

## New Zealand Data Sheet

### WARNING: SERIOUS MENINGOCOCCAL INFECTION

SOLIRIS<sup>®</sup> increases the risk of meningococcal infections

- Vaccinate patients with a meningococcal vaccine at least 2 weeks prior to receiving the first dose of SOLIRIS<sup>®</sup>; revaccinate according to current medical guidelines for vaccine use.
- Monitor patients for early signs of meningococcal infections, evaluate immediately if infection is suspected, and treat with antibiotics if necessary.

### SOLIRIS<sup>®</sup>

Eculizumab 'rnc', concentrated solution for intravenous infusion (CAS registry number: 219685-50-4).

### DESCRIPTION

SOLIRIS<sup>®</sup> (eculizumab 'rnc') is a genetically-engineered humanized monoclonal antibody directed against the  $\alpha$ -chain of the C5 complement protein. The antibody is a glycosylated hybrid IgG2-IgG4 kappa immunoglobulin containing human light- and heavy-chain variable region framework sequences, murine complementarity-determining region sequences, and human constant region sequences. Eculizumab 'rnc' is composed of two identical 448 amino acid heavy chains and two identical 214 amino acid light chains, and has a molecular weight of approximately 148 kDa.

The eculizumab 'rnc' antibody is produced by murine myeloma cell culture and purified by standard bioprocess chromatographic technology, including specific viral inactivation and filtration steps.

SOLIRIS<sup>®</sup> is a sterile, clear, colourless, preservative-free 10 mg/mL solution for intravenous infusion, and is supplied in 30 mL (300 mg) single-use vials. The product is formulated at pH 7, and each vial contains 300 mg of eculizumab 'rnc', 13.8 mg monobasic sodium phosphate monohydrate, 53.4 mg dibasic sodium phosphate heptahydrate, 263.1 mg sodium chloride, 6.6 mg polysorbate 80 (vegetable origin) and Water for Injection.

### PHARMACOLOGY

#### Mechanism of Action

A genetic mutation in patients with Paroxysmal Nocturnal Haemoglobinuria (PNH) leads to the generation of populations of abnormal red blood cells (known as PNH RBCs) that are deficient in terminal complement inhibitors, rendering PNH RBCs sensitive to persistent terminal complement-mediated destruction. The subsequent intravascular haemolysis is the primary disease manifestation in PNH patients. The destruction and loss of these PNH cells result in low blood counts (anaemia), and also fatigue, difficulty in functioning, pain, dark urine and kidney disease, shortness of breath, and blood clots.

Eculizumab 'rnc', the active ingredient in SOLIRIS<sup>®</sup>, is a terminal complement inhibitor that specifically binds to the complement protein C5 with high affinity, thereby inhibiting its cleavage to C5a and C5b and preventing the generation of the terminal complement complex

C5b-9. SOLIRIS<sup>®</sup> therefore restores terminal complement regulation in the blood of PNH patients and inhibits terminal complement mediated intravascular haemolysis in PNH patients. Eculizumab ‘rnc’ preserves the early components of complement activation that are essential for opsonisation of microorganisms and clearance of immune complexes.

*In Vitro* Binding Specificity: The specificity of SOLIRIS<sup>®</sup> for C5 in human serum was evaluated in two *in vitro* studies. The species specificity of SOLIRIS<sup>®</sup> was assessed by determining its ability to inhibit haemolytic activity in non-human sera (4 primate and 4 non-primate species) using a complement-mediated haemolytic assay. The results of this study demonstrate that SOLIRIS<sup>®</sup> does not inhibit C5 activity in sera from the species tested. The tissue cross-reactivity of SOLIRIS<sup>®</sup> was evaluated by assessing binding to a panel of 38 human tissues. C5 expression in the human tissue panel examined in this study is consistent with published reports of C5 expression, as C5 has been reported in smooth muscle, striated muscle, and renal proximal tubular epithelium. No unexpected tissue cross-reactivity was observed.

### **Pharmacodynamics**

The pharmacodynamic profile of SOLIRIS<sup>®</sup> was assessed using an *in vitro* serum complement haemolysis assay that measures the extent of terminal complement inhibition in the serum of patients receiving SOLIRIS<sup>®</sup>. Administration of SOLIRIS<sup>®</sup> results in a rapid and sustained reduction in terminal complement activity. Eculizumab ‘rnc’ serum concentrations of approximately  $\geq 35 \mu\text{g/mL}$  are sufficient for essentially complete inhibition of terminal complement-mediated intravascular haemolysis in PNH patients.

Administration of SOLIRIS<sup>®</sup> in an initial phase/maintenance regimen of 600 mg/week for the first 4 weeks and 900 mg in the fifth week of the initial phase, followed by a 900 mg maintenance dose every other week resulted in a rapid and sustained reduction in complement-mediated haemolytic activity. SOLIRIS<sup>®</sup> when administered as recommended provides a blood concentration sufficient to completely block haemolysis within 60 minutes; red blood cell destruction, as indicated by lactate dehydrogenase (LDH) levels, is significantly reduced by one week. In the Phase 3 study in PNH patients, C04-001, the dosing regimen was sufficient to maintain plasma SOLIRIS<sup>®</sup> levels to essentially completely block terminal complement activation in 39/40 patients measured for the entire 26 week study period demonstrating that the proposed dosing regimen is adequate.

### **Pharmacokinetics**

The pharmacokinetics (PK) of SOLIRIS<sup>®</sup> were studied in patients with PNH using total serum concentrations (free and bound drug). A population PK analysis with standard 1-compartmental model was conducted on the multiple dose PK data from 40 patients receiving the recommended SOLIRIS<sup>®</sup> regimen. In this model, the clearance of SOLIRIS<sup>®</sup> for a typical PNH patient weighing 70 kg was 22 mL/hr and the volume of distribution was 7.7 L. The half-life was  $272 \pm 82$  hours (mean  $\pm$  SD). The mean observed peak and trough serum concentrations of SOLIRIS<sup>®</sup> by week 26 were  $194 \pm 76 \mu\text{g/mL}$  and  $97 \pm 60 \mu\text{g/mL}$ , respectively.

Pharmacodynamic activity correlates directly with eculizumab ‘rnc’ serum concentrations and maintenance of trough levels above  $\geq 35 \mu\text{g/mL}$  results in essentially complete blockade of haemolytic activity in the majority of patients.

Studies have not been conducted to evaluate the PK of SOLIRIS<sup>®</sup> in special patient populations identified by gender, race, age (paediatric or geriatric), or the presence of renal or hepatic impairment.

## CLINICAL TRIALS

The safety and efficacy of SOLIRIS<sup>®</sup> in PNH patients with haemolysis were assessed in a randomised, double-blind, placebo-controlled 26-week study (C04-001); PNH patients were also treated with SOLIRIS<sup>®</sup> in a single arm 52-week study (C04-002); and in a long-term extension study (E05-001). Patients received meningococcal vaccination prior to receipt of SOLIRIS<sup>®</sup>. In all studies, the dose of SOLIRIS<sup>®</sup> was 600 mg study drug every  $7 \pm 2$  days for 4 weeks, followed by 900 mg  $7 \pm 2$  days later, then 900 mg every  $14 \pm 2$  days for the study duration. SOLIRIS<sup>®</sup> was administered as an intravenous infusion over 25 - 45 minutes.

### C04-001 Study

PNH patients with at least four transfusions in the prior 12 months, flow cytometric confirmation of at least 10% PNH cells and platelet counts of at least 100,000/microlitre were randomised to either SOLIRIS<sup>®</sup> (n = 43) or placebo (n = 44). Prior to randomisation, all patients underwent an initial observation period to confirm the need for RBC transfusion and to identify the haemoglobin concentration (the "set-point") which would define each patient's haemoglobin stabilisation and transfusion outcomes. The haemoglobin set-point was less than or equal to 9 g/dL in patients with symptoms and was less than or equal to 7 g/dL in patients without symptoms. Endpoints related to haemolysis included the numbers of patients achieving haemoglobin stabilisation, the number of RBC units transfused, fatigue, and health-related quality of life. To achieve a designation of haemoglobin stabilisation, a patient had to maintain a haemoglobin concentration above the haemoglobin set-point and avoid any RBC transfusion for the entire 26-week period. Haemolysis was monitored mainly by the measurement of serum LDH levels, and the proportion of PNH RBCs was monitored by flow cytometry. Patients receiving anticoagulants and systemic corticosteroids at baseline continued these medications. Major baseline characteristics were balanced (see Table 1). Because of the study sample size and duration, the effects of SOLIRIS<sup>®</sup> on thrombotic events could not be determined.

**Table 1: Patient Demographics and Characteristics in C04-001 and C04-002 Studies**

Parameter	C04-001 Study		C04-002 Study
	Placebo N = 44	SOLIRIS <sup>®</sup> N = 43	SOLIRIS <sup>®</sup> N = 97
Mean Age (SD)	38.4 (13.4)	42.1 (15.5)	41.1 (14.4)
Gender - Female (%)	29 (65.9)	23 (53.5)	49 (50.5)
History of Aplastic Anaemia or MDS (%)	12 (27.3)	8 (18.7)	29 (29.9)
Patients with history of thrombosis (events)	8 (11)	9 (16)	42 (91)
Concomitant Anticoagulants (%)	20 (45.5)	24 (55.8)	59 (61)
Concomitant Steroids/Immunosuppressant Treatments (%)	16 (36.4)	14 (32.6)	46 (47.4)
Discontinued treatment	10	2	1
PRBC in previous 12 months [median (Q1,Q3)]	17.0 (13.5, 25.0)	18.0 (12.0, 24.0)	8.0 (4.0, 24.0)
Mean Hgb level (g/dL) at set-point (SD)	7.7 (0.75)	7.8 (0.79)	N/A
Pre-treatment LDH levels (median, U/L)	2,234.5	2,032.0	2,051.0
Free Haemoglobin at baseline (median, mg/dL)	46.2	40.5	34.9

Patients treated with SOLIRIS<sup>®</sup> had significantly reduced ( $p < 0.001$ ) haemolysis resulting in improvements in anaemia as indicated by increased haemoglobin stabilisation and reduced need for RBC transfusions compared to placebo treated patients (see Table 2). These effects were seen among patients within each of the three pre-study RBC transfusion strata (4 - 14 units; 15 - 25 units; > 25 units). After 3 weeks of SOLIRIS<sup>®</sup> treatment, patients reported less fatigue and improved health-related quality of life.

**Table 2: Efficacy Outcomes in C04-001 and C04-002**

	C04-001 Study			C04-002 Study	
	Placebo N = 44	SOLIRIS <sup>®</sup> N = 43	P - Value	SOLIRIS <sup>®</sup> N = 97	P Value
Percentage of patients with stabilised Haemoglobin levels at end of study	0	49	< 0.001	N/A	
PRBC transfused during treatment (median)	10	0	< 0.001	0.0	< 0.001
Transfusion Avoidance during treatment (%)	0	51	< 0.001	51 <sup>1</sup>	< 0.001
				51 <sup>2</sup>	< 0.001
LDH levels at end of study (median, U/L)	2,167	239	< 0.001	269	< 0.001
LDH AUC at end of study (median, U/L x Day)	411,822	58,587	< 0.001	-632,264	< 0.001
Free Haemoglobin at end of study (median, mg/dL)	62	5	< 0.001	5	< 0.001
FACIT-Fatigue (effect size) after 6 months treatment	1.13		<0.001	1.01 <sup>1</sup>	< 0.001
FACIT-Fatigue (effect size) after 12 months treatment	N/A			1.14 <sup>2</sup>	< 0.001

<sup>1</sup>Assessed after 26-week treatment in C04-002. <sup>2</sup>Assessed at C04-002 study completion (52 weeks).

#### C04-002 Study

PNH patients with at least one transfusion in the prior 24 months and at least 30,000 platelets/microlitre received SOLIRIS<sup>®</sup> over a 52-week period. Concomitant medications included anti-thrombotic agents in 63% of the patients and systemic corticosteroids in 40% of the patients. Baseline characteristics are shown in Table 2. Overall, 96 of the 97 enrolled patients completed the study (one patient died following a thrombotic event). A reduction in intravascular haemolysis as measured by serum LDH levels was sustained for the treatment period and resulted in increased transfusion avoidance, a reduced need for RBC transfusion and less fatigue. See Table 2.

#### E05-001 Study

From the 195 patients that originated in C04-001, C04-002, or C02-001, 187 SOLIRIS-treated PNH patients were enrolled in a long-term extension study (E05-001). All patients sustained a reduction in intravascular haemolysis over a total SOLIRIS<sup>®</sup> exposure time ranging from 10 to 54 months. Across all enrolled PNH patients, the thrombosis rate was significantly reduced with SOLIRIS<sup>®</sup> treatment as compared to the thrombosis rate prior to commencement of SOLIRIS<sup>®</sup> treatment. However, the majority of patients received concomitant anticoagulants; the effects of anticoagulant withdrawal during SOLIRIS<sup>®</sup> therapy were not studied. See Table 3.

**Table 3: Thromboembolic Event Efficacy Outcomes**

	<b>E05-001 (All studies combined)</b>
Pre-Treatment	
Patients (n)	195
Thromboembolic Events (n)	124
Patient Years (n)	1683.4
Thromboembolic Event Rate (n per 100 patient years)	7.37
SOLIRIS <sup>®</sup> Treatment	
Patients (n)	195
Thromboembolic Events (n)	3
Patient Years (n)	281.0
Thromboembolic Event Rate (n per 100 patient years)	1.07 (P<0.001)

**INDICATIONS**

SOLIRIS<sup>®</sup> is indicated for the treatment of patients with paroxysmal nocturnal haemoglobinuria (PNH) to reduce haemolysis.

**CONTRAINDICATIONS**

Do not initiate SOLIRIS<sup>®</sup> therapy in patients:

- with unresolved serious *Neisseria meningitidis* infection.
- who are not currently vaccinated against *Neisseria meningitidis*.

**PRECAUTIONS****Serious Meningococcal Infections**

The use of SOLIRIS<sup>®</sup> increases a patient's susceptibility to serious meningococcal infections (septicaemia and/or meningitis). All patients without a history of prior meningococcal vaccination must receive the meningococcal vaccine at least 2 weeks prior to receiving the first dose of SOLIRIS<sup>®</sup> and revaccinated according to current medical guidelines for vaccine use. Quadravalent, conjugated meningococcal vaccines are strongly recommended. Vaccination may not prevent meningococcal infections.

All patients must be monitored for early signs and symptoms of meningococcal infections and evaluated immediately if an infection is suspected. Physicians should strongly consider discontinuation of SOLIRIS<sup>®</sup> during the treatment of serious meningococcal infections.

In clinical studies, 2 out of 196 PNH patients developed serious meningococcal infections while receiving treatment with SOLIRIS<sup>®</sup>; all were vaccinated prior to receiving SOLIRIS<sup>®</sup> therapy. [see *Adverse Reactions*].

**Other Infections**

SOLIRIS<sup>®</sup> blocks terminal complement; therefore patients may have increased susceptibility to infections, especially with encapsulated bacteria. Use caution when administering SOLIRIS<sup>®</sup> to patients with any systemic infection.

### **Monitoring After SOLIRIS<sup>®</sup> Discontinuation**

Since SOLIRIS<sup>®</sup> therapy increases the number of PNH cells [in study 1, the proportion of PNH RBCs increased among SOLIRIS<sup>®</sup>-treated patients by a median of 28% from baseline (range from -25% to 69%)], patients who discontinue treatment with SOLIRIS<sup>®</sup> may be at increased risk for serious haemolysis. Serious haemolysis is identified by serum LDH levels greater than the pre-treatment level, along with any of the following: greater than 25% absolute decrease in PNH clone size (in the absence of dilution due to transfusion) in one week or less; a haemoglobin level of <5 gm/dL or a decrease of >4 gm/dL in one week or less; angina; change in mental status; a 50% increase in serum creatinine level; or thrombosis. Monitor any patient who discontinues SOLIRIS<sup>®</sup> for at least 8 weeks to detect serious haemolysis and other reactions.

If serious haemolysis occurs after SOLIRIS<sup>®</sup> discontinuation, consider the following procedures/treatments: blood transfusion (packed RBCs), or exchange transfusion if the PNH RBCs are >50% of the total RBCs by flow cytometry; anticoagulation; corticosteroids; or reinstitution of SOLIRIS<sup>®</sup>.

In clinical studies, 16 of 196 PNH patients discontinued treatment with SOLIRIS<sup>®</sup>. Patients were followed for evidence of worsening haemolysis and no serious haemolysis was observed.

### **Thrombosis Prevention and Management**

The effect of withdrawal of anticoagulant therapy during SOLIRIS<sup>®</sup> treatment has not been established. Therefore, treatment with SOLIRIS<sup>®</sup> should not alter anticoagulant management.

### **Laboratory Monitoring**

Serum LDH levels increase during haemolysis and may assist in monitoring SOLIRIS<sup>®</sup> effects. In addition to measuring serum LDH levels, PNH patients should be monitored for signs and symptoms of intravascular haemolysis. PNH patients may require dose adjustment within the recommended 14+/-2 day dosing schedule during the maintenance phase (up to every 12 days). In clinical studies, six patients achieved a reduction in serum LDH levels only after a decrease in the SOLIRIS<sup>®</sup> dosing interval from 14 to 12 days. All other patients achieved a reduction in serum LDH levels with the 14 day dosing interval [*see Pharmacology and Clinical Trials*].

### **Infusion Reactions**

As with all protein products, administration of SOLIRIS<sup>®</sup> may result in infusion reactions, including anaphylaxis or other hypersensitivity reactions. In clinical trials, no PNH patients experienced an infusion reaction which required discontinuation of SOLIRIS<sup>®</sup>. SOLIRIS<sup>®</sup> administration should be interrupted in all patients experiencing severe infusion reactions and appropriate medical therapy administered.

### **Carcinogenicity**

No studies have been conducted to assess the carcinogenic potential of eculizumab ‘rmc’.

### **Genotoxicity**

No studies have been conducted to assess the genotoxic potential of eculizumab ‘rmc’.

### **Effects on Fertility**

No studies have been conducted to assess the effects of eculizumab ‘rmc’ on male and female fertility. In animal studies with a murine anti-C5 antibody, no adverse effects on the fertility of treated mice were observed.

### Use in Pregnancy – Category B2

There are no adequate and well-controlled studies of SOLIRIS® in pregnant women. Eculizumab ‘rmc’ is expected to cross the placenta. In animal studies with a murine anti-C5 antibody given during the period of organogenesis, there were no clearly treatment-related findings in fetuses of mice exposed to 60 mg/kg/week, a dose comparable to the human dose of eculizumab ‘rmc’ on a mg/kg basis. When maternal exposure to the murine antibody occurred from the time of implantation to the end of lactation, a slightly higher number of male offspring became moribund or died in the group given 60 mg/kg/week. The relevance to use of SOLIRIS® is unclear. SOLIRIS® should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

### Use in Lactation

It is not known whether eculizumab ‘rmc’ is secreted into human milk. IgG is secreted in human milk, so it is likely that eculizumab ‘rmc’ will be present in human milk. SOLIRIS® should be given to a breastfeeding woman only if clearly needed and after a careful risk/benefit analysis has been conducted. Consideration should be given to avoiding breastfeeding for the first 24 hours after birth.

### Paediatric Use

The safety and effectiveness of SOLIRIS® therapy in paediatric patients below the age of 18 have not been established.

### Geriatric Use

In PNH studies, 15 patients 65 years of age or older were treated with SOLIRIS®. Although there were no apparent age-related differences observed in these studies, the number of patients aged 65 and over is not sufficient to determine whether they respond differently from younger patients.

## ADVERSE REACTIONS

### Clinical Trial Experience

Meningococcal infections are the most important adverse reactions experienced by patients receiving SOLIRIS® therapy. In PNH clinical studies, two patients experienced meningococcal sepsis. Both patients had previously received a meningococcal vaccine. In clinical studies among patients without PNH, meningococcal meningitis occurred in one unvaccinated patient [*see Precautions*].

The data described below reflect exposure to SOLIRIS® in 196 adult patients with PNH, age 18-85, of whom 55% were female. All had signs or symptoms of intravascular haemolysis. SOLIRIS® was studied in a placebo-controlled clinical study (in which 43 patients received SOLIRIS® and 44, placebo); a single arm clinical study and a long-term extension study. 182 patients were exposed for greater than one year. All patients received the recommended SOLIRIS® dose regimen.

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. Table 4 summarizes the adverse reactions that occurred at a numerically higher rate in the SOLIRIS® group than the placebo group and at a rate of 5% or more among patients treated with SOLIRIS®.

**TABLE 4**  
**ADVERSE REACTIONS REPORTED IN 5% OR MORE OF SOLIRIS TREATED PATIENTS**  
**AND GREATER THAN PLACEBO IN THE CONTROLLED CLINICAL STUDY**

Reaction	SOLIRIS® N = 43 N (%)	Placebo N = 44 N (%)

Headache	19 (44)	12 (27)
Nasopharyngitis	10 (23)	8 (18)
Back pain	8 (19)	4 (9)
Nausea	7 (16)	5 (11)
Fatigue	5 (12)	1 (2)
Cough	5 (12)	4 (9)
Herpes simplex infections	3 (7)	0
Sinusitis	3 (7)	3 (7)
Respiratory tract infection	3 (7)	1 (2)
Constipation	3 (7)	2 (5)
Myalgia	3 (7)	1 (2)
Pain in extremity	3 (7)	1 (2)
Influenza-like illness	2 (5)	1 (2)

In the placebo-controlled clinical study, serious adverse reactions occurred among 4 (9%) patients receiving SOLIRIS<sup>®</sup> and 9 (21%) patients receiving placebo. The serious reactions included infections and progression of PNH. No deaths occurred in the study and no patients receiving SOLIRIS<sup>®</sup> experienced a thrombotic event; one thrombotic event occurred in a patient receiving placebo.

Among 193 patients with PNH treated with SOLIRIS<sup>®</sup> in the single arm, clinical study or the follow-up study, the adverse reactions were similar to those reported in the placebo-controlled clinical study. Serious adverse reactions occurred among 16% of the patients in these studies.

The most common serious adverse reactions were: viral infection (2%), headache (2%), anaemia (2%), and pyrexia (2%).

### **Immunogenicity**

Infrequent, low titre antibody responses have been detected in SOLIRIS<sup>®</sup> treated patients across all PNH and non-PNH studies with a frequency (3.4%) similar to that of placebo (4.8%). No patients have developed neutralizing antibodies following therapy with SOLIRIS<sup>®</sup>, and there has been no observed correlation of antibody development to clinical response or adverse events. The immunogenicity data reflect the percentage of patients whose test results were considered positive for antibodies to SOLIRIS<sup>®</sup> in an enzyme linked immunosorbent assay (ELISA) and are highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody positivity in the assay may be influenced by several factors including sample handling, timing of sample collection, concomitant medications and underlying disease. For these reasons, comparison of the incidence of antibodies to SOLIRIS<sup>®</sup> with the incidence of antibodies to other products may be misleading.

### **Drug Interactions**

Drug interaction studies have not been performed with SOLIRIS<sup>®</sup>.

### **DOSAGE AND ADMINISTRATION**

Patients must be administered a meningococcal vaccine at least two weeks prior to initiation of SOLIRIS<sup>®</sup> therapy and revaccinated according to current medical guidelines for vaccine use [see *Precautions*].

### **Recommended Dosage Regimen**

SOLIRIS<sup>®</sup> therapy consists of:

- 600 mg every 7 days for the first 4 weeks, followed by
- 900 mg for the fifth dose 7 days later, then
- 900 mg every 14 days thereafter.

SOLIRIS<sup>®</sup> should be administered at the recommended dosage regimen time points, or within two days of these time points [*see Precautions*].

### **Dose Modifications**

A fixed dosage regimen was studied in clinical studies in PNH. There are no recommended modifications to the dosing regimen for SOLIRIS<sup>®</sup>.

### **Instructions for Use (Aseptic Technique)**

#### **Preparation for Administration**

SOLIRIS<sup>®</sup> must be diluted to a final admixture concentration of 5 mg/mL using the following steps:

- Withdraw the required amount of SOLIRIS<sup>®</sup> from the vial into a sterile syringe.
- Transfer the recommended dose to an infusion bag.
- Dilute SOLIRIS<sup>®</sup> to a final concentration of 5 mg/mL by adding the appropriate amount (equal volume of diluent to drug volume) of 0.9% Sodium Chloride Injection, USP; 0.45% Sodium Chloride Injection, USP; 5% Dextrose in Water Injection, USP; or Ringer's Injection, USP to the infusion bag.

Product is for single use in one patient only. Discard any unused portion left in a vial, as the product contains no preservatives.

The final admixed SOLIRIS<sup>®</sup> 5 mg/mL infusion volume is 120 mL for 600 mg doses or 180 mL for 900 mg doses. Gently invert the infusion bag containing the diluted SOLIRIS<sup>®</sup> solution to ensure thorough mixing of the product and diluent. Discard any unused portion left in a vial, as the product contains no preservatives.

Prior to administration, the admixture should be allowed to adjust to 18° to 25° C. The admixture must not be heated in a microwave or with any heat source other than ambient air temperature. The SOLIRIS<sup>®</sup> admixture should be inspected visually for particulate matter and discoloration prior to administration.

### **Administration**

*Do Not Administer As An Intravenous Push Or Bolus Injection*

The SOLIRIS<sup>®</sup> admixture should be administered by intravenous infusion over 35 minutes via gravity feed, a syringe-type pump, or an infusion pump. Admixed solutions of SOLIRIS<sup>®</sup> are stable for 24 hours at 2° to 8° C and at 18° to 25° C. To reduce microbiological hazard, use as soon as practicable after preparation. If storage is necessary, hold at 2° to 8° C for not more than 24 hours.

If an adverse reaction occurs during the administration of SOLIRIS<sup>®</sup>, the infusion may be slowed or stopped at the discretion of the physician. If the infusion is slowed, the total infusion time should not exceed two hours. Monitor the patient for at least one hour following completion of the infusion for signs or symptoms of an infusion reaction.

### **OVERDOSAGE**

No case of overdose has been reported during clinical studies.

## **PRESENTATION AND STORAGE CONDITIONS**

### **Stability and Storage**

SOLIRIS<sup>®</sup> (eculizumab ‘rmc’) is supplied as 300 mg single-use vials containing 30 mL of 10 mg/mL sterile, preservative-free SOLIRIS<sup>®</sup> solution per vial.

Single unit 300 mg carton: Contains one (1) 30 mL vial of SOLIRIS<sup>®</sup> (10 mg/mL).

SOLIRIS<sup>®</sup> vials must be stored in the original carton until time of use under refrigerated conditions at 2 ° to 8° C and protected from light. Do not use beyond the expiration date stamped on the carton. Store in the original package in order to protect from light.

*DO NOT FREEZE. DO NOT SHAKE.*

After dilution, the product should be used immediately. Diluted solutions of SOLIRIS<sup>®</sup> are stable for 24 hours. If a diluted solution has been prepared more than 4 hours prior to administration, it should be stored at 2° to 8° C for not more than 24 hours.

## **POISONS SCHEDULE AND CLASSIFICATION OF MEDICINE**

S4. Prescription Medicine

### **NAME AND ADDRESS OF SPONSOR**

In Australia:  
Alexion Pharmaceuticals Australasia Pty Ltd  
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AUST R 138885

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This product, or its use, is covered by Australian Patent No. 735596  
SOLIRIS<sup>®</sup> is a registered trademark of Alexion Pharmaceuticals Inc., USA

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