▼ This medicinal product is subject to additional monitoring in Australia. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse events at www.tga.gov.au/reporting-problems.

AUSTRALIAN PRODUCT INFORMATION – SPEVIGO (spesolimab), rch infusion vial

1 NAME OF THE MEDICINE

spesolimab (rch)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 7.5 mL vial of SPEVIGO solution for intravenous infusion contains 450 mg of spesolimab (60 mg/mL).

Excipients with known effect:

Each 450 mg/7.5 mL vial contains 386 mg of sucrose.

For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

SPEVIGO 60 mg/mL solution for intravenous infusion is a colourless to slightly brown-yellow, clear to slightly opalescent solution.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

SPEVIGO is indicated for the treatment of flares in adult patients with generalised pustular psoriasis.

4.2 DOSE AND METHOD OF ADMINISTRATION

Treatment with SPEVIGO should be initiated and supervised by physicians experienced in the management of patients with inflammatory skin diseases.

Dosage

The recommended dose of SPEVIGO is a single dose of 900 mg (2 x 450 mg/7.5 mL vials) administered as an intravenous infusion. If flare symptoms persist, an additional 900 mg dose may be administered 1 week after the initial dose.

Method of Administration

SPEVIGO must be diluted before use (see Instructions for Use / Handling). SPEVIGO is administered as a continuous intravenous infusion through an intravenous line containing a sterile, non-pyrogenic, low protein binding in-line filter (pore size of 0.2 µm) over 90 minutes.

In the event that the infusion is slowed or temporarily stopped, the total infusion time (including stop time) should not exceed 180 minutes (see Section 4.4 Special Warnings and Precautions for Use).

Instructions for Use / Handling

Prior to use, the unopened vial may be kept at room temperature (up to 30°C) for up to 24 hours, if stored in the original package in order to protect from light.

The vial should be visually inspected before use. SPEVIGO is a colourless to slightly brownish-yellow, clear to slightly opalescent solution. If the solution is cloudy, discoloured, or contains large or coloured particulates, the vial should be discarded.

Aseptic technique must be used to prepare the solution for infusion. Draw and discard 15 mL from a 100 mL container of sterile 0.9% sodium chloride solution and replace slowly with 15 mL SPEVIGO

(complete content from two vials of 450 mg/7.5 mL). Mix gently before use. The diluted SPEVIGO infusion solution should be used immediately.

SPEVIGO must not be mixed with other medicinal products. A pre-existing intravenous line may be used for administration of SPEVIGO. The line must be flushed with sterile 0.9% sodium chloride solution prior to and at the end of infusion. No other infusion should be administered in parallel via the same intravenous access.

SPEVIGO does not contain preservatives. SPEVIGO is for single use in one patient only. Discard any residue.

4.3 CONTRAINDICATIONS

Severe or life-threatening hypersensitivity to SPEVIGO or to any of the excipients (see Section 6.1 List of Excipients).

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Traceability

In order to improve traceability of biological medicinal products, the trade name and the batch number of the administered product should be clearly recorded in the patient file.

Infections

SPEVIGO may increase the risk of infections. During the 1-week placebo-controlled period in the Effisayil-1 trial, infections were reported in 17.1% of patients treated with SPEVIGO compared with 5.6% of patients treated with placebo (see Section 4.8 Adverse Effects (Undesirable Effects)).

In patients with a chronic infection or a history of recurrent infection, the potential risks and expected clinical benefits of treatment should be considered prior to prescribing SPEVIGO. Treatment with SPEVIGO should not be initiated in patients with any clinically important active infection until the infection resolves or is adequately treated. Patients should be instructed to seek medical advice if signs or symptoms of clinically important infection occur after treatment with SPEVIGO.

Pre-treatment Evaluation for Tuberculosis

Patients should be evaluated for tuberculosis (TB) infection prior to initiating treatment with SPEVIGO. SPEVIGO should not be administered to patients with active TB infection.

Anti-TB therapy should be considered prior to initiating SPEVIGO in patients with latent TB or a history of TB in whom an adequate course of treatment cannot be confirmed. After SPEVIGO treatment, patients should be monitored for signs and symptoms of active TB.

Hypersensitivity and Infusion-Related Reactions

Hypersensitivity and infusion-related reactions may occur with monoclonal antibodies such as SPEVIGO. Hypersensitivity may include immediate reactions such as anaphylaxis and delayed reactions such as drug reaction with eosinophilia and systemic symptoms (DRESS).

Immediate hypersensitivity reactions, including anaphylactic reactions have been reported in patients treated with SPEVIGO (see Section 4.8 Adverse effects (Undesirable effects).

If a patient develops signs of anaphylaxis or other serious hypersensitivity, SPEVIGO should be discontinued immediately and appropriate treatment should be initiated (see Section 4.3 Contraindications).

If a patient develops mild or moderate infusion-related reaction, SPEVIGO should be stopped and appropriate medical therapy should be considered (e.g. systemic antihistamines and/or corticosteroids). Upon resolution of the reaction, the infusion may be restarted at a slower infusion rate with gradual increase to complete the infusion (see Section 4.2 Dose and Method of Administration).

Two cases of DRESS were reported in Study Effisayil-1 in subjects with generalised pustular psoriasis (GPP) who were treated with spesolimab. The cases reported showed no and a low diagnostic certainty, respectively, and confounding factors were present.

Immunisations

No specific studies have been conducted in patients who have recently received live viral or live bacterial vaccines. The interval between live vaccinations and initiation of SPEVIGO therapy should be at least 4 weeks. Live vaccines should not be administered for at least 16 weeks after treatment with SPEVIGO.

Peripheral Neuropathy

The potential for peripheral neuropathy with SPEVIGO is unknown. Cases of peripheral neuropathy have been reported in clinical trials with spesolimab.

Among approximately 750 subjects exposed to spesolimab during clinical development, cases were reported as Guillain-Barre Syndrome (GBS) in 3 subjects who received different doses of spesolimab via various methods of administration in clinical trials for unapproved indications. Based on the Brighton criteria for GBS definition, one case met level 4 (i.e. reported event of GBS, with insufficient evidence to meet the case definition); the other two cases did not meet the criteria.

Physicians should be vigilant for symptoms potentially indicative of new-onset peripheral neuropathy.

Excipients

This medicinal product contains less than 1 mmol sodium (23 mg) per 900 mg dose, that is to say essentially ‘sodium free’.

Use in Patients with Renal and/or Hepatic Impairment

SPEVIGO has not been studied in these patient populations. These conditions are generally not expected to have any clinically relevant impact on the pharmacokinetics of monoclonal antibodies and no dose adjustments are considered necessary.

Use in the Elderly

No dose adjustment is required. There is limited information in patients aged 65 years and older.

Paediatric Use

The safety and efficacy of SPEVIGO in children below the age of 18 years have not been established. No data is available.

Effects on laboratory tests

The effects of SPEVIGO on laboratory tests have not been established. No data is available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

No interaction studies have been performed. Live vaccines should not be given concurrently with SPEVIGO (see Section 4.4 Special Warnings and Precautions for Use).

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on Fertility

There are no data available on the effect of spesolimab on human fertility. Pre-clinical studies in mice using a surrogate, mouse specific anti-IL36R monoclonal antibody did not indicate direct or indirect harmful effects with respect to fertility on either sex from antagonism of IL36R.

Use in Pregnancy (Category B1)

There are limited data from the use of spesolimab in pregnant women. Human IgG is known to cross the placental barrier; therefore, spesolimab may be transmitted from the mother to the developing fetus. Pre-clinical studies using a surrogate, mouse specific anti-IL-36R monoclonal antibody do not indicate direct or indirect harmful embryofetal development effects. As a precautionary measure, it is recommended to avoid the use of SPEVIGO in pregnancy, unless the expected clinical benefit clearly outweighs the potential risks.

Use in Lactation

It is unknown whether spesolimab is excreted in human milk. There are no data on the effects on the breastfed infant, or the effects on milk production. Spesolimab is a monoclonal antibody and is

expected to be present in human milk. A risk to newborns/infants cannot be excluded. A decision must be made whether to discontinue breast-feeding or to abstain from SPEVIGO therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

SPEVIGO has no or negligible influence on the ability to drive and use machines.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

Summary of the safety profile

Adverse events occurring in at least 10% of patients in either treatment arm in the Effisayil-1 trial up to 1 week are summarised in Table 1.

Table 1 Adverse Events reported for more than 10% of patients in either treatment group on Placebo or SPEVIGO 900 mg i.v. in Effisayil-1 trial up to 1 week.

System Organ Class Preferred Term	**Up to Week 1**	
	Placebo N (%)	**SPEVIGO 900 mg i.v. N (%)**
Number of patients	18 (100.0)	35 (100.0)
Patients with any AE	12 (66.7)	27 (77.1)
Infections and infestations	1 (5.6)	6 (17.1)
Blood and lymphatic system disorders	2 (11.1)	1 (2.9)
Metabolism and nutrition disorders	2 (11.1)	3 (8.6)
Nervous system disorders	3 (16.7)	4 (11.4)
Dizziness	2 (11.1)	0
Skin and subcutaneous tissue disorders	9 (50.0)	18 (51.4)
Pustular psoriasis	7 (38.9)	13 (37.1)
Musculoskeletal and connective tissue disorders	2 (11.1)	4 (11.4)
General disorders and administration site conditions	5 (27.8)	9 (25.7)
Pyrexia	4 (22.2)	2 (5.7)
Investigations	2 (11.1)	4 (11.4)

Percentages are calculated using total number of patients in the treatment class as the denominator. MedDRA version used for reporting: 23.1. End of time at risk: min of (Day 7, the day of EoS). All AEs starting up to the end of time at risk are included.

The safety data provided in Table 2 are based on Effisayil-1, a double-blind, randomised trial comparing a single intravenous 900 mg dose of SPEVIGO (n = 35) with placebo (n = 18) in patients with generalised pustular psoriasis for up to 12 weeks after treatment and four double-blind, placebo-controlled trials of 254 spesolimab-treated patients who received doses up to 1200 mg intravenous or subcutaneous spesolimab for other diseases, as well as open-label extension trials, and post-marketing experience.

The most frequent adverse reaction associated with SPEVIGO are infections.

Tabulated summary of adverse reactions

The adverse reactions are listed by absolute frequency. Frequencies are defined as very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), or very rare (<1/10,000), and not known (cannot be estimated from the available data).

Table 2 Summary of Adverse Reactions

MedDRA System Organ Class Terminology	SPEVIGO Adverse Reactions	Frequency
Infections and Infestations	Urinary tract infection Upper respiratory tract infection	Common Very Common
Immune system disorders	Hypersensitivity[a]	Not known
Skin and Subcutaneous Tissue Disorders	Pruritus	Common
General Disorders and Administration Site Conditions	Injection site reactions Fatigue	Very common* Common

[a] derived from open label extension trials and post-marketing experience

*Not reported in Effisayil-1

Infections

During the 1-week placebo-controlled period in Effisayil-1, infections were reported in 17.1% of patients treated with SPEVIGO compared with 5.6% of patients treated with placebo. Serious infection (urinary tract infection) was reported in 1 patient (2.9%) in the SPEVIGO group and no patients in the placebo group. Infections observed in clinical trials with spesolimab were generally mild to moderate with no distinct pattern regarding pathogen or type of infection.

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)

Two cases of DRESS were reported in Effisayil-1 in subjects with GPP who were treated with SPEVIGO. RegiSCAR DRESS validation scoring (with the following categories: "no", “possible”, “probable” and “possible DRESS”) was applied to the reported cases. Reported cases were assessed as “no DRESS” and “possible DRESS”. Therefore, the causality assessment with spesolimab has not been established.

Hypersensitivity

Hypersensitivity comprises immediate systemic hypersensitivity reactions, including anaphylactic reaction. Immediate systemic hypersensitivity reactions have been reported in open-label extension trials and the post-marketing setting.

Injection site reactions

Injection site reactions include injection site erythema, injection site swelling, injection site pain, injection site induration, and injection site warmth. Injection site reactions were typically mild-to-moderate in severity.

4.9 OVERDOSE

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

There is no clinical experience with overdoses of SPEVIGO. The highest dose of SPEVIGO administered in clinical trials was 1200 mg. Adverse events observed in subjects receiving single or repeated doses up to 1200 mg were consistent with the known safety profile of SPEVIGO.

In the event of overdose, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions and symptomatic treatment be instituted as appropriate.

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: Immunosuppressants, Interleukin Inhibitors; ATC code: L04AC22.

Mechanism of action

Spesolimab is a humanised antagonistic monoclonal immunoglobulin G1 (IgG1) antibody blocking human IL36R signalling. Binding of spesolimab to IL36R prevents the subsequent activation of IL36R by cognate ligands (IL36 α, β and γ) and downstream activation of pro-inflammatory and pro-fibrotic pathways. IL36R signalling is differentiated from TNF-α, integrin and IL-23 inhibitory pathways by directly and simultaneously blocking both inflammatory and pro-fibrotic pathways. Genetic human studies have established a strong link between IL36R signalling and skin inflammation.

Following treatment with SPEVIGO in patients with GPP, reduced levels of C-reactive protein (CRP), interleukin (IL)-6, T helper cell (Th1/Th17) mediated cytokines, keratinocyte-mediated inflammation, neutrophilic mediators, and proinflammatory cytokines were observed in serum and skin at week 1 compared to baseline and was associated with a decrease in clinical severity. These reductions in biomarkers became more pronounced at the last measurement at week 8 in Effisayil-1.

Clinical Trials

A randomised, double-blind, placebo-controlled study (Effisayil-1) was conducted to evaluate the clinical efficacy and safety of SPEVIGO in adult patients with flares of Generalised Pustular Psoriasis (GPP), as diagnosed per European Rare And Severe Psoriasis Expert Network (ERASPEN) criteria, regardless of IL36RN mutation status. Patients were randomised if they had a flare of GPP of moderate-to-severe intensity, as defined by a Generalised Pustular Psoriasis Physician Global Assessment (GPPGA) total score (which ranges from 0 [clear] to 4 [severe]) of at least 3 (moderate), presence of fresh pustules (new appearance or worsening of pustules), GPPGA pustulation sub score of at least 2 (mild), and at least 5% of body surface area (BSA) covered with erythema and the presence pustules. Patients were required to discontinue systemic and topical therapy for GPP prior to receiving study drug.

The primary endpoint of the study was the proportion of patients with a GPPGA pustulation sub score of 0 (indicating no visible pustules) at Week 1 after treatment. The key secondary endpoint of the study was the proportion of patients with GPPGA total score of 0 or 1 (clear or almost clear skin) at Week 1. Additional secondary endpoints at Week 4 were the proportion of patients with a 75% reduction in the Psoriasis Area and Severity Index for Generalised Pustular Psoriasis (GPPASI 75), and patient-reported outcomes including change from baseline in Pain Visual Analog Scale (VAS) score, change from baseline in Psoriasis Symptom Scale (PSS) score, and change from baseline in Functional Assessment of Chronic Illness Therapy (FACIT) Fatigue score.

A total of 53 patients were randomised (2:1) to receive a single intravenous dose of 900 mg SPEVIGO (n = 35) or placebo (n = 18). Patients in either treatment arm who still experienced flare symptoms at Week 1 were eligible to receive a single intravenous dose of open-label 900 mg SPEVIGO, resulting in 12 patients (34%) in the SPEVIGO arm receiving a second dose of SPEVIGO and 15 patients (83%) in the placebo arm receiving one dose of SPEVIGO on Day 8. In addition, 6 patients (4 SPEVIGO arm; 2 placebo arm) received rescue treatment with a single 900 mg dose of intravenous SPEVIGO for reoccurrence of a flare after Day 8.

The study population consisted of 32% men and 68% women. The mean age was 43 (range: 21 to 69) years; 55% of patients were Asian and 45% were Caucasian. Most patients included in the study had a GPPGA pustulation sub score of 3 (43%) or 4 (36%), and patients had a GPPGA total score of 3 (81%) or 4 (19%). 24.5% of patients had been previously treated with biologic therapy for GPP.

At Week 1, there was a statistically significant difference in the proportion of patients achieving a GPPGA pustulation sub score of 0 (indicating no visible pustules) and GPPGA total score of 0 or 1 (clear or almost clear skin) in the SPEVIGO arm compared with placebo (see Table 3).

Table 3. GPPGA Pustulation Sub Score and GPPGA Total Score at Week 1

	Placebo	SPEVIGO 900 mg i.v.
Number of Patients Analysed	18	35
Patients Achieving a GPPGA Pustulation Sub Score of 0, n (%)	1 (5.6)	19 (54.3)
Risk Difference Versus Placebo, % (95% CI)	48.7 (21.5, 67.2)	
p-value*	0.0004	
Patients Achieving a GPPGA Total Score of 0 or 1, n (%)	2 (11.1)	15 (42.9)
Risk Difference Versus Placebo, % (95%, CI)	31.7 (2.2, 52.7)	
p-value*	0.0118	

GPPGA = Generalised Pustular Psoriasis Physician Global Assessment; i.v. = intravenous

*One-sided p-value

In patients randomised to SPEVIGO, pustular clearance (GPPGA pustulation sub score of 0) was achieved as early as one day after treatment in 11.4% (4/35) of patients. The effect of up to two doses of SPEVIGO on GPPGA pustulation sub score and GPPGA total score was sustained until Week 12.

Of the 12 patients from the SPEVIGO group who received a second dose of SPEVIGO on Day 8, 41.7% (5 patients) achieved pustular clearance and 16.7% (2 patients) achieved a GPPGA total score of 0 or 1 at Week 2, i.e. 1 week after the second dose administration.

Of the 23 patients who received a single dose of SPEVIGO on Day 1, 82.6% (19 patients) achieved pustular clearance and 65.2% (15 patients) achieved a GPPGA total score of 0 or 1 at Week 2. By Week 12, the proportion of patients with pustular clearance and GPPGA total score of 0 or 1 remains at 65.2% (15 patients) and 60.9% (14 patients), respectively.

For both primary and key secondary endpoints, treatment effect was observed for all patients regardless of the IL-36 mutation status. This study did not include sufficient numbers of subjects to determine if there are differences in response according to biological sex, age, race, baseline GPPGA pustulation sub score, and baseline GPPGA total score.

Immunogenicity

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

In patients with GPP treated with spesolimab in Effisayil-1, anti-drug antibodies (ADA) formed with a median onset of 2.3 weeks. Following administration of intravenous spesolimab 900 mg, 24% of patients had a maximum ADA titer greater than 4000 and were Neutralising antibody (Nab)-positive by end of the trial (Weeks 12 to 17).

Females appeared to have higher immunogenicity response; the percentage of patients with ADA titer greater than 4000 was 30% in females, and 12% in males, respectively.

In some patients with ADA titer values greater than 4000, plasma spesolimab concentrations were reduced, with no apparent impact on pharmacokinetics at ADA titers below 4000. In the presence of ADA, efficacy was observed upon re-treatment of recurring flares with SPEVIGO in an open label extension trial. There was no apparent correlation between the presence of ADA to spesolimab and hypersensitivity reactions.

5.2 PHARMACOKINETIC PROPERTIES

A population pharmacokinetic model was developed based on data collected from healthy subjects, patients with GPP and patients with other diseases. After a single intravenous dose of 900 mg, the population pharmacokinetic model-estimated $AUC_{0-\infty}$ (95% CI) and C_{max} (95% CI) in a typical ADA-negative patient with GPP were 4750 (4510, 4970) µg·day/mL and 238 (218, 256) µg/mL, respectively.

Distribution

Based on the population pharmacokinetic analysis, the typical volume of distribution at steady state was 6.4 L.

Metabolism

The metabolic pathway of spesolimab has not been characterised. As a humanised IgG1 monoclonal antibody, spesolimab is expected to be degraded into small peptides and amino acids via catabolic pathways in a manner similar to endogenous IgG.

Excretion

In the linear dose range (0.3-20 mg/kg), based on the population pharmacokinetic model, spesolimab clearance (95% CI) in a typical GPP patient without ADA, weighing 70 kg was 0.184 (0.175, 0.194) L/day. The terminal-half-life was 25.5 (24.4, 26.3) days.

Linearity/non-linearity

At low doses, spesolimab exhibited target-mediated drug disposition (TMDD) kinetics after single intravenous dose administration. At doses from 0.01 to 0.3 mg/kg, both clearance (CL) and terminal half-life were dose dependent, and systemic exposure (AUC) increased more than dose proportionally with dose. The saturation of the nonlinear elimination pathway occurred at about 0.3 mg/kg as spesolimab AUC increased approximately linearly with dose from 0.3 to 20 mg/kg, and CL and terminal half-life were independent of dose.

Pharmacokinetics in specific populations

Elderly/Gender/Race

Based on population pharmacokinetic analyses, age, gender and race do not have an effect on the pharmacokinetics of spesolimab.

Hepatic and Renal Impairment

As a monoclonal antibody, spesolimab is not expected to undergo hepatic or renal elimination. No formal trial of the effect of hepatic or renal impairment on the pharmacokinetics of spesolimab was conducted.

Population pharmacokinetic analysis did not identify mild hepatic impairment or mild or moderate renal impairment as having an influence on the systemic exposure of spesolimab.

Body Weight

Spesolimab concentrations were lower in subjects with higher body weight. The impact of body weight on spesolimab plasma concentrations is not expected to be clinically meaningful.

Paediatric Population

The pharmacokinetics of spesolimab in paediatric patients has not yet been studied.

Drug-Drug Interactions (Studies)

No formal drug interaction studies have been conducted with spesolimab. Population pharmacokinetic analyses indicated that concomitant use of immunosuppressants or oral corticosteroids did not have a direct impact on the pharmacokinetics of spesolimab.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

Genotoxicity studies have not been conducted with spesolimab.

Carcinogenicity

Carcinogenicity studies have not been conducted with spesolimab. A carcinogenicity risk assessment based on scientific literature revealed no carcinogenic potential in IL36 receptor deficient mice.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

SPEVIGO also contains glacial acetic acid, polysorbate 20, sodium acetate trihydrate, sucrose, arginine hydrochloride and water for injections.

6.2 INCOMPATIBILITIES

No incompatibilities have been observed between SPEVIGO and infusion sets composed of polyvinylchloride (PVC), polyethylene (PE), polypropylene (PP), polybutadiene and polyurethane (PUR), and in-line filter membranes composed of polyethersulfone (PES, neutral and positively charged) and positively charged polyamide (PA).

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store at 2 to 8 degrees Celsius (2-8°C). Do not freeze. Protect from light.

Chemical and physical in-use stability of the diluted solution has been demonstrated for 21 hours at 2-8°C followed by up to 6 hours at ≤ 30°C including 3 hours infusion time.

To reduce microbiological hazard, use as soon as practicable after dilution. If storage of the diluted solution is necessary, it should be held at 2-8°C for not more than 24 hours and is the responsibility of the user. For the time between preparation and start of administration the solution for infusion should be protected from light following local standard procedures.

6.5 NATURE AND CONTENTS OF CONTAINER

SPEVIGO 60 mg/mL solution for infusion is presented as a nominal 7.5 mL fill volume in a 10 mL clear glass vial, closed with a rubber stopper and secured with a dark blue crimp cap.

SPEVIGO is supplied in packs of 2 vials.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 PHYSICOCHEMICAL PROPERTIES

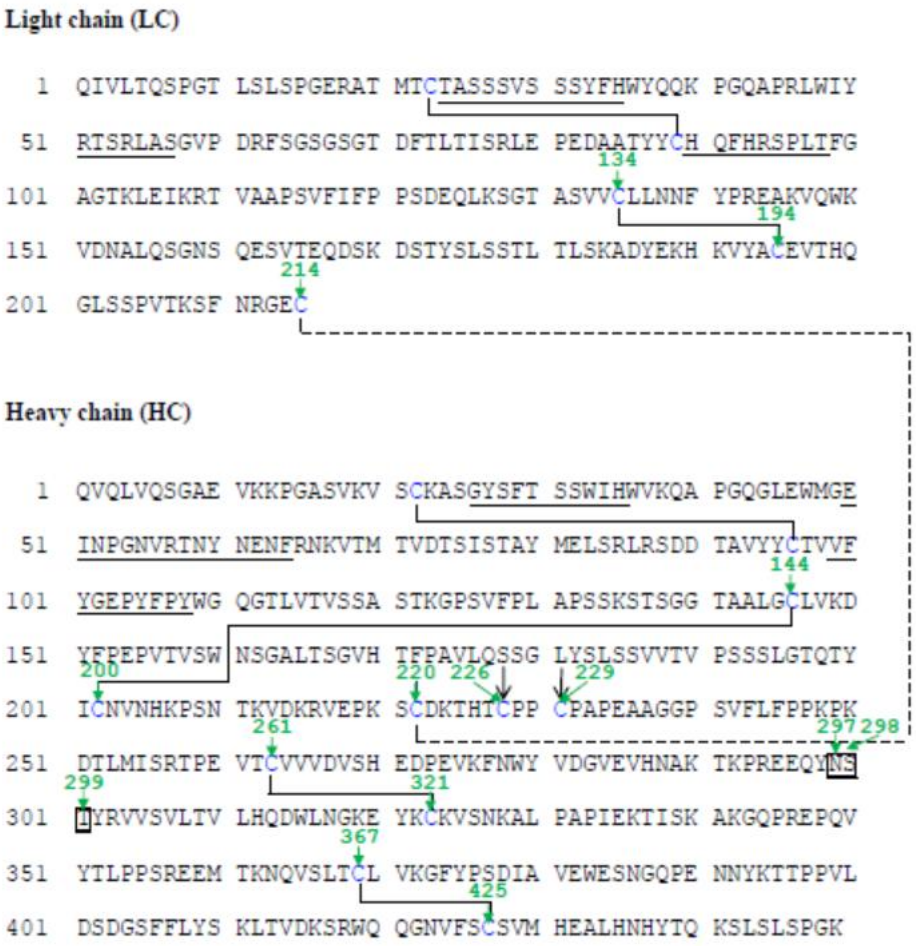
Spesolimab is an (Fc)-engineered humanised antibody of the IgG1 isotype that is directed against human IL-36 receptor (IL36R). Spesolimab drug substance is a colourless to slightly brownish-yellow, clear to slightly opalescent solution. The final formulated spesolimab drug substance has a pH of 5.5 and an osmolality of 125 – 165 mOsm/kg.

Chemical structure

Molecular formula: $C_{6480}H_{9988}N_{1736}O_{2012}S_{46}$

Molecular mass: 146 kDa

Structural formula: Spesolimab is composed of two heterodimers. Each of the heterodimers is composed of a heavy and a light polypeptide chain. Each heavy chain is composed of 449 amino acids and each light chain contains 215 amino acids. The four polypeptide chains of the antibody molecule are covalently linked together by disulfide bonds between Cys222 of the heavy chain and Cys 215 of the light chain. The two heavy chains are connected within the hinge region by two inter-chain disulfide bonds Cys228 – Cys228 and Cys231 – Cys 231.



CAS number

2097104-58-8

7 MEDICINE SCHEDULE (POISONS STANDARD)

S4 – Prescription Only Medicine

8 SPONSOR

Boehringer Ingelheim Pty Limited
ABN 52 000 452 308
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North Ryde NSW 2113
www.boehringer-ingelheim.com.au

9 DATE OF FIRST APPROVAL

24 November 2023

10 DATE OF REVISION

19 March 2025

SUMMARY TABLE OF CHANGES

Section Changed	Summary of New Information
4.4	Update to ‘Hypersensitivity and infusion-related reactions’ warning statement
4.8	Addition of ‘hypersensitivity’ as new adverse reaction and associated statement Update to reported frequencies for ‘Upper respiratory tract infection’ and ‘Injection site reactions’