swissmedic

Date: 9 June 2026
Swissmedic, Swiss Agency for Therapeutic Products

Swiss Public Assessment Report

RYSTIGGO

International non-proprietary name:	rozanolixizumab
Pharmaceutical form:	solution for injection
Dosage strength(s):	280 mg / 2mL
Route(s) of administration:	subcutaneous (s.c.) infusion
Marketing authorisation holder:	UCB-Pharma SA
Marketing authorisation no.:	69227
Decision and decision date:	approved on 12 February 2025

Note:

This assessment report is as adopted by Swissmedic with all information of a commercially confidential nature deleted.

SwissPARs are final documents that provide information on submissions at a particular point in time. They are not updated after publication.

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1 Terms, Definitions, Abbreviations

Ab	Antibody
AChR	Anti-Acetylcholine Receptors
ADA	Anti-drug antibody
ADME	Absorption, distribution, metabolism, elimination
AE	Adverse event
ALT	Alanine aminotransferase
API	Active pharmaceutical ingredient
AST	Aspartate aminotransferase
ATC	Anatomical Therapeutic Chemical Classification System
AUC	Area under the plasma concentration-time curve
$AUC_{0\text{-}24h}$	Area under the plasma concentration-time curve for the 24-hour dosing interval
CI	Confidence interval
C_{max}	Maximum observed plasma/serum concentration of drug
CYP	Cytochrome P450
DDI	Drug-drug interaction
EMA	European Medicines Agency
ERA	Environmental risk assessment
FcRn	neonatal Fc Receptor
FDA	Food and Drug Administration (USA)
GI	Gastrointestinal
GLP	Good Laboratory Practice
gMG	generalised Myasthenia Gravis
HPLC	High-performance liquid chromatography
IC/EC_{50}	Half-maximal inhibitory/effective concentration
ICH	International Council for Harmonisation
Ig	Immunoglobulin
INN	International non-proprietary name
ITT	Intention-to-treat
LoQ	List of Questions
MAH	Marketing authorisation holder
Max	Maximum
MG	Myasthenia Gravis
MG-ADL	Myasthenia Gravis Activities of Daily Living
Min	Minimum
MRHD	Maximum recommended human dose
MuSK	Muscle-Specific Kinase
N/A	Not applicable
NO(A)EL	No observed (adverse) effect level
OLE	Open Label Extension
PBPK	Physiology-based pharmacokinetics
PD	Pharmacodynamics
PIP	Paediatric investigation plan (EMA)
PK	Pharmacokinetics
PopPK	Population pharmacokinetics
PSP	Pediatric study plan (US FDA)
QMG	Quantitative Myasthenia Gravis
RMP	Risk management plan
SAE	Serious adverse event
SwissPAR	Swiss Public Assessment Report
TEAE	Treatment-emergent adverse event

TPA	Federal Act of 15 December 2000 on Medicinal Products and Medical Devices (SR 812.21)
TPO	Ordinance of 21 September 2018 on Therapeutic Products (SR 812.212.21)

2 Background information on the procedure

2.1 Applicant's request(s)

New active substance status
The Applicant requested new active substance status for rozanolixizumab in the above-mentioned medicinal product.

Orphan drug status
The Applicant requested orphan drug status in accordance with Article 4 paragraph 1 letter a^{decies} no. 2 TPA. Orphan drug status was granted on 9 March 2023.

Work-sharing procedure
The Applicant requested a work-sharing procedure with Australia's TGA and Health Canada.
The Access NAS (new active substance) work-sharing initiative is a collaboration between regulatory authorities – specifically Australia's Therapeutic Goods Administration (TGA), Health Canada (HC), Singapore's Health Sciences Authority (HSA), the UK Medicines & Healthcare products Regulatory Agency (MHRA) and Swissmedic – and the pharmaceutical industry. The work-sharing initiative involves the coordinated assessment of NAS applications that have been filed in at least two jurisdictions.

2.2 Indication and dosage

2.2.1 Requested indication

RYSTIGGO is indicated as an add-on to standard therapy for the treatment of generalised myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) or anti-muscle-specific tyrosine kinase (MuSK) antibody positive.

2.2.2 Approved indication

RYSTIGGO is indicated as an add-on to standard therapy for the treatment of generalised myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) or anti-muscle-specific tyrosine kinase (MuSK) antibody positive (see section "Clinical Efficacy").

2.2.3 Requested dosage

Summary of the requested standard dosage:

The recommended dosage of RYSTIGGO is based on body weight, as shown below in Table 1.

Table 1:

Body Weight	**≥ 35 to <50 kg**	**≥ 50 to < 70 kg**	**≥ 70 to < 100 kg**	**≥ 100 kg**
Weekly dosage (mg)	280 mg	420 mg	560 mg	840 mg
Weekly dosage (ml)	2 ml	3 ml	4 ml	6 ml

Administer the recommended dosage as a subcutaneous infusion once weekly for 6 weeks.

2.2.4 Approved dosage

(see appendix)

2.3 Regulatory history (milestones)

Application	19 October 2023
Formal control completed	18 November 2023
List of Questions (LoQ)	15 March 2024
Response to LoQ	14 May 2024
Second List of Questions (LoQ)	28 June 2024
Response to second LoQ	28 August 2024
Preliminary decision	22 October 2024
Response to preliminary decision	26 November 2024
Final decision	12 February 2025
Decision	approval

3 Medical context

Myasthenia gravis (MG) is a rare chronic autoimmune disease characterised by variable levels of weakness and fatigability of skeletal muscles caused by impaired acetylcholine (ACh) mediated transmission at neuromuscular junctions. In approximately 85% of patients, MG goes beyond ocular muscles and affects muscle groups throughout the body including those involved in swallowing and respiration. This condition is designated as generalised myasthenia gravis (gMG). In 80 to 85% of all MG patients, there is evidence for pathogenic autoantibodies targeted against anti-acetylcholine receptors (AChR). Nearly 6% of patients are tested positive for autoantibodies against muscle-specific kinase (MuSK). 10% to 15% of patients are double seronegative for AChR/MuSK autoantibodies. There is still an unmet medical need in the field of gMG, especially in those gMG patients who are seronegative for AChR-Abs and MuSK autoantibodies.

Rozanolixizumab is a recombinant, humanised anti-neonatal Fc receptor (FcRn) IgG4P mAb. Rozanolixizumab binds with high affinity and specificity to human FcRn and thereby competitively blocks IgG binding to FcRn. The natural ligands of FcRn are IgG and albumin which, following pinocytic uptake into the endosomes, are salvaged by FcRn, which carries these proteins away from the lysosome to be released back into the plasma instead of becoming degraded. By blocking the FcRn, Rozanolixizumab enhances IgG catabolism, thereby non-specifically reducing total IgG levels (including MG-specific auto-Abs). Rozanolixizumab is administered subcutaneously (SC).

4 Quality aspects

Swissmedic has not assessed the primary data relating to quality aspects submitted with this application and is adopting the results of the assessment of the foreign reference authority (see section 2.1 Applicant’s request / Work-sharing procedure).

5 Nonclinical aspects

5.1 Pharmacology

The results of the nonclinical pharmacology studies support the proof of concept and the selection of the cynomolgus monkey for nonclinical safety assessment of rozanolixizumab. In surface plasmon resonance assays, rozanolixizumab demonstrated similar mean affinity (K_D) for human and cynomolgus monkey FcRn at pH 7.4 (55 and 57 pM) and pH 6.0 (44 and 42 pM). The affinity of rozanolixizumab for mouse and rat FcRn was much weaker (nanomolar range), and no binding to rabbit FcRn could be detected. The K_D of rozanolixizumab for human FcRn expressed on Madin-Darby canine kidney cells was ~0.4 nM (pH 7.4 and pH 6.0). Rozanolixizumab inhibited IgG recycling and transcytosis by FcRn in these cells with IC_{50} values of 0.4 and 1 nM, respectively. Slightly (2-fold) lower binding affinity and potency of rozanolixizumab were observed in studies using cells expressing cynomolgus monkey FcRn; this is not considered relevant due to the high doses used in the toxicity studies. The capacity of rozanolixizumab to reduce plasma IgG levels was studied *in vivo* in a human FcRn transgenic mouse model and in cynomolgus monkeys. Intravenous (IV) treatment of mice expressing human FcRn with 10-100 mg/kg rozanolixizumab resulted in a dose-dependent accelerated clearance of human IgG in mouse plasma. Rozanolixizumab was also able to reduce total endogenous IgG plasma levels in cynomolgus monkeys after subcutaneous (SC) or IV administration at ≥5 mg/kg. The effect on monkey IgG plasma levels was used as a marker for the pharmacodynamic (PD) response in the toxicity studies. The results of studies in mice with an anti-mouse FcRn surrogate antibody support the use of rozanolixizumab for the treatment of diseases that are related to the formation of autoantibodies. The lack of a nonclinical efficacy study in a specific model for myasthenia gravis is accepted.
The off-target binding potential of rozanolixizumab was evaluated *in vitro* for >4500 human proteins expressed on the surface of HEK293 cells. Based on the results of these studies, rozanolixizumab is highly specific for its target, the α chain of the FcRn receptor.
Since rozanolixizumab is an IgG4, the risk for Fcy receptor-related reactions is considered low.
No stand-alone safety pharmacology studies were conducted, but relevant parameters were evaluated in the repeat-dose toxicity studies in cynomolgus monkeys. No rozanolixizumab-related effects on cardiovascular, respiratory or central nervous system function were observed.
No nonclinical studies on pharmacodynamic drug interactions were conducted. Based on the pharmacological mode of action, use of rozanolixizumab will increase the clearance of other IgG-based medicinal products. This is stated in the Information for healthcare professionals.

5.2 Pharmacokinetics

Validated analytical methods were used to quantify total and free rozanolixizumab levels as well as ADA in plasma from cynomolgus monkeys in the GLP-compliant toxicity studies. Total endogenous plasma IgG levels (marker for the PD response) were determined using a qualified non-GLP method.
The pharmacokinetics (PK) of rozanolixizumab in cynomolgus monkeys were characterised following IV and SC administration. Absorption after SC administration to monkeys was slow (T_{max} 8-48 h); bioavailability was approximately 60%. In a PK/PD study, non-linear PK was observed with IV dosing at 5-30 mg/kg; the rapid decline in rozanolixizumab plasma concentrations at lower doses and a supraproportional increase in AUC were considered related to target-mediated drug disposition and saturation of the clearance process at higher doses. Mean half-lives ($t_{1/2}$) determined with the highest doses in the repeat-dose toxicity studies (150 mg/kg IV or SC) were between 16 and 30 h, i.e. much shorter than typical $t_{1/2}$ of IgGs in monkeys. The PK of rozanolixizumab in monkeys is considered comparable to the PK in humans.
Repeated every 3 days dosing of monkeys at 150 mg/kg SC was associated with accumulation in the 26-week study and the enhanced pre- and postnatal development (ePPND) study. Plasma exposures achieved in the toxicity studies at the 150 mg/kg doses were 36- to 228-fold above the clinical exposure (based on mean AUC for free rozanolixizumab).

As expected for a foreign protein, rozanolixizumab induced the production of ADA in cynomolgus monkeys. In some animals, the presence of ADAs correlated with reduced rozanolixizumab plasma exposure and/or loss of the PD response. However, the validity of the toxicity studies was not affected, because most high-dose animals were sufficiently exposed and showed the PD response until the end of the treatment period.
In line with ICH S6(R1), no dedicated studies on the distribution, metabolism and excretion of rozanolixizumab were conducted. In the ePPND study, some infants from maternal animals treated with the high dose had detectable rozanolixizumab in plasma on Postnatal Day 1 (PND 1), but not on PND 7. The mean infant/maternal animal concentration ratio on PND 1 was 0.0233. Based on these data, rozanolixizumab transfer across the placenta may occur, but is low. The transfer of rozanolixizumab into milk was not examined.

5.3 Toxicology

The pivotal toxicity studies with rozanolixizumab were conducted in cynomolgus monkeys, which are a pharmacologically relevant species. Tissue cross-reactivity studies showed similar staining in human and cynomolgus monkey tissues, which further supports the selection of the cynomolgus monkey as a species for safety assessment. Rhesus monkey was explored as a possible species for toxicity testing following observations of gastrointestinal effects, headaches, and pyrexia in the first-in-human study, because no such reactions had been observed in cynomolgus monkeys. However, no signs of toxicity comparable to the adverse events observed in the clinical study were noted in three male rhesus monkeys following IV administration of 150 mg/kg rozanolixizumab. Toxicity studies in rodents were not conducted, because rozanolixizumab showed significantly reduced affinity to mouse and rat FcRn; this is accepted, based on ICH S6(R1).

Repeat-dose toxicity was assessed in studies with treatment durations of up to 26 weeks, followed by 8-week recovery periods. The maximum dose level in all studies was 150 mg/kg every 3 days, administered either via SC injection (4-, 13-, and 26-week studies) or intravenously (4- and 13-week studies). The vehicle/control item corresponded to the clinical formulation. Treatment with rozanolixizumab was generally well tolerated in these studies. A pharmacology-related marked reduction in plasma IgG levels (up to -85%) was observed with dosing at 50 or 150 mg/kg. In addition, slight, reversible decreases in serum albumin were observed with rozanolixizumab treatment in all studies, although the binding epitope of the antibody on FcRn does not overlap with the residues that are involved in the binding of albumin[1]. The Applicant discussed the effect on serum albumin levels with a possible steric blocking of the albumin binding portion of FcRn by the FcRn-bound rozanolixizumab. In the clinical studies, no relevant effects on serum albumin levels were observed with rozanolixizumab treatment.
In the 13-week study, an increased incidence of perivascular mononuclear cell infiltrates in the brain (meninges and cerebral parenchyma) was observed after treatment in the rozanolixizumab groups when compared to the control group. The findings were considered non-adverse due to their minimal severity and lack of associated neuronal degeneration or glial response. The Applicant considered them as spontaneous background findings, i.e. unrelated to the treatment with rozanolixizumab, which was justified with literature references, the lack of relationship to dose and PD response, and higher incidence of meningeal infiltrates in control animals at the end of recovery. In addition, no such observations were made in the 26-week study.
In the 26-week study, one female monkey was terminated early due to loss of PD effect and reduced rozanolixizumab plasma exposure, which was considered related to the development of ADAs. Except for increased levels of complement factor C3a and C-reactive protein, the animal had not shown any test item-related effects on in-life parameters. Increased C3a was also measured in another female; this animal showed a strong ADA response and reduced plasma exposure during the treatment. Both

[1] Smith B, Kiessling A, Lledo-Garcia R *et al.*: Generation and characterization of a high affinity anti-human FcRn antibody, rozanolixizumab, and the effects of different molecular formats on the reduction of plasma IgG concentration. MABS 2018, Vol. 10, No. 7, 1111–1130.

females had histopathology findings of perivascular inflammatory cell infiltration in various organs, as well as increased cellularity in axillary and inguinal lymph nodes. Based on immunohistochemistry examinations, the inflammatory responses in these animals were considered related to immune complex formation and deposition. The inflammatory findings in the lung of one female were considered adverse. Therefore, there is no NOAEL for females in the 26-week study, because only one dose level (150 mg/kg) was used. However, the findings of ADA-related immune complex disease in rozanolixizumab-treated monkeys are considered of low clinical relevance.

In accordance with ICH S6(R1), no genotoxicity studies were conducted with rozanolixizumab. The Applicant provided an adequate justification for not conducting carcinogenicity studies and submitted an assessment on the carcinogenic potential of rozanolixizumab. Based on the weight of evidence from the literature data and the nonclinical data for rozanolixizumab, the risk for tumorigenic potential of rozanolixizumab is considered low.

In line with ICH S6(R1), the potential for rozanolixizumab to induce effects on fertility was assessed in the 26-week study in sexually mature cynomolgus monkeys. No effects were observed on the evaluated parameters, which included menstrual cycle, semen evaluation, testicular evaluation by ultrasound, organ weights and histopathology of reproductive organs.
An ePPND study based on the recommendations in ICH S6(R1) was conducted with rozanolixizumab to assess the potential for effects on pregnancy and development. Cynomolgus monkeys were treated from gestation day (GD) 20 until delivery with 0, 50 or 150 mg/kg rozanolixizumab SC every 3 days. In both rozanolixizumab-treated groups, increased prenatal loss (mainly between GD 20 and 50) was observed compared to the control group, with the values in the 150 mg/kg rozanolixizumab group exceeding the range of the historical control data for the test facility. Although pregnancy loss is a common finding in cynomolgus monkeys, a relationship with the administration of rozanolixizumab to the maternal animals cannot be excluded. This should be considered with regard to the use of rozanolixizumab during pregnancy and is addressed in the Information for healthcare professionals. No effects of rozanolixizumab treatment were observed in the PPND study on parturition or postnatal development of surviving infants (observation up to PND 180). The study included measurement of IgG plasma levels in infants. As expected from the pharmacological mode of action, rozanolixizumab significantly inhibited the placental transfer of maternal IgGs to fetuses, resulting in reduced infant plasma IgG levels at birth. This is also expected with clinical use of rozanolixizumab; the Information for healthcare professionals addresses the possible risks of reduced passive protection and use of live vaccines in newborns. During the postnatal observation period of the PPND study, the IgG plasma levels in infants of rozanolixizumab-treated maternal animals increased to control levels or greater; this is considered related to the biosynthesis of IgG production by the infant.

Local tolerance was evaluated in the repeat-dose toxicity studies. Minimal to marked inflammation was observed at the SC injection sites with rozanolixizumab treatment; the reactions were reversible. Injection site reactions were also common findings in the clinical studies with rozanolixizumab.

Rozanolixizumab showed no relevant cytokine induction potential *in vitro*. Possible effects on the immune system were investigated *in vivo* as part of the toxicity studies in cynomolgus monkeys. No rozanolixizumab-related effects were observed by immunophenotyping (blood and lymphoid tissues) and measurement of cytokines. There were also no pharmacology-related adverse pathology findings in lymphoid tissues. Immune complex disease was observed in two female monkeys in the 26-week study, but the clinical relevance is considered to be low (see above).
T cell-dependent antibody response (TDAR) was assessed in the 13- and 26-week studies. Following immunisation with keyhole limpet haemocyanin (KLH) during treatment, rozanolixizumab-treated animals showed decreased anti-KLH IgG titres. Following another immunisation during recovery, anti-KLH IgG peak titres were in the normal physiological range. The reduced anti-KLH IgG levels during the treatment period were considered related to the pharmacological mode of action of rozanolixizumab, i.e. increased clearance of IgG. The possible risks by the reduced IgG response/titres (increased susceptibility to infectious agents, lower efficacy of vaccination) are addressed in the Information for healthcare professionals. In the ePPND study, no effects on TDAR were observed in infants from rozanolixizumab-treated maternal animals; immunisation was on PNDs 126 and 147.

The main results from the nonclinical safety studies are adequately described and evaluated for human relevance in the RMP.

Since rozanolixizumab is a protein, the risk for the environment is considered negligible.

5.4 Nonclinical conclusions

Overall, the Applicant submitted a comprehensive set of studies on the pharmacology, pharmacokinetics and toxicology of rozanolixizumab. The proof of concept was shown. In the toxicity studies in a pharmacologically relevant species, no safety risks were identified that would preclude the use of rozanolixizumab in patients with myasthenia gravis. Potential safety risks are adequately addressed in the Information for healthcare professionals. From the nonclinical standpoint, there is no objection against approval.

6 Clinical aspects

6.1 Clinical pharmacology

The PK and PD profiles of rozanolixizumab in healthy subjects following single IV and SC doses (1 mg/kg, 4 mg/kg, 7 mg/kg, 10 mg/kg, 280 mg, and 560 mg) were evaluated in three Phase 1 trials. Furthermore, PK and PD data collected in two Phase 2 and three Phase 3 studies were used exclusively for population PK as well as population PK/PD analyses.

Biopharmaceutical development
A liquid formulation and a lyophilised formulation of rozanolixizumab were used during clinical development, from which the liquid formulation is the proposed commercial formulation. The proposed commercial drug product that was manufactured using drug substance from the proposed commercial process was administered in the Phase 3 clinical studies. Overall, no biopharmaceutical/ bioequivalence studies were conducted.
Based on a population PK/PD analysis, it was demonstrated that rozanolixizumab steady state exposure was increased following the administration of the lyophilised formulation.
The final to-be-marketed rozanolixizumab drug product is supplied as a sterile, preservative-free, colourless to pale brownish yellow, clear to slightly opalescent 140 mg/ml solution for subcutaneous injection in a 6 mL (6R) glass vial.

Pharmacokinetics
ADME
Following SC administration, the maximum concentrations of rozanolixizumab were reached after approximately two days in healthy subjects. Based on the population PK analysis, absolute bioavailability was estimated at 67% using IV and SC data from healthy subjects and patients with immune thrombocytopenia.
The trough concentrations were close to, or below, the limit of quantification (BLQ) in the majority of patients, suggesting limited rozanolixizumab accumulation.
In line with target-mediated drug disposition (TMDD), non-linear PK was observed for rozanolixizumab. Overall, rozanolixizumab exposure increased greater than dose-proportionally over a dose range from 1 mg/kg to 20 mg/kg.
Disease population was not identified as a statistically significant covariate, suggesting no relevant exposure differences between healthy subjects and generalised myasthenia gravis (gMG) patients.
Based on the simulations with the population PK/PD model, it is recommended that rozanolixizumab may be administered up to 4 days after the scheduled time point in case of a missed dose. Thereafter, the original dosing schedule may be resumed until the treatment cycle is completed.

Based on the population PK analyses, the mean estimate of the apparent volume of distribution was 6.6 L for a typical gMG patient weighing 76 kg.

No studies regarding the metabolism of rozanolixizumab have been conducted considering the biological nature of the molecule.

In line with TMDD, rozanolixizumab has two elimination pathways consisting of a FcRn-independent linear clearance pathway and a non-linear elimination pathway driven by target binding. The FcRn-independent linear clearance is considered a minor pathway for rozanolixizumab at clinically relevant doses of ~7 mg/kg and ~10 mg/kg.
Based on population PK analysis, the mean estimate for apparent CL/F was 0.89 L/day for a typical gMG patient weighing 76 kg. Since the half-life of unbound rozanolixizumab is concentration-dependent, it was not calculated. Within one week after administration, rozanolixizumab plasma concentrations were undetectable.

Special populations / Intrinsic factors

Renal and hepatic impairment is not expected to have an impact on the PK of monoclonal antibodies (mAbs), therefore no dedicated studies in these populations were conducted.
The population PK analysis revealed that mild to moderate renal impairment did not have an impact on the clearance of rozanolixizumab . The available data did not allow the identification and classification of hepatically impaired patients based on the Child-Pugh criteria.

To support the dose selection, an exploratory population PK/PD analysis using PK and total IgG data following IV and SC administration from one Phase 2 study and two Phase 1 studies was conducted. Using PK and total IgG data following SC administration from three Phase 1 studies, two Phase 2 studies and two Phase 3 studies, the final population PK/PD model for rozanolixizumab was developed to identify factors that account for variability of the rozanolixizumab PK and PD.
rozanolixizumab PK and total IgG serum concentrations were modelled simultaneously describing the link between PK, FcRn receptor occupancy, and reduction in IgG. The PK of rozanolixizumab was well described with a 1-compartment model with first-order absorption and a first-order elimination from the central compartment, in addition to a TMDD using the quasi-equilibrium approximation. The turnover of IgG was described by an indirect-response model. The final population PK/PD model included the following covariates: body weight on FcRn-independent apparent clearance (FcRn-independent CL/F), apparent volume of distribution (V/F), and baseline IgG, presence of anti-drug antibodies (ADAs)/neutralising antibodies (NAbs) on FcRn independent CL/F, formulation on mean absorption time (MAT), ITP patient on V/F, and baseline steroid use on baseline IgG and maximum effect (E_{max}).
A substantial proportion of rozanolixizumab plasma concentrations fell below the lower limit of quantification (LLOQ) and were therefore excluded. Nevertheless, the model performed adequately based on prediction-corrected visual predictive checks (pcVPCs) and goodness-of-fit (GOF) plots. As expected for a mAb, body weight had the largest impact on the PK of rozanolixizumab. However, this did not translate into a clinically relevant effect on total IgG. Overall, no dose adjustments are required based on any of the investigated covariates including age, sex or race.

Interactions
No *in vitro* or clinical interaction studies were conducted.
An effect of rozanolixizumab on CYPs, UGTs or transporters by its metabolism, chemical properties or mechanism of action is unlikely. Since cytokine levels appeared to be unaffected in the Phase 3 studies, no impact on CYP expression is anticipated.
Rozanolixizumab has been designed not to interfere with albumin binding to FcRn. In the Phase 3 studies, only minimal reductions of the albumin levels were observed. Therefore, no interactions with highly protein-bound drugs are expected.

Pharmacodynamics
Mechanism of action and primary pharmacology
Myasthenia gravis is an organ-specific, antibody-mediated autoimmune disease. The pathogenic autoantibodies against the acetylcholine receptor (AChR) and muscle-specific kinase (MuSK) are primarily of the immunoglobulin G (IgG)1 or IgG3 and IgG4 isotypes, respectively. rozanolixizumab drug substance is a recombinant, humanised anti-neonatal Fc receptor (FcRn) IgG4P monoclonal antibody. By binding to IgG and albumin, FcRn reduces their lysosomal degradation. By blocking FcRn, treatment with rozanolixizumab is thought to enhance the catabolism of IgGs and thereby potentially reduce pathogenic autoantibodies.

Secondary pharmacology (safety)
No thorough-QT study was conducted. mAbs harbour a low risk of prolonging the QT interval.

Pharmacodynamic interactions with other medicinal products or substances
Due to the mechanism of action of rozanolixizumab, exposures of concomitantly administered IgG-based drugs and Fc–peptide fusion proteins may be decreased.
Vaccination during rozanolixizumab treatment has not been studied.

The use of high-dose oral steroids can induce low IgG levels. As part of the population PK/PD analyses, baseline steroid usage was identified as a statistically significant covariate on baseline total IgG and E_{max} of the PK-IgG model. However, the difference in IgG reduction was not considered clinically relevant. No impact on the MG-ADL score was observed.

Exposure efficacy/safety relationship
Using MG-ADL score data from the Phase 3 study MG0003, an exposure-efficacy analysis was conducted. The effect of rozanolixizumab on the MG-ADL score was linked to IgG inhibition, which was well described by a direct response model with a placebo effect. Myasthenia Gravis Foundation of America disease class at baseline was included as a predictor of the baseline MG-ADL score. No other evaluated covariates, including baseline IgG concentration, age, sex, region, type of autoantibody, baseline steroid usage, duration of disease, and prior thymectomy, were found to be statistically significant. Since only very few subjects with a body weight >100 kg were included, the predictive performance of the model in patients >100 kg may be limited. Based on the pcVPCs, no significant difference in the treatment effect can be observed between the ~7 mg/kg and ~10 mg/kg doses. Of note, body weight was not identified as a statistically significant covariate on MG-ADL score.
The models were extended with anti-AChR and anti-MuSK autoantibody data from one Phase 2 study and two Phase 3 studies in gMG. The association between anti-AChR and MG-ADL score was best described by a direct response model with a time-dependent placebo effect. Higher baseline anti-AChR concentration was associated with increased $E_{maxMG–ADL}$, whereas no other evaluated covariates, including age, sex, region, baseline steroid usage, duration of disease, thymectomy at baseline, were found to be statistically significant. Again, no significant difference in the treatment effect can be observed between the ~7 mg/kg and ~10 mg/kg doses based on the pcVPCs. Only limited data of MuSK-positive participants were available.

Graphical exploration of adverse events of focus (AEOF) revealed that the frequency of headache of any grade was increased at doses higher than 300 mg. The frequency was highest for the first dose and decreased for later doses. Gastrointestinal disturbances of any grade increased with dose, which was driven by moderate events.

6.2 Dose finding and dose recommendation

Dosing in Phase 1 and Phase 2 studies. Rozanolixizumab has been studied with body weight-normalised dosing (mg/kg) in Phase 1 and Phase 2 studies. In gMG Phase 2 study MG0002, rozanolixizumab SC was administered using body weight-based dosing (mg/kg) at doses of 4 mg/kg and 7 mg/kg (rozanolixizumab or placebo was administered Q1W for 3 weeks in 2 dosing periods followed by an 8-week Follow-up Period starting from the last dose). There were clinically relevant improvements in MG-ADL following treatment with rozanolixizumab 7 mg/kg compared with placebo, and PD data showed maximum reductions in total IgG serum concentrations of approximately 70% from Baseline after repeated doses of 7 mg/kg.

Dosing in Phase 3 gMG studies. A dose ≈7 mg/kg was selected for the Phase 3 programme to replicate and confirm the MG-ADL improvements. A dose ≈10 mg/kg was included to assess whether additional benefit could be gained through either a greater magnitude of effect or shorter time to onset of clinical response, while maintaining a positive benefit-risk profile. The weight-tiered approach with 5 different fixed doses across 4 body weight tiers (35 kg to <50 kg; 50 kg to <70 kg; 70 kg to <100 kg; ≥100 kg) was introduced to simplify dosing.

Dose recommendation proposed for marketing authorisation in gMG patients. The Applicant proposed a dose of ≈7 mg/kg for labelling in gMG patients based on clinical efficacy shown across efficacy endpoints, and an acceptable safety profile with no incremental benefit on the primary endpoint with ≈10 mg/kg in pivotal study MG0003.

6.3 Efficacy

Pivotal study MG0003
The pivotal trial to support marketing authorisation for the treatment of gMG is MG0003, a completed multicentre, randomised, double-blind, placebo-controlled, 3-arm repeat dose study evaluating the efficacy and safety of two doses of rozanolixizumab (≈7 mg/kg and ≈10 mg/kg) and matching placebo in adult gMG patients with MG Foundation of America (MGFA) Class II to IVa, and being considered for additional treatment such as intravenous immunoglobulin (IVIg) or plasma exchange (PLEX) and with a historic positive record of autoantibodies against AChR or MuSK. Patients with severe weakness affecting oropharyngeal or respiratory muscles or (imminent) MG crisis were excluded from the study programme. Rozanolixizumab was used as an add-on to the patient's established MG medication.
Study periods include an up to 4-week Screening Period, a 6-week double-blind Treatment Period including 6 SC infusions of rozanolixizumab (at 1-week intervals) and an 8-week blinded Observation Period that began a week after the last infusion. Completers of the 6-week Treatment Period could roll over into the 8-week Observation Period. Randomisation into treatment groups was 1:1:1 and was stratified by MG-specific AChR+ or MuSK+ status. Rozanolixizumab SC was administered based on a weight-tiered approach across 4 body weight tiers to simplify dosing. The same dosing was used in the Open Label Extension (OLE) studies MG0004 and MG0007. The assessment tools referring to the primary and the first three secondary endpoints included the well-established and validated clinical scales Myasthenia Gravis Activities of Daily Living (MG-ADL) scale (patient rated), Myasthenia gravis Composite scale (MG-C) and Quantitative Myasthenia Gravis (QMG) scale (both physician rated). Minimal clinically important differences (MCID) have been defined for all three scales (change of 2 points on MG-ADL, and 3 points on MG-C and QMG, respectively). A sequential hierarchical test procedure was applied for the primary and secondary efficacy endpoints to protect the overall significance level for the multiplicity of endpoints and treatment groups.
Overall, 200 patients were randomised (66 in the ≈7 mg/kg, 67 in the ≈10 mg/kg and 67 in the placebo group). Baseline characteristics suggest less severe gMG for patients in the ≈7 mg/kg dose group as compared to the ≈10 mg/kg dose group. The numbers of subjects in the rozanolixizumab treatment groups <50 mg (N=8), ≥65 years (N=33), MG-ADL <5 (N=27) and MGFA Class IV (N=5) were limited. Similar to the proportion seen in the general gMG patient population, 10.5% of all patients had MuSK+ auto-Abs. 64% of subjects completed MG0003. 5.3% of rozanolixizumab-treated subjects discontinued due to adverse events (AEs). 29/133 rozanolixizumab-treated subjects experienced MG worsening during the Observation Period and chose to receive the subsequent rozanolixizumab cycle in one of the OLE studies MG0004 or MG0007 instead of receiving rescue therapy with IVIg or PLEX.

Open label extension study MG0007
At the time of marketing authorisation application, OLE MG0007 was an ongoing randomised Phase 3 OLE study. Study participants from MG0003 who completed the End of study Visit were re-randomised in MG0007 to both rozanolixizumab in a ratio of 1:1. Dose switches were allowed throughout MG0007. During the Observation and Non-treatment Periods, patients were assessed for symptom worsening at regular 4-week intervals. According to investigator judgement during these periods, patients were eligible to initiate another 6-week Treatment Period with rozanolixizumab based on symptom worsening (defined as an increase of 2.0 points on the MG-ADL scale or 3.0 points on the QMG scale). A 4-week interval was maintained between treatment periods unless IgG levels returned to ≥2 g/L. 165 out of 200 patients included in MG0003 entered MG0007. 88/165 patients were assigned to the ≈7 mg/kg group and 77/165 patients were assigned to the ≈10 mg/kg group. At the time of data cutoff, no participants had completed the study. 123/157 patients were ongoing in the study and 34/157 patients had discontinued the study, most frequently due to AEs (12.7%).

Efficacy results – pivotal study MG0003. At Day 43 (i.e. one week after the last infusion of the treatment cycle), the primary endpoint '*change in MG-ADL scores from Baseline*' showed clinically meaningful improvement that was statistically significantly different compared to placebo for both ≈7 mg/kg and ≈10 mg/kg rozanolixizumab treatment groups (<0.001). MG-ADL responder status was achieved by 68% in the ≈7 mg/kg and 61% in the ≈10 mg/kg dose group as compared to 28% of

placebo-treated subjects. The median time to first MG-ADL response was estimated to be 16 days and 22 days for the ≈7 mg/kg and ≈10 mg/kg rozanolixizumab treatment groups, respectively (indicating that the probability of a response is 50% at those timepoints).
Secondary efficacy endpoints MG-C and QMG also yielded clinically meaningful improvements in the least square (LS) mean score from Baseline that were statistically significantly different compared to placebo or both rozanolixizumab treatment groups (all p-values <0.001).

Efficacy results – OLE study MG0007. The clinical efficacy of rozanolixizumab observed in MG0003 was similar in MG0007, with improvements across all the efficacy endpoints following repeated cyclic treatment with ≈7 mg/kg and ≈10 mg/kg, with effect sizes similar to those observed in the parent study MG0003. Responses for MG-ADL were seen as early as Day 8 of each treatment cycle, with a median time to MG-ADL response of 15 days for the majority of each of the first 5 treatment cycles. The treatment-free interval was ~9 weeks between the first 2 cycles and ~7 to 8 weeks between Cycle 2 and Cycle 3. Patients treated over more cycles showed a trend for shorter treatment-free intervals (minimum 29 days). 65% of 23 subjects who rolled over from MG0003 due to MG worsening during the MG Observation Period achieved responder status at Weeks 5 and 7, and 56% at Week 9 of MG0007. The numbers of patients treated in later cycles declined continuously and do not allow robust conclusions. Efficacy regarding repeated cyclic treatment in the anti-MuSK+ subgroup was clinically meaningful and similar to the benefits observed in MG0003. 14 patients (6 in the ≈7 mg/kg treatment group and 8 in the ≈10 mg/kg treatment group) needed rescue therapy (IVIg or PEX) in MG0007.

6.4 Safety

The safety evaluation of rozanolixizumab in gMG includes a comparison of data from 200 patients who received placebo (N=67) or rozanolixizumab administered at approximate doses (≈) of ≈7 mg/kg (N=64) or ≈10 mg/kg (N=69) in MG0003 (i.e. the pivotal Phase 3 double-blind, randomised study). However, the primary safety analysis refers to the pooled Pool S2, which included all rozanolixizumab-treated study participants who have undergone ≥1 Treatment Cycle (i.e. ≥1 dose of rozanolixizumab in any 6-week Treatment Period), and the Treatment Cycle has been followed by an (up to) 8-week Follow-up Period starting from the last infusion in MG0003 and MG0007.

Safety – pivotal study MG0003

Exposure to study treatment (in days) was similar across placebo and rozanolixizumab treatment groups. Approximately 80% in the placebo and the ≈7 mg/kg treatment groups received all 6 infusions as compared to 70% in the ≈10 mg/kg dose group. 5.3% of rozanolixizumab-treated patients discontinued the study due to TEAEs (3.1% in the ≈7 mg/kg vs. 3.0% in the placebo group). There were no fatal SAEs. The overall TEAE incidence was similar in both rozanolixizumab dose groups and considerably lower in the placebo group (81% in the ≈7 mg/kg group, 83% in the ≈10 mg/kg group and 67% in the placebo group). Individual TEAEs across rozanolixizumab treatment groups reported in ≥5% of patients in either rozanolixizumab group were headache (45.3% vs. 19.4%), diarrhoea (25% vs. 13.4%), pyrexia (12.5% vs. 1.5%, nausea (7.8% vs. 7.5%), and arthralgia (6.3% vs. 3.0%), myalgia, vomiting, hypertension, nasopharyngitis. For serious TEAEs, the incidence was lower in the ≈7 mg/kg dose group as compared to placebo (7.8% vs. 9.0%) and comparable for severe AEs (4.7% vs. 4.5%). Headache also represents the most common severe individual TEAE (one patient in the ≈7 mg/kg group), followed by TEAEs related to MG worsening. Most frequent individual serious TEAEs are related to MG worsening (1.6% vs. 4.5%). Moderate reductions in mean albumin levels were observed at all timepoints for both rozanolixizumab treatment groups. IgG value ≤1 g/L was present in 11 participants. This is to be expected from the mechanism of action.

Safety - Pooled analyses (Pool S2)

Pool S2 includes 188 subjects (94 subjects in the ≈7 mg/kg dose group and 94 subjects in the ≈10 mg/kg dose group). 29.3% of rozanolixizumab-treated subjects discontinued the study with the most frequent reason being AEs, followed by lack of efficacy (1.6%). The incidence of TEAEs leading to temporal withdrawal of the investigational medicinal product (IMP) was 17.0%. Over all 678 cycles,

169/188 (89.9%) study participants experienced 1526 TEAEs. By cycle, the incidence of any TEAEs did not increase with repeated cyclic treatment, but nor did it decrease substantially. Most TEAEs were reported during treatment periods. 5 participants (all MG0007) died, including 4 participants who died before the data cutoff date of 08.07.2022, and 1 participant who died post data cutoff. In four of the five fatal cases, infection contributed to the fatal course.
Most common TEAEs across both dose groups included headache (46.3%, migraine 2.7%), diarrhoea (28.7%), pyrexia (18.1%), nausea (14.9%), COVID-19 infection (13.8%), arthralgia (11.2%), and blood IgG decreased (10.6%). Other important TEAEs were infection (oral herpes, herpes zoster, UTI, bronchitis, interferon gamma release assay positive), lymphocyte count decreased, injection site reactions and pruritus. The type of individual TEAEs did not change with repeated cyclic treatment. 50 patients experienced 76 severe TEAEs. Most common severe TEAEs in Pool S2 were MG worsening (5.9%) and headache (4.3%). With repeated cyclic treatment, no increase in severe or serious TEAEs was observed. 22.3% of study participants experienced a total of 56 serious TEAEs and 15.4% of rozanolixizumab-treated patients experienced TEAEs leading to discontinuation. With repeated cyclic treatment, the most common TEAEs leading to study discontinuation in the rozanolixizumab overall group were related to MG worsening, leading to protocol-mandated withdrawal due to receiving rescue therapy. The incidence of TEAEs leading to temporary withdrawal of the IMP was 17% across both dose groups and cycles (range over cycles 1 to 7: 4.2% to 9.3%). The most common preferred terms related to temporary withdrawal reflect temporary withdrawal criteria related to decreased IgG levels and COVID-19 specified in the protocols. The findings suggest frequent interruptions due to low IgG and/or infections.

6.5 Final clinical benefit risk assessment

The Applicant conducted an adequate clinical pharmacology program, and the PK profile of rozanolixizumab generally conforms to that of a mAb. Based on the population PK/PD analyses, no dose adjustment is necessary based on any of the evaluated covariates including, amongst others, age, sex, and race. Overall, the proposed dosing regimen is supported based on the PK/PD.

The pivotal placebo-controlled trial MG0003 involved a single treatment cycle, while repeated cyclic treatment has been studied in OLE MG0007. The latter study provides evidence for a clinical meaningful treatment benefit in at least 50% of gMG subjects receiving rozanolixizumab as an add-on to their established MG standard therapy. For this group, rozanolixizumab represents a promising treatment option if clinical response cannot be achieved with conventional gMG therapy. It is also noteworthy that the subgroup of anti-MuSK+ patients experienced a consistent and clinically meaningful treatment benefit in both clinical trials. The safety profile appears acceptable when close clinical monitoring is ensured. To address open clinical issues, specific information has been implemented in the Information for healthcare professionals (e.g. limited overall efficacy and safety dataset for repeated cyclic treatment with low rozanolixizumab dose, use in patients >65 years and <50 kg body weight, discontinuation of low rozanolixizumab dose treatment in QMG non-responders after two subsequent unsuccessful cycles, no early re-treatment (<4 weeks), patients <50 kg body weight, elderly patients).

To reflect the study design and the study population, the following indication wording has been finally approved:

RYSTIGGO is indicated as an add-on to standard therapy for the treatment of generalised myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) or anti-muscle-specific tyrosine kinase (MuSK) antibody positive.

7 Risk management plan summary

The RMP summaries contain information on the medicinal products′ safety profiles and explain the measures that are taken to further investigate and monitor the risks, as well as to prevent or minimise them.
The RMP summaries are published separately on the Swissmedic website. It is the responsibility of the marketing authorisation holder to ensure that the content of the published RMP summaries is accurate and correct. As the RMPs are international documents, their summaries might differ from the content in the Information for healthcare professionals / product information approved and published in Switzerland, e.g. by mentioning risks that occur in populations or indications not included in the Swiss authorisations.

8 Appendix

Approved Information for healthcare professionals

Please be aware that the following version of the Information for healthcare professionals for RYSTIGGO was approved with the submission described in the SwissPAR. This Information for healthcare professionals may have been updated since the SwissPAR was published.

Please note that the valid and relevant reference document for the effective and safe use of medicinal products in Switzerland is the Information for healthcare professionals currently authorised by Swissmedic (see www.swissmedicinfo.ch).

Note:
The following Information for healthcare professionals has been translated by the MAH. It is the responsibility of the authorisation holder to ensure the translation is correct. The only binding and legally valid text is the Information for healthcare professionals approved in one of the official Swiss languages.

Placeholder for text approval stamp

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected new or serious adverse reactions. See the "Undesirable effects" section for advice on the reporting of adverse reactions.

RYSTIGGO

Composition

Active substances

Rozanolixizumab is a recombinant, humanised anti-neonatal Fc receptor (FcRn) immunoglobulin G 4P (IgG4P) monoclonal antibody produced in Chinese Hamster Ovary (CHO) by recombinant DNA technology.
One ml contains 140 mg of rozanolixizumab.

Excipients

L-histidine, L-histidine hydrochloride monohydrate, L-proline, Polysorbate 80, Water for injection.

Pharmaceutical form and active substance quantity per unit

Solution for injection.
For subcutaneous (s.c.) infusion.
Each vial contains sufficient volume for a 2 ml (280 mg of rozanolixizumab) dose to be administered.
Colourless to pale brownish-yellow, clear to slightly opalescent solution.

Indications/Uses

Rystiggo is indicated as an add-on to standard therapy for the treatment of generalised myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) or anti-muscle-specific tyrosine kinase (MuSK) antibody positive (see section “Clinical Efficacy”).

Dosage/Administration

Rystiggo should be prescribed and monitored by physicians experienced in the treatment of patients with neuromuscular or neuro-inflammatory disorders.

Dosage

To ensure traceability of biotechnological medicinal products, it is recommended that the trade name and batch number should be documented for each treatment.

A treatment cycle consists of one dose per week for six weeks administered via the subcutaneous route.
The following table indicates the recommended total weekly dose of rozanolixizumab according to the patient's 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
Number of vials to be used*	1	2	2	3

*each vial contains excess volume for priming of the infusion line, see "Mode of administration".

There is no data with patients under 35 kg and over 155 kg. Patients with Myasthenia Gravis Foundation of America (MGFA) Class IVb and V were not studied in the Rystiggo clinical trial program.

Subsequent treatment cycles are administered according to clinical evaluation.
The frequency of treatment cycles may vary by patient. In case symptoms worsen and require additional treatment (defined as an increase of 3 points on the Quantitative Myasthenia Gravis (QMG) scale and/or of 2 points on the Myasthenia Gravis Activities of Daily Living (MG-ADL) scale since the end of the last treatment cycle), patients may receive another 6-week treatment cycle.
In the clinical development program, most participants had treatment-free intervals of 4-13 weeks between cycles. The minimum interval between two treatment cycles is four weeks (i.e. start of the subsequent cycle at least 28 days after the last dose of the previous cycle).
Treatment benefit must be regularly assessed. If a patient does not respond to two consecutive six-week treatment cycles (defined as an improvement of less than 3 points on the QMG scale and/or less than 2 points on the MG-ADL scale compared to the start of the respective cycle), treatment with Rystiggo should not be continued.

If a scheduled infusion is missed, Rystiggo may be administered up to 4 days after the scheduled time point. Subsequently, the original dosing schedule should be resumed until the treatment cycle is completed.

Special dosage instructions

Patients with hepatic disorders
No data are available in patients with hepatic impairment. No dose adjustment is considered necessary as the pharmacokinetics of rozanolixizumab are unlikely to be affected by hepatic impairment (see section *Pharmacokinetics*).

Patients with renal disorders
Limited safety and efficacy data are available in patients with mild to moderate renal impairment (eGFR > 45ml/min/1.73m^2). No data are available in patients with severe renal impairment. No dose adjustment is considered necessary as the pharmacokinetics of rozanolixizumab are unlikely to be affected by renal impairment (see section *Pharmacokinetics*).

Elderly patients
No dose adjustment is required (see section *Pharmacokinetics*). No data are yet available on safety and efficacy in patients ≥85 years. The data available for the age group ≥65 to 85 years is limited (see *Warnings and precautions* and *Adverse reactions*).

Children and adolescents
The safety and efficacy of rozanolixizumab in children and adolescents aged <18 years have not been established. No data are available. Rystiggo has not been approved for the use in the pediatric population.

Mode of administration

For subcutaneous infusion using a pump.

Infusion pumps, syringes and infusion sets suitable for subcutaneous administration of medicinal products must be used. It is recommended to use pumps where administered volume can be pre-set as each vial contains excess volume for priming of the infusion line.

It is recommended that rozanolixizumab is administered subcutaneously preferably into the lower right or lower left part of the abdomen, below the belly button. Other infusion sites have not been studied in the clinical development program. Infusions should not be given into areas where the skin is tender, erythematous, or indurated.
During administration of all single doses of the entire first treatment cycle and administration of the first dose of the second treatment cycle of rozanolixizumab, appropriate treatment for injection and hypersensitivity-related reactions should be readily available (see section *Warnings and Precautions*).

Infusion rate
Rozanolixizumab is administered using an infusion pump at a constant flow rate up to 20 ml/hr.

Before administering rozanolixizumab, the *Instructions for handling* must be read carefully.

Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section “Composition”.

Warnings and precautions

Clinical monitoring
In the clinical study program, the efficacy and safety of repeated cyclic treatment with the approved dosage of Rystiggo were only investigated in a limited number of patients. Rystiggo is a symptom driven cyclic treatment.
In view of individual, unpredictable differences in clinical response, patients should be closely monitored. In the clinical study programme, despite repeated cyclic treatment with Rystiggo at a dose of approximately (≈) 7mg/kg or ≈ 10mg/kg, 13.8% of patients reported a worsening of the underlying disease up to myasthenic crisis (2.1%) (see section *Clinical Efficacy* and *Adverse Reactions*).
No data are available on the efficacy and safety of Rystiggo for the treatment of myasthenic crisis.

Body weight <50kg
In the clinical study program, only a very limited number of patients with a body weight below 50 kg was examined. The efficacy of repeated cyclic treatment with rozanolixizumab has not yet been reliably demonstrated in this group (see section *Clinical efficacy*).

Elderly patients
In the clinical study program, only a limited number of patients aged ≥65 to 85 years was studied . The treatment effect of repeated cyclic treatment was lower in this age group and less robust compared to patients <65 years. At the same time, older patients showed a less favourable side effect profile: in a double-blind and one open-label extension study, 39.6% of older patients (≥65 years) experienced severe adverse effects compared to 30.7% in the group <65 years. A myasthenic crisis occurred in 6.3% of patients aged ≥65 years and in 0.7% of patients aged <65 years (see section *Clinical efficacy*).

Myasthenic crisis
Treatment with rozanolixizumab in patients with impending or manifest myasthenic crisis has not been studied.
Rozanolixizumab is not approved for the treatment of impending or manifest myasthenic crisis. In the case of impending or manifest myasthenic crisis, the interaction between rozanolixizumab and

established therapies for myasthenic crisis must be taken into account, as rozanolixizumab may impair the efficacy of these therapies (see Section *Interactions*).

Aseptic meningitis

Drug-induced aseptic meningitis has been reported following treatment with rozanolixizumab (see Section *Undesirable effects*). If symptoms consistent with drug-induced aseptic meningitis develop, diagnostic workup and treatment should be initiated according to the standard of care.

Hypogammaglobulinemia

Due to its mechanism of action, Rystiggo can lead to a significant drop in immunoglobulin G (IgG) levels (see section *Undesirable effects*). In the clinical development program, treatment with Rystiggo was temporarily interrupted if the total serum IgG fell <1g/L, regardless of whether an infection was present at the same time. As soon as the IgG level was ≥2g/L again, treatment with Rystiggo could be resumed. In the case of a non-serious persistent or recurrent infection with a total serum IgG ≥1 and <2g/L, treatment with Rystiggo was also temporarily suspended until the infection had subsided and the IgG had returned to ≥2g/L.

Infections

As rozanolixizumab causes transient reduction in IgG levels the risk of infections may increase (see Section *Properties/Effects*).

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

Vaccination

Immunisation with vaccines during rozanolixizumab therapy has not been studied. The safety of immunisation with live or live-attenuated vaccines and the response to immunisation with vaccines are unknown. All vaccines should be administered according to immunisation guidelines and at least 4 weeks before initiation of treatment with rozanolixizumab. For patients that are on treatment with rozanolixizumab, vaccination with live or live-attenuated vaccines is not recommended. For all other vaccines, the vaccinations should take place at least 2 weeks after the last infusion of a treatment cycle and 4 weeks before initiating the next cycle with rozanolixizumab.

Hypersensitivity

Infusion reactions such as rash or angioedema may occur (see section *Undesirable effects*). In the clinical study program, these were mild to moderate. Patients should be monitored during treatment with rozanolixizumab and for 15 minutes after the administration of rozanolixizumab is complete for

clinical signs and symptoms of hypersensitivity reactions. If a hypersensitivity reaction occurs during administration (see section *Undesirable effects*), rozanolixizumab infusion should be discontinued and appropriate measures should be initiated if needed. Once resolved, administration may be resumed.

Immunogenicity

In the pooled cyclic treatment data from the phase 3 program, after 1 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. There was no apparent impact of immunogenicity on efficacy (see section *Properties/Effects*). However, study participants with ADAs were more than twice as likely to report certain side effects compared to study participants without ADAs (see *Adverse effects* section).

Excipient proline

This medicinal product contains 29 mg of proline in each ml.
Administration to patients with hyperprolinaemia should be limited to cases where there are no other alternatives treatments available.

Interactions

No interaction studies have been performed. As rozanolixizumab interferes with the neonatal Fc receptor (FcRn) recycling mechanism of immunoglobulin G (IgG), the serum concentrations of IgG-based medicinal products (e.g. monoclonal antibodies and intravenous immunoglobulin [IVIg]) and Fc–peptide fusion proteins are expected to be decreased if administered concomitantly with rozanolixizumab. Two weeks after a rozanolixizumab infusion, a clinically relevant effect of rozanolixizumab on the PK or efficacy of these drugs is unlikely to occur. It is recommended to initiate these drugs 2 weeks after a rozanolixizumab infusion and monitor for attenuated efficacy of these medications when administered concomitantly with rozanolixizumab.

Interactions with highly-protein bound medications or medications that are substrates, inducers or inhibitors of cytochrome P450 enzymes or transporters are unlikely.
Treatment with IV or SC immunoglobulins, PLEX/plasmapheresis and immunoadsorption may reduce circulating levels of rozanolixizumab.

Pregnancy, lactation

Pregnancy

Limited data does not allow to draw conclusion on the use of rozanolixizumab in pregnant women. Animal studies have shown an effect on early losses in pregnacy. In addition, as expected by the pharmacological mode of action of rozanolixizumab, offspring from treated dams had very low levels of IgG at birth. In animals, rozanolixizumab showed no effect on fetal development, parturition or postnatal development (see Section *Preclinical data*).Treatment of pregnant women with rozanolixizumab should only be considered if the clinical benefit outweighs the risks.
As rozanolixizumab is expected to reduce maternal IgG levels, and is also expected to inhibit the transfer of maternal IgG to the foetus, reduction in passive protection to the newborn is anticipated. Therefore, risks and benefits of administering live / live attenuated vaccines to infants from rozanolixizumab-treated pregnant women during the first 2 months post birth should be weighed against each other (see section *Warnings and Precautions*, subsection “Vaccination”).

Lactation

It is unknown whether rozanolixizumab is excreted in human milk. Maternal IgG is generally known to be excreted in low amounts in breast milk during the first days after birth, which is decreasing further soon afterwards. Based on these theoretical considerations, a risk to breast-fed infants cannot be excluded, especially in the first days after birth. After this early phase, the decision whether to discontinue rozanolixizumab or breast-feeding should be based on the potential benefits of breastfeeding, the clinical need of the mother for tratment with rozanolixizumab and the potential adverse effects of rozanolixizumab on the breastfed infant.

Fertility

The effects of rozanolixizumab on human fertility is not known. Animal studies do not indicate harmful effects with respect to fertility (see section *Preclinical Data*).

Effect on ability to drive and use machines

No studies have been conducted on the effect of rozanolixizumab on the ability to drive and use machines. Theoretical considerations suggest no or negligible influence on the ability to drive and use machines.

Undesirable effects

Summary of the safety profile
A total of 133 patients have been treated with rozanolixizumab in a double-blinded placebo-controlled clinical study in Myasthenia Gravis. The most commonly reported adverse reactions in the double-blind and one open-label extension study (188 patients) were headache (51.6%), diarrhoea (33.5%), upper respiratory tract infections (25.5%), pyrexia (20.7%), nausea (17.6%), infusion/injection reactions (12.2%), and arthralgia (12.2%) .

List of adverse reactions

Adverse reactions from clinical studies in gMG are listed below, classified by MedDRA System Organ Class (SOC). Within each SOC, the adverse reactions are ranked by frequency, with the most frequent reactions first.

Frequency categories are defined as follows: Very common (≥ 1/10); Common (≥ 1/100 to < 1/10); Uncommon (≥ 1/1000 to < 1/100); Rare (≥ 1/10,000 to < 1/1000); Very rare (< 1/10,000), not known (cannot be estimated from the available data).

Table 1: List of adverse reactions

MedDRA System Organ Class	Frequency category	Adverse Reactions
Blood and lymphatic system disorders	Very common	Reduced IgG blood levels (11.2%)
Infections and infestations	Very common	Upper respiratory tract infections (25.5%)[1]
	Common	Viral infections [2] Lower respiratory tract infections[3] Herpes viral infections[4]
Nervous system disorders	Very common	Headache (51.6%)[5]
	Rare	Aseptic meningitis
Respiratory tract, chest and mediastinum disorders	Common	Oropharyngeal pain
Gastrointestinal disorders	Very common	Diarrhoea (33.5%) Abdominal pain (16.5%) [6] Nausea (17.6%)
	Common	Vomiting
Skin and subcutaneous tissue disorders	Common	Rash[7]
	Uncommon	Angioedema[8]
Musculoskeletal and connective tissue and bone disorders	Very common	Arthralgia (12.2%)
	Common	Myalgia Neck pain Muscle spasms
General disorders and administration site conditions	Very common	Pyrexia (20.7%) Reactions at the injection/infusion site (12.2%)[9]
	Common	Influenza-like illness Chest pain

[1] Includes acute and chronic sinusitis, laryngitis, nasopharyngitis, pharyngitis, rhinitis, sinusitis, tonsillitis, upper respiratory tract infection

[2] Includes viral gastroenteritis, viral respiratory tract infection, viral infection, viral upper respiratory tract infection, but excludes COVID-19 infections
[3] Includes bronchitis, lower respiratory tract infection, pneumonia
[4] Includes herpes simplex, herpes virus, herpes zoster, ophthalmic herpes simplex, oral herpes infections
[5] Includes headaches and migraines
[6] Includes abdominal pain, abdominal pain upper, abdominal discomfort
[7] Includes rash, papular rash and erythematous rash
[8] Includes swollen tongue
[9] Includes but not limited to injection site bruising, injection site rash, injection site reaction, injection site erythema, injection site pruritus, infusion site erythema, infusion site reaction.

Description of specific adverse reactions and additional information

Headache

In MG0003, headache was the most common event reported in 58 (43.6 %) and 13 (19.4%) of the patients treated with rozanolixizumab and placebo, respectively. Headache occurred most frequently after the first infusion of rozanolixizumab and within 1 to 4 days after infusion. Headaches were nonserious, mostly mild or moderate and there was no increase in incidences of headache with repeated cyclic treatment.

Immunogenicity

The detection of anti-drug antibodies (ADAs) is highly dependent on the sensitivity and specificity of the test. In addition, the observed incidence of antibody positivity (including neutralising antibodies) in a test can be influenced by several factors, including test methodology, sample handling, timing of sample collection, concomitant medication and underlying disease. For this reason, comparing the incidence of antibodies to rozanolixizumab with the incidence of antibodies to other drugs may be misleading.

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. The reduction in total IgG by rozanolixizumab in neutralising antibody-positive patients was not different from patients who were antidrug antibody-negative.

There was no apparent impact of immunogenicity on efficacy and overall safety.

The rate for certain events (upper abdominal discomfort, upper respiratory tract infections, decreased number of neutrophil granulocytes, hypertension, dys/paraesthesia, dyspnea, dyslipidemia) was at least two times higher in study participants with ADAs than in study participants without ADAs. A direct causal relationship between the occurrence of these side effects and ADAs has not yet been demonstrated. Patients without ADAs were more frequently treated with immunosuppresants, systemic steroids and chemotherapeutic agents.

Reporting suspected adverse reactions after authorisation of the medicinal product is very important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions online via the ElViS portal (Electronic Vigilance System). You can obtain information about this at www.swissmedic.ch.

Overdose

Signs and symptoms

There are 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.

Treatment

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

Properties/Effects

ATC code

L04AG16

Mechanism of action

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

By the same mechanism, rozanolixizumab decreases the concentration of pathogenic IgG autoantibodies associated with gMG. Clinical data with rozanolixizumab have not identified any clinically relevant impact on levels of albumin, which binds at a different site on FcRn.

Pharmacodynamics

Weekly subcutaneous administration of rozanolixizumab resulted in a rapid and sustained reduction in total IgG serum concentrations, with significant 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. Similar effects were observed for all subclasses of IgG.

Clinical efficacy

Phase 3 studies

The safety and efficacy of rozanolixizumab was evaluated in patients with generalized myasthenia gravis in 3 Phase III studies. Patients were at least 18 years of age, had a body weight ≥35 kg, had a diagnosis of generalized myasthenia gravis, had autoantibodies against AChR or MuSK, had a disease stage class II to IVa according to the Myasthenia Gravis Foundation of America (MGFA) classification, a MG-Activities of Daily Living (MG-ADL, a patient reported outcome measure) score of at least 3 (with ≥3 points from non-ocular symptoms) and, a Quantitative Myasthenia Gravis (QMG) score of at least 11 and met the criteria for additional treatment with plasmapheresis (plasma exchange (PLEX)) or intravenous immunoglobulins (IVIg).
Patients were not permitted in the study if they had:

- clinically relevant active infection or serious infections, mycobacterial infections, hepatitis B, hepatitis C, HIV infections
- current or medical history of primary immunodeficiency or IgA deficiency, history of splenectomy, or transplantation (solid organ transplant or hematopoietic stem cell/marrow transplant)
- thymectomy in the 6 months prior to initiation therapyor thymoma at any time that required chemotherapy and/or radiotherapy and active neoplastic disease or history of neoplastic disease within the past 5 years
- been treated with PLEX, IVIg 1 month and monoclonal antibodies 3 to 6 months prior to starting treatment
- a serum total IgG level ≤ 5.5 g/l or an absolute neutrophil count < 1 500 cells/mm3

The safety and efficacy of rozanolixizumab was evaluated in patients with gMG in the pivotal phase 3 study MG0003. Long-term safety, tolerability and efficacy of rozanolixizumab were evaluated in 2 phase 3 open-label extension (OLE) studies, with in OLE (MG0007) administering rozanolixizumab as 6-week treatment cycles based on clinical needs over a period of up to 2 years.

Study MG0003

The study MG0003 evaluated 200 patients for up to 18 weeks where patients were randomised to receive weight-tiered doses of rozanolixizumab equivalent to approximately (≈) 7 mg/kg or ≈10 mg/kg, or placebo. Treatment consisted of one dose per week for a period of 6 weeks followed by an 8-week observation period.

The efficacy of rozanolixizumab was evaluated with respect to impact on MG-ADL, MG-C, QMG and a range of other patient reported outcomes instruments including the MG Symptoms PRO scores.
The primary endpoint was the change from Baseline to Day 43 in the MG-ADL score. Secondary

efficacy endpoints were a change from Baseline to Day 43 in MG-C score and QMG score as well as MG-ADL responder status at Day 43.

In general, patient demographics and baseline disease characteristics were balanced across treatment groups. The majority of patients in the rozanolixizumab ≈7 mg/kg group were female (59.1 %), below 65 years of age (74.2 %), were of predominantly White (62.1 %) or Asian (13.5 %) race, and presented with MGFA class II or III gMG (95.4%). The median age at MG diagnosis was 44.0 years, and the median time since diagnosis was 5.3 years. The autoantibody distribution were 7.6 % anti-MuSK positive, 90.9 % anti-AChR positive. Overall, 95.5 % of patients received at least one MG baseline medication that continued during the study, including 83.3 % receiving acetylcholinesterase inhibitors, as well as 63.6 % receiving corticosteroids, and 47.0 % receiving immunosuppressants at stable doses.

In the rozanolixizumab and placebo groups, the median MG-ADL total score was 8.0, and the median QMG total score was 15.0, at the beginning of the study.

Results for the primary and secondary efficacy endpoints are provided in Table 2 below. A statistically significant and clinically meaningful improvement at Day 43 in MG symptoms was observed in MG-ADL, MG-C, and QMG scores for both rozanolixizumab treatment groups versus placebo.

Table 2: Efficacy outcomes change from Baseline to Day 43

	Placebo (N=67)	**Rozanolixizumab ≈7 mg/kg (N=66)**
MG-ADL		
Baseline Mean	8.4	8.4
Change from Baseline 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
MG-C		
Baseline Mean	15.6	15.9
Change from Baseline 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		
Baseline Mean	15.8	15.4
Change from Baseline 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.

An MG-ADL responder had to have at least a 2-point improvement from Baseline. The proportion of MG-ADL responders at Day 43 in the ≈7mg/kg rozanolixizumab group (46 [71,9%]) was more than double compared with the placebo group (20 [31.3%]). The proportion of QMG responders on day 43 was 39,1% in the placebo group compared to 54,7% in the ≈7 mg/kg rozanolixizumab group. A QMG responder had to show an improvement of at least 3 points compared to baseline at any time during the treatment and observation period of the study.
Rozanolixizumab treatment was associated with a rapid improvement in MG-ADL, MG-C and QMG response already seen in patients one week after the initial dose. The highest levels of improvement were reported from Day 36 to Day 43 for the ≈7mg/kg grouprozanolixizumab treatment group.

OLE studies

The OLE study MG0007 investigated the efficacy of repeated 6-week rozanolixizumab treatment cycles. Patients who showed a deterioration, in the opinion of the investigator (might include increase of at least 2 points on the MG-ADL scale or 3 points on the QMG scale) could receive a further treatment cycle. A total of 25 patients received more than 3 treatment cycles with ≈7mg/kg rozanolixizumab. Individual patients received up to 15 cycles. Patients who responded to repeated treatment with ≈7mg/kg rozanolixizumab showed a stable treatment response to the administration of further treatment cycles.
In the group of patients treated exclusively with the approved dosage of rozanolixizumab, the response rates according to the MG-ADL scale in cycles 1 to 4 were between 55,3% and 87,5%, and according to the QMG scale between 57,9% and 71,4%.

Efficacy in elderly population

Study MG0003 also evaluated the efficacy of rozanolixizumab treatment groups versus placebo in elderly patients (≥65 years of age) which represented 17 patients in the exclusively ≈7mg/kg rozanolixizumab group. The difference compared to placebo-treated patients in the improvement of the MG-ADL score on day 43 compared to baseline was -2.287 (SE 1.257) in the group ≥65 years compared to -2.577 (SE 0.524) in the age group <65 years.
In the OLE study MG0007, 14 elderly patients (≥65 years) were treated with repeated cycles of rozanolixizumab at the approved dose (1 cycle received 14 patients, 2 cycles 12 patients, 3 cycles 7 patients, 4 and more cycles: ≤5 patients). The mean improvement in the MG-ADL score on day 43 compared to baseline of the respective cycle was lower than in the group <65 years (cycle 1: -2.5 (SD 3.6) vs. -3.4 (SD 3.2), cycle 2: -1.6 (SD 3.8) vs. -2.7 (SD 2.5), cycle 3: -1.7 (SD 3.1) vs. -3.3 (SD 2.6) points).

Efficacy in AChR and MuSK autoantibody positive participants

Subgroup analysis by MG-specific autoantibodies, MuSK+ and AChR+, was performed. MG-ADL, MG-C and QMG responder rates >40% for anti-AChR+ participants (28 participants in cycle 1, 27 participants in cycle 2, 21 participants in cycle 3 and 15 participants in cycle 4) and >50% for anti-MuSK-positive participants (4 participants in each cycle 1 to 4) were observed at Day 43 upon repeated cyclic treatment for Cycles 1 to 4. These data refer to study participants who were treated exclusively with the approved dosage of ≈7mg/kg body weight of rozanolixizumab.

Efficacy in patients with a body weight <50kg

The number of study participants with a body weight <50kg who received repeated cyclic treatment with only ≈7mg/kg rozanolixizumab in OLE MG0007 was small (cycle 1-5: up to 4 study participants per cycle). In this group, MG-ADL responder rates varied between 0 and 100% across cycles 1 to 5, with the mean change in MG-ADL score in three of the five cycles failing to reach the clinical meaningfulness threshold, defined as at least ≥2 points at day 43 vs. baseline of the respective cycle.

Paediatric population

See section *Dosage/Administration* for information on paediatric use.

Pharmacokinetics

Absorption

Following subcutaneous administration of rozanolixizumab, peak plasma levels are achieved after approximately 2 days. The absolute bioavailability of rozanolixizumab after subcutaneous 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 active substance 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.

Linearity/non-linearity

Rozanolixizumab exhibited nonlinear pharmacokinetics typical for a monoclonal antibody that undergoes target-mediated drug disposition.

At steady-state, maximum plasma concentrations and area under the concentration time curve (AUC) were predicted to be 3-fold and 4-fold higher at weight-tiered doses of ≈10 mg/kg as compared to ≈7 mg/kg, respectively.

Kinetics in specific patient groups

Renal or hepatic impairment

No dedicated studies have been conducted in patients with renal or hepatic impairment. However, renal or hepatic impairment is not expected to affect the pharmacokinetics of rozanolixizumab. Based on a population pharmacokinetic analysis, renal function (estimated glomerular filtration rate [eGFR] 38-161 ml/min/1.73m2) or hepatic biochemical and function tests (ALT, AST, alkaline phosphatase and bilirubin) had no clinically significant effect on rozanolixizumab apparent linear clearance.

Age, sex, or race

A population pharmacokinetic analysis did not reveal a clinically significant impact of age (from 18 years of age to 89 years of age), sex or race on the pharmacokinetics of rozanolixizumab.

Preclinical data

Repeated dose toxicity

Non-clinical data reveal no special hazard for humans based on studies of repeated dose toxicity. Administration to Cynomolgus and Rhesus monkeys resulted in the expected reduction in IgG.
T-cell dependent antibody response (TDAR) during the treatment phase elicited normal IgM levels and a low IgG response due to accelerated degradation. However, boost immunization after rozanolixizumab clearance resulted in normal IgM and IgG response.

Carcinogenicity

No carcinogenicity studies have been performed.

Genotoxicity

As rozanolixizumab is a monoclonal antibody no genotoxicity studies have been conducted.

Reproductive toxicity

In a study with treatment of cynomolgus monkeys from day 20 of gestation, the incidence of miscarriages was increased in the rozanolixizumab groups compared to the control group (especially between day 20 and 50 of gestation). No effects of rozanolixizumab treatment on fetal development, birth and postnatal development were observed. Offsprings from treated dams had very low levels of

IgG as expected from the pharmacology. IgG level recovered to control values or greater within 60 days. There was no impact on immune function of the pups of treated mothers as assessed by a TDAR assay.

Impairment of fertility

No fertility studies (male or female) were conducted.

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

Other Information

Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products for infusion.

Shelf life

Do not use this medicine after the expiry date marked as “EXP” on the pack.

Special precautions for storage

Store in the refrigerator (2-8°C).

Do not freeze.

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

Keep out of the reach of children.

Authorisation number

69227.

Packs

2 ml solution in vial (Type I glass) with a elastomeric stopper sealed with a crimp seal and flip off cap. Pack size: 1 vial [A].

Marketing authorisation holder

UCB-Pharma AG, Bulle

Date of revision of the text

October 2024

Instructions for handling

Material specificities

The rozanolixizumab solution for injection can be administered using polypropylene syringes as well as infusion sets containing polyethylene (PE), low density polyethylene (LDPE), polyester, polyvinyl chloride (PVC without DEHP), polycarbonate (PC), fluorinated ethylene polypropylene (FEP), urethane/acrylate, polyurethane, meta-acrylonitrile butadiene styrene (MABS), silicone or cyclohexanone. Do not use administration devices labelled as containing di(2-ethylhexyl)phthalate (DEHP).

In order to avoid potential interruptions in delivery of rozanolixizumab, the following criteria should berespected:

- Syringe pump occlusion alarm limits must be set to the maximum setting
- Administration tubing length of 61 cm or shorter is recommended
- An infusion set with a needle of 26 G gauge or with a larger diameter should be used

Before administering rozanolixizumab, the instructions for use must be read carefully.

Rozanolixizumab does not contain preservatives and each vial is for single use only. Therefore, 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.

The following information is intended for healthcare professionals only.

Instructions for use for Healthcare Professionals
Handling Rystiggo By Means of A Device-Assisted Infusion Technique
eg an Infusion Pump

For subcutaneous use only

The number of vials (2 ml per vial) to be used depends on the body weight of the patient. To administer the 280 mg dose to patients weighing ≥ 35 to < 50 kg, 2 ml are necessary. To administer

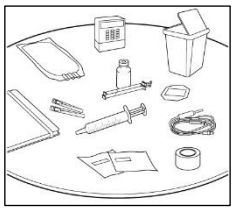
the 420 mg dose to patients weighing ≥ 50 kg to < 70 kg, 3 ml are necessary. To administer the 560 mg dose to patients weighing ≥ 70 to < 100 kg, 4 ml are necessary. To administer the 840 mg dose to patients weighing ≥ 100 kg, 6 ml are necessary.

Read ALL the instructions below before you administer rozanolixizumab solution.

1. Remove Rystiggo from the box:

- Allow vials to reach room temperature. This may take a minimum of 30 minutes up to 120 minutes. Do not use heating devices.
- Check each vial before using:
  - Expiration date: Do not use beyond expiration date.
  - Colour: 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.
  - Cap: Do not use if protective cap of the vial is missing or defective.

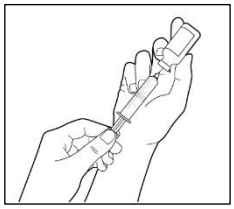
2. Gather all items:



- Collect all items for the infusion. In addition to the vial unit(s), collect the following, which are not supplied: syringe, syringe needle(s), alcohol wipe, infusion set, tape or transparent dressing, infusion pump and sharps container.

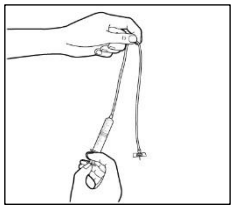
3. Use aseptic technique when preparing and administering this product

4. Prepare Rystiggo for infusion



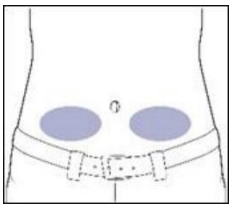
- Use transfer needles to fill the syringe
- Take the protective cap off the vial and clean the vial stopper with an alcohol wipe. Let dry.
- Extract the entire content of the vial into the syringe. A small amount will remain in the vial and should be discarded.
- For multiple vials, use a fresh needle and repeat previous steps.
- Remove the needle from the syringe and attach the infusion set to the syringe.

5. Prepare the infusion



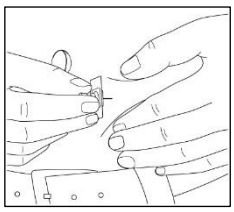
- Follow instructions provided with the infusion pump to prepare the pump, and prime the infusion line. Administer immediately after priming the infusion set.
- Each vial contains excess volume (to allow priming of the infusion line); therefore, pre-set the pump to deliver the prescribed volume. For pumps that cannot be pre-set, after priming the infusion line, adjust the volume to be administered by expelling any excess volume.

6. Prepare the infusion site



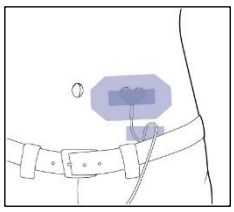
- Choose an infusion area: lower right or lower left part of the abdomen, below the belly button. Never infuse into areas where the skin is tender, bruised, red or hard. Avoid infusing into scars or stretch marks.
- Clean the infusion site using alcohol wipe. Allow to dry.

7. Insert the infusion set needle



- Take an abdominal skinfold between two fingers.
- Insert the infusion set needle into the subcutaneous tissue.

8. Secure the needle to the skin

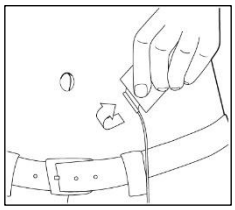


- If necessary, use tape or transparent dressing to hold the needle in place.

9. Start infusion

- Follow the manufacturer's instructions for using the pump.

10. End infusion



- 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.

11. Clean up

- Discard in a sharps container all items with remaining product i.e. partially used vials, infusion set and any administration supplies.