSTIGGO in pregnancy are not known.
- are breastfeeding or plan to breastfeed. It is not known if RYSTIGGO passes into your breast milk.

Other warnings you should know about:

RYSTIGGO is not approved for children and adolescents under 18 years of age because it has not been studied in this age group.

It is not known whether RYSTIGGO may affect your fertility. Talk to your healthcare professional if you are planning on having children.

RYSTIGGO may cause serious side effects, including:

- Inflammation of the membranes that surround the brain and spinal cord (aseptic meningitis). Aseptic meningitis has been observed in association with this medicine. Seek immediate medical attention if you develop symptoms of aseptic meningitis such as severe headache, fever, stiffness of the neck, nausea, vomiting and/or intolerance to bright light.
- This medicine contains a protein that can cause allergic reactions in some people. Tell your healthcare provider right away if you have signs or symptoms of an infusion reaction (allergic reaction) during and for 15 minutes after treatment. Some of the signs and symptoms of an infusion reaction (allergic reaction) may include: rash, swelling, itching, hives, trouble breathing, low blood pressure, fainting.
- Tell your healthcare provider right away if you have signs or symptoms of an infection before starting or during treatment with RYSTIGGO. Some of the signs and symptoms may include fever, chills, frequent and/or painful urination, cough, runny nose, wheezing, shortness of breath, fatigue, sore throat, excess phlegm, nasal discharge, back pain, and/or chest pain.

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

- Tell your healthcare professional or pharmacist if you are using, have recently used or might use any other medicines.
- Taking RYSTIGGO with other medicines may result in the loss of effect of the other medications. Other medicines may impair the effect of RYSTIGGO. Tell your healthcare professional if you are taking or planning to take other medicines.

How to take RYSTIGGO:

- Take RYSTIGGO exactly as directed by your healthcare professional.
- RYSTIGGO is given as an infusion under the skin (subcutaneous use). It is injected into the tummy area, in the lower right or lower left below the belly button. Injections should not be given into areas where the skin is tender, bruised, red or hard.
- RYSTIGGO can be injected by your healthcare professional using an infusion pump (also known as a syringe pump) or using a syringe manual push.
- RYSTIGGO can also be self-injected or injected by a caregiver using only the syringe manual push, after proper training by a healthcare professional on how to properly administer RYSTIGGO.
    - Before you take RYSTIGGO, make sure your healthcare professional goes through the important information with you and/or your caregiver and shows you how to properly prepare and inject RYSTIGGO.
    - Read the "Instructions for Use – Self-administration via Syringe Manual Push" at the end of this leaflet before using RYSTIGGO. This leaflet includes additional important details for the safe and proper use of RYSTIGGO.

Usual dose:

RYSTIGGO is given once every week for 6 weeks (treatment cycle). Your healthcare professional will tell you when to administer your future treatment cycles.

Your healthcare professional will calculate the correct dose for you taking into account your weight:

- if you weigh at least 100 kg, the recommended dose is 840 mg (requiring 6 mL per administration)
- if you weigh from 70 kg to less than 100 kg, the recommended dose is 560 mg (requiring 4 mL per administration)
- if you weigh from 50 kg to less than 70 kg, the recommended dose is 420 mg (requiring 3 mL per administration)
- if you weigh from 35 kg to less than 50 kg, the recommended dose is 280 mg (requiring 2 mL per administration)

Overdose:

If you think you, or a person you are caring for, have taken too much RYSTIGGO, contact a healthcare professional, hospital emergency department, regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669) immediately, even if there are no signs or symptoms.

Missed dose:

If you miss a dose, you may give the injection for up to 4 days after the missed dose. Thereafter, the next dose should be given according to the original dosing schedule until the treatment cycle is completed.

Do not stop using this medicine without talking to your healthcare professional first. Interrupting or stopping treatment with RYSTIGGO may cause your symptoms of generalised myasthenia gravis to come back. Your healthcare professional will advise you on how long you should be treated with this medicine.

If you have any further questions on the use of this medicine, ask your healthcare professional.

Possible side effects from using RYSTIGGO:

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

Very common: may affect more than 1 in 10 people

- Headache (including migraine)
- Diarrhea
- Fever (pyrexia)

Common: may affect up to 1 in 10 people

- Feeling sick (nausea)
- Upper respiratory tract infections (e.g., common cold, runny or stuffy nose, sinusitis)
- Joint pain (arthralgia)
- Skin rash, sometimes with red bumps (rash papular)
- Injection site reaction, injection site rash, redness of the skin (erythema), inflammation, discomfort and infusion site pain
- Stomach ache
- Viral infections (including shingles and cold sores)

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 (canada.ca/drug-device-reporting) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

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

Storage:

Store in a refrigerator (2°C to 8°C or 36°F to 46°F).

Do not freeze. Do not shake.

Keep RYSTIGGO in the original box to protect it from light.

RYSTIGGO may be removed from the refrigerator, kept at room temperature (up to 25°C/77°F) in the original outer carton package, for only one single period of up to 20 days. Do not use this medicine after this time period. There is a space on the box so you can write the date it was taken out of the refrigerator.

Keep out of reach and sight of children.

If you want more information about RYSTIGGO:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes the Patient Medication Information by visiting the Health Canada Drug Product Database website (Drug Product Database: Access the database); the manufacturer's website (www.ucb-canada.ca); or by calling 1-866-709-8444.

This leaflet was prepared by UCB Canada Inc.

Date of Authorization: 2026-10-14

RYSTIGGO® is a registered trademark of UCB Biopharma SRL.

INSTRUCTIONS FOR USE - Self-administration via Syringe Manual Push

[Pr]RYSTIGGO®

rozanolixizumab injection

Read all of these instructions before using RYSTIGGO. Your healthcare professional should show you or a caregiver how to inject RYSTIGGO before you use it for the first time. Do not inject yourself or someone else until you have been shown how to inject RYSTIGGO the right way. This information does not replace talking to your healthcare professional about your medical condition or treatment.

The table below shows the recommended dose (per administration) taking into account the patient's weight.

Body weight	**≥ 35 to <50 kg**	**≥ 50 to < 70 kg**	**≥ 70 to < 100 kg**	**≥ 100 kg**
Recommended dose (mg)	280 mg	420 mg	560 mg	840 mg
Amount of medication required per administration (mL)	2 mL	3 mL	4 mL	6 mL

! <u>Important information you need to know before giving yourself or someone else RYSTIGGO</u>

- For under the skin (subcutaneous) use only.
- Use each vial only once.
- Check your dose – you may need more than 1 vial to prepare your prescribed dose.
- **Do not** use RYSTIGGO if the expiry date has passed.
- Before using RYSTIGGO, check if the dose on the box(es) is the same as your prescribed dose. **Do not** use if the dose is not the same as your prescription. Contact your doctor or nurse for next steps.
- **Do not** use the vial if the liquid is cloudy or has particles you can see. The medicine should be colourless to pale brownish-yellow, clear to slightly opalescent (pearly white).



- **Do not** shake the vial.
- **Do not** use the vial if the protective cap is missing or broken. If any of the vials are broken or do not have a cap, report and return them to the pharmacy.

How to store RYSTIGGO

- Store in a refrigerator (2 °C to 8 °C).
- **Do not** freeze.
- Keep RYSTIGGO in the original box to protect it from light.
- Remove the box from the refrigerator before your infusion. For a more comfortable infusion, let the vial reach room temperature before you use this medicine. This may take 30 to 120 minutes. Do not warm in any other way.
- If the vial has been stored at room temperature (see PATIENT MEDICATION INFORMATION, Storage section), it can be used immediately.



! Keep this medicine out of the sight and reach of children.

Step-by-step instructions

1. <u>Get ready</u>

Step 1: Gather all the supplies you will need on a clean and flat work surface:

- **Included** in the RYSTIGGO box(es):
    - RYSTIGGO vial
    - RYSTIGGO Package Leaflet which includes the Instructions for Use

! Check your dose – you may need more than 1 vial to prepare your prescribed dose.

- **Not included** in the RYSTIGGO box:
    - Syringe (5 -10 ml depending on your prescribed dose)
    - Transfer needle(s) or a vented vial adaptor
    - Infusion set with a 26G or larger diameter needle. The infusion tubing should be 61 cm in length or shorter.
    - Alcohol wipes.
    - Transparent or see-through dressing
    - Tape
    - Adhesive bandage.
    - Sharps disposal container
    - Clean container (bowl) or paper towel to collect extra liquid when filling the infusion line.

Step 2: Clean your work surface and hands

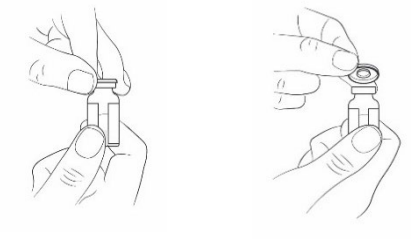
- Clean your work surface with disinfectant and wash your hands carefully with soap and water or use a hand sanitiser. Dry them with a clean towel.

2. Prepare the vial(s) and syringe

! Check your dose – you may need more than 1 vial to prepare your prescribed dose.

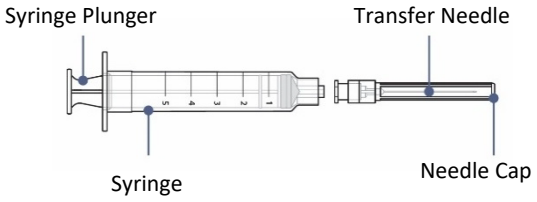
Step 3: Remove the protective cap from the vial(s)

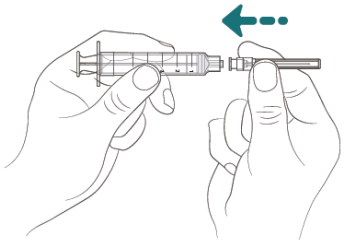
- Take the protective cap off the vial(s) by holding the edge and lifting upwards.
- Clean the rubber stopper with an alcohol wipe. Allow to air-dry.
- Leave the aluminium shield in place.
- Check your dose - if you need more than one vial to prepare your prescribed dose, remove all the caps and clean the stoppers.



! If you are using a vented vial adaptor instead of a transfer needle, you can skip directly to Step 7.

Step 4: Attach the transfer needle to the syringe

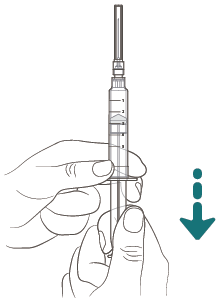




- Remove the syringe and transfer needle from the packaging. Do not touch the tip of the syringe or the base of the needle to avoid germs.
- With the needle cap still on, gently push or twist the transfer needle onto the syringe until it is firmly connected.

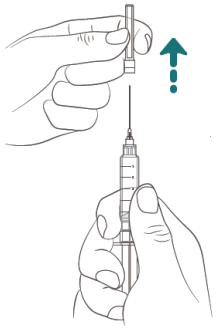
Step 5: Draw air into the syringe

- Keep the needle cap on while you are doing this.
- Slowly pull down on the syringe plunger to draw air into the syringe.
- Fill the syringe with about the same amount of air as the amount of medicine in the vial.



Step 6: Remove the needle cap from the transfer needle

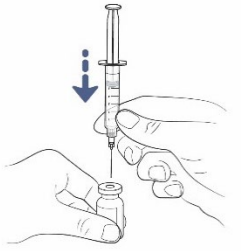
- Hold the syringe with one hand.
- With your other hand, hold the transfer needle cap and pull it straight off the needle
- Place the cap on the table to throw away later.
- **Do not** touch the needle tip.
- **Do not** let the needle tip touch anything after you remove the cap.



Step 7: Insert the transfer needle or vented vial adaptor directly into the vial
Follow the instructions for the infusion method you are using:

<u>Using transfer needle</u>

- Place the vial on the table and insert the transfer needle straight through the rubber stopper.



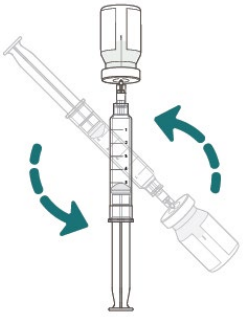
<u>Using vial adaptor</u>

- Place the vial on the table and insert the **vial adaptor** straight through the rubber stopper.
- Attach the syringe to the vented vial adaptor.



Step 8: Turn the vial and syringe

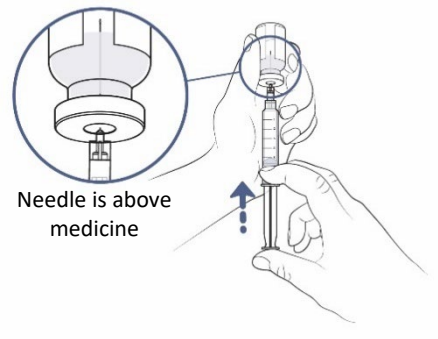
- Now turn the vial and syringe upside-down.
- Keep the transfer needle or vented vial adaptor inside the vial.



! If you are using a vented vial adaptor, you can skip directly to Step 11.

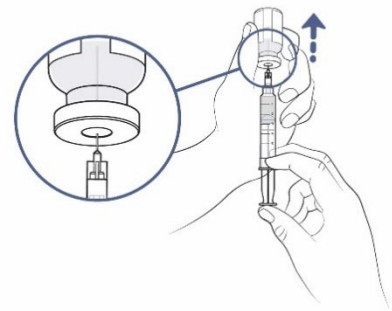
Step 9: Push air from the syringe into the vial

- Check that the transfer needle now points upwards and make sure the needle tip is in the space above the medicine.
- Slowly push the syringe plunger upwards to push all the air from the syringe into the vial. Keep your thumb pressed on the syringe plunger the whole time – so you do not let air into the syringe.
- Keep the needle tip in the space above the medicine the whole time.
- **Do not** push air into the medicine as this can create bubbles.



Step 10: Get ready to fill the syringe

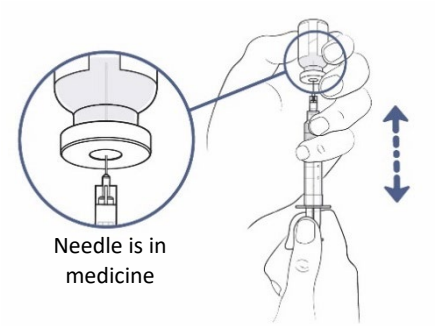
- Keep your thumb pushed on the syringe plunger. With your other hand, pull the vial **slowly and carefully** upwards so the needle tip is fully covered by the liquid medicine.



Step 11: Fill the syringe with as much medicine as possible

! Check your dose – you may need more than 1 vial to prepare your prescribed dose.

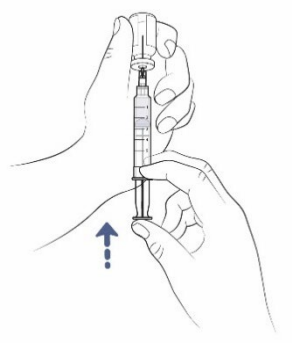
- Now slowly pull the syringe plunger down and fill the syringe with medicine.
  If you are using a transfer needle to fill the syringe, do the following:
  - Keep pulling the vial slowly and carefully upwards to keep the tip of the needle fully covered by the liquid.
  - Adjust the needle tip to keep it in the liquid. This will help you to take as much medicine out of the vial(s) as possible.
- You should now have more medicine in the syringe than your prescribed dose. You will adjust this later.



! There will also be a very small amount of the medicine that you cannot take out of the vial. You will throw this away with the vial later.

! If you are using a vented vial adaptor, detach the syringe from the vented vial adaptor. Leave the vented vial adaptor in the vial. You can throw this away at the end of the infusion. You can now skip directly to Step 14.

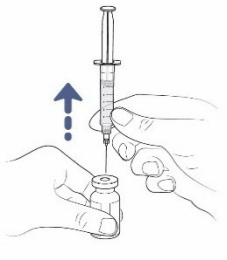
Step 12: Remove air from the syringe

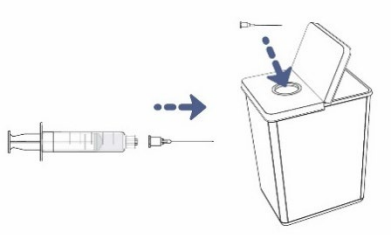




- If there is any space between the liquid in the syringe and the top of the syringe, slowly push the plunger to push air back into the vial.
- If you see air bubbles in the syringe, you can remove them by tapping gently on the syringe with your index finger. Now slowly push the plunger to push air back into the vial.

Step 13: Remove the transfer needle from the vial and the syringe





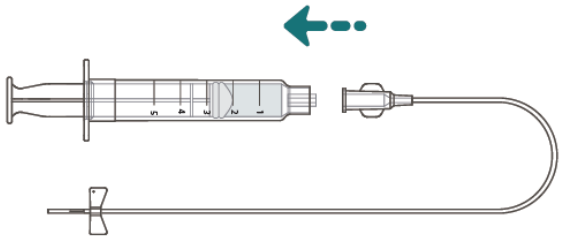
- Turn the vial and syringe over and put the vial on the work surface.
- Remove the transfer needle and syringe from the vial by pulling straight up on the syringe.
- Remove the transfer needle from the syringe by pulling or twisting carefully on the base of the needle.
- **Do not** touch the needle. **Do not** put the needle cap back on.
- Throw the needle away in the sharps disposal container.
- If you are using a vented vial adaptor instead of a needle, it is not necessary to remove the vented vial adaptor from the vial before throwing them away.

Step 14: Re-check your dose

- If you need to use another vial to prepare your prescribed dose, repeat Steps 4-13 with the same syringe and a new transfer needle or vented vial adaptor to avoid contamination.

3. Prepare for infusion

Step 15: Attach the infusion set onto the syringe

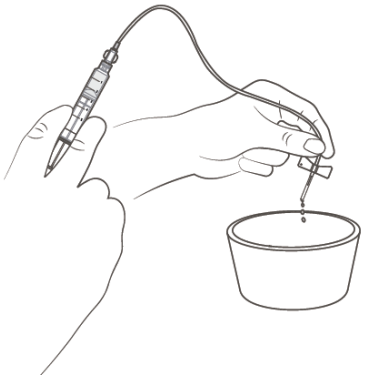


Infusion set

- Place the syringe on the clean work surface while you are preparing the infusion line.
- Remove the infusion set from the protective pouch.
- Remove the cap from the end of the infusion set by twisting it off. Place the cap on the work surface to throw away later.
- Attach the infusion set onto the syringe until firmly connected. **Do not** touch the tip of the syringe or the base of the infusion set to avoid germs.
- **Do not** remove the needle cap from the infusion set needle.

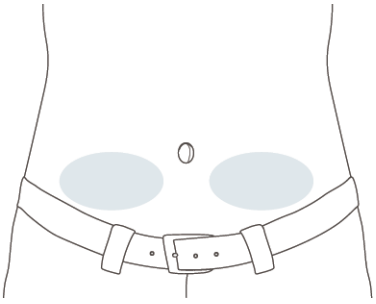
Step 16: Fill the infusion set with medicine

- Make sure you have a bowl or paper towel in front of you – you can use it to collect any medicine from the infusion line that is not needed.
- Keep the cap on the infusion line needle and hold it over the bowl. Now hold the syringe in a vertical position and fill the infusion line with medicine by pushing gently on the syringe plunger.
- **The amount of liquid left in the syringe must match your prescribed dose.**



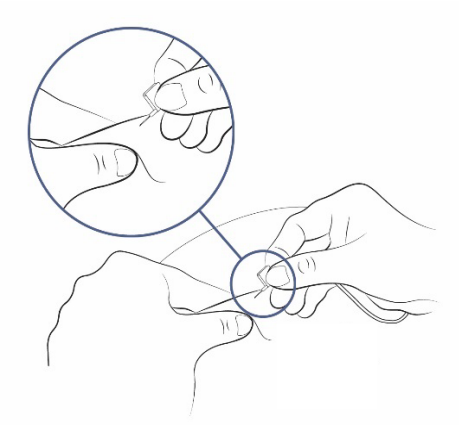
Step 17: Choose and prepare the infusion site

- Choose an infusion site to the lower left or lower right side of the belly (abdomen), below the level of the belly button.
    - **Do not** use an area of skin which:
        - is tender, bruised, red or hard
        - has scars or stretch marks.
- Prepare the infusion site:
    - Clean the infusion area with an alcohol wipe for 30-seconds and allow it to air-dry. Do not touch the area after it has been cleaned.



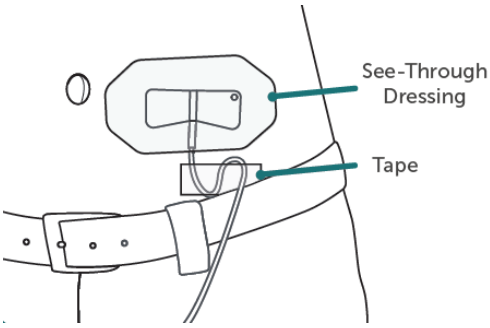
Step 18: Insert the infusion set needle

- Carefully remove the needle cap from the infusion set needle.
- Fold the butterfly wings together and hold them with your thumb and index finger of one hand.
- With your other hand, pinch the skin between 2 fingers to make a fold.
- Push the needle into the middle of the skin and push it under the skin.
- The needle should go in easily. If it is difficult, you can pull the needle out slightly.
- There are different types of infusion sets (some without a butterfly-type needle and some that allow the needle to be withdrawn leaving behind a small, flexible tube (called a cannula)). Your nurse or doctor will explain to you how to use your infusion set.



Step 19: Secure the infusion set

- Use a transparent or see-through dressing to hold the infusion set in place. Some infusion sets have a built-in adhesive.
- You can use tape to hold the infusion line on your skin.



For illustration only. Your specific supplies may look different.

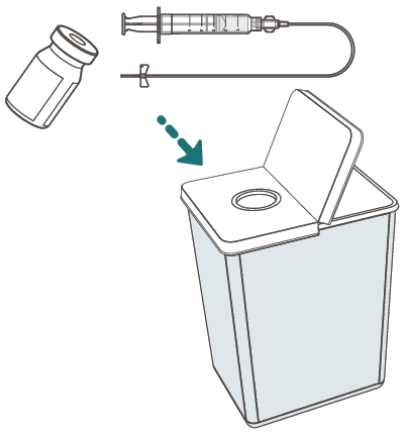
4. <u>Infuse and finish</u>

Step 20: Start the infusion for Syringe Manual Push

- Sit back comfortably and push firmly on the syringe plunger to infuse the medicine.
- You should infuse the medicine at a speed that feels comfortable to you (infusion times are usually around 5 minutes but may range from 1 minute to 30 minutes). Keep pushing until there is no more medicine left in the syringe.
- Before and during the infusion, make sure that the infusion line does not twist or bend. If this happens, the flow of medicine can be interrupted. In this case, correct the bend in the infusion line and try again.
- If it feels uncomfortable or if any of the medicine flows back into the infusion line, you can push more slowly.

! Note: There will be some medicine left in the infusion line. This is normal and you can throw it away in the sharps disposal container.

Step 21: Finish the infusion and clean up



- After you finish the infusion, **do not** try to take the dressing off the needle. Remove them both from your skin together and throw them away with the syringe in the sharps disposal container.
- There may be a drop or two of liquid at the infusion site after you take out the needle. This is normal.
- Cover the infusion site with a clean dressing, such as an adhesive bandage.
- Throw away any used vial(s) and leftover medicine into the sharps disposal container.
- Throw away any other used supplies in your household waste.

! Always keep the sharps disposal container out of the sight and reach of children.