NATIONAL PHARMACEUTICAL REGULATORY DIVISION (NPRA)
MINISTRY OF HEALTH MALAYSIA

TECHNICAL EVALUATION SUMMARY FOR NEW REGISTRATION APPLICATION (ORPHAN DRUG)

PRODUCT NAME:
Soliris 10mg/ml Concentrate for Solution for Infusion (MAL24096027ACZ)

ACTIVE INGREDIENT:
Eculizumab 10mg/mL

PRODUCT REGISTRATION HOLDER:
AstraZeneca Sdn. Bhd.

PRODUCT MANUFACTURER:
Alexion Pharma International Operations Limited, Dublin, Ireland

APPROVAL DATE:
5 September 2024 (DCA 400)

1.0 BACKGROUND INFORMATION

a. The DCA has previously registered Soliris 300mg/30ml, concentrate for solution for infusion (MAL12045001ACZ; PRH: DKSH Malaysia Sdn Bhd) for the treatment of adult paroxysmal nocturnal haemoglobinuria (PNH) and atypical haemolytic uremic syndrome (aHUS) in adults and paediatrics. However, the registration of this product was terminated on Oct 2018 due to low usage.

b. The current application is submitted by another PRH (AstraZeneca) and involve more indications (pediatric PNH, generalized myasthenia gravis [gMG] and neuromyelitis optica spectrum disorder [NMOSD]) and different/additional drug substance and drug product manufacturing sites compared to the previous product.

c. The designation of Orphan Medicine for Soliris®, for PNH (D59.5), aHUS (D58.8), Myasthenia gravis (G70.0) and NMOSD (G36.0) was approved in the Drug Evaluation Committee Meeting (Mesyuarat JKPP 08/2023; date of designation: 6th September 2023).

1.1 PROPOSED INDICATION:

Soliris is indicated in adults and children for the treatment of:

- Paroxysmal nocturnal haemoglobinuria (PNH).
  Evidence of clinical benefit is demonstrated in patients with haemolysis with clinical symptom(s) indicative of high disease activity, regardless of transfusion history
- Atypical haemolytic uremic syndrome (aHUS)
- Refractory generalized myasthenia gravis (gMG) in patients aged 6 years and above who are anti-acetylcholine receptor (AChR) antibody-positive

Soliris is indicated in adults for the treatment of:

- Neuromyelitis optica spectrum disorder (NMOSD) in patients who are anti-aquaporin-4 (AQP4) antibody-positive with a relapsing course of the disease

1.2 PROPOSED POSOLOGY:

Soliris must be administered by a healthcare professional and under the supervision of a physician experienced in the management of patients with haematological, renal, neuromuscular or neuro-inflammatory disorders.

Home infusion may be considered for patients who have tolerated infusions well in the clinic. The decision of a patient to receive home infusions should be made after evaluation and recommendation from the treating physician. Home infusions should be performed by a qualified healthcare professional.

Paroxysmal Nocturnal Haemoglobinuria (PNH) in adults

The PNH dosing regimen for adult patients (≥18 years of age) consists of a 4-week initial phase followed by a maintenance phase:

- Initial phase: 600 mg of Soliris administered via a 25 – 45 minute (35 minutes ± 10 minutes) intravenous infusion every week for the first 4 weeks.
- Maintenance phase: 900 mg of Soliris administered via a 25 – 45 minute (35 minutes ± 10 minutes) intravenous infusion for the fifth week, followed by 900 mg of Soliris administered via a 25 – 45 minute (35 minutes ± 10 minutes) intravenous infusion every 14 ± 2 days.

atypical Haemolytic Uremic Syndrome (aHUS), refractory generalized Myasthenia Gravis (gMG) and Neuromyelitis Optica Spectrum Disorder (NMOSD) in adults

The aHUS, refractory gMG, and NMOSD dosing regimen for adult patients (≥18 years of age) consists of a 4-week initial phase followed by a maintenance phase:

- Initial phase: 900 mg of Soliris administered via a 25 – 45 minute (35 minutes ± 10 minutes) intravenous infusion every week for the first 4 weeks.
- Maintenance phase: 1,200 mg of Soliris administered via a 25 – 45 minute (35 minutes ± 10 minutes) intravenous infusion for the fifth week, followed by 1,200 mg of Soliris administered via a 25 – 45 minute (35 minutes ± 10 minutes) intravenous infusion every 14 ± 2 days.

Refractory gMG
Available data suggest that clinical response is usually achieved by 12 weeks of Soliris treatment. Discontinuation of the therapy should be considered in a patient who shows no evidence of therapeutic benefit by 12 weeks.

Paediatric patients in PNH, aHUS, or refractory gMG
Paediatric PNH, aHUS, or refractory gMG patients with body weight ≥ 40 kg are treated with the adult dosing recommendations.

In paediatric PNH, aHUS, and refractory gMG patients with body weight below 40 kg, the Soliris dosing regimen consists of:

Patient Body Weight	**Initial Phase**	**Maintenance Phase**
30 to <40 kg	600 mg weekly for the first 2 weeks	900 mg at week 3; then 900 mg every 2 weeks
20 to <30 kg	600 mg weekly for the first 2 weeks	600 mg at week 3; then 600 mg every 2 weeks
10 to <20 kg	600 mg single dose at week 1	300 mg at week 2; then 300 mg every 2 weeks
5 to <10 kg	300 mg single dose at week 1	300 mg at week 2; then 300 mg every 3 weeks

Soliris has not been studied in patients with PNH or refractory gMG who weigh less than 40kg. The posology of Soliris to be used in paediatric patients with PNH or refractory gMG patients weighing less than 40 kg is identical to the weight-based dose recommendation provided for paediatric patients with aHUS. Based on the pharmacokinetic (PK)/pharmacodynamic (PD) data available in patients with aHUS and PNH treated with Soliris, this body-weight based dose regimen for paediatric patients is expected to result in an efficacy and safety profile similar to that in adults. For patients with refractory gMG weighing less than 40 kg this body-weight based dose regimen is also expected to result in an efficacy and safety profile similar to that in adults.

Soliris has not been studied in paediatric patients with NMOSD.

Supplemental dosing of Soliris is required in the setting of concomitant plasmapheresis (PP), plasma exchange (PE), or fresh frozen plasma infusion (PI) as described below:

Type of Plasma Intervention	Most Recent Soliris Dose	Supplemental Soliris Dose With Each PP/PE/PI Intervention	Timing of Supplemental Soliris Dose
Plasmapheresis or plasma exchange	300 mg	300 mg per each plasmapheresis or plasma exchange session	Within 60 minutes after each plasmapheresis or plasma exchange.
	≥600 mg	600 mg per each plasmapheresis or plasma exchange session	
Fresh frozen plasma infusion	≥300 mg	300 mg per infusion of fresh frozen plasma	60 minutes prior to each infusion of fresh frozen plasma

Abbreviations: PP/PE/PI = plasmapheresis/plasma exchange/plasma infusion

Supplemental dose of Soliris is required in the setting of concomitant intravenous immunoglobulin (IVIg) treatment as described below:

Most Recent Soliris Dose	Supplemental Soliris Dose	Timing of Supplemental Soliris Dose
≥ 900 mg	600 mg per IVIg cycle	As soon as possible after IVIg cycle
≤ 600 mg	300 mg per IVIg cycle	

Abbreviation: IVIg = intravenous immunoglobulin

Treatment monitoring
aHUS patients should be monitored for signs and symptoms of thrombotic microangiopathy (TMA). Soliris treatment is recommended to continue for the patient's lifetime, unless the discontinuation of Soliris is clinically indicated.

Elderly
Soliris may be administered to patients aged 65 years and over. There is no evidence to suggest that any special precautions are needed when older people are treated – although experience with Soliris in this patient population is still limited.

Renal impairment
No dose adjustment is required for patients with renal impairment.

Hepatic impairment
The safety and efficacy of Soliris have not been studied in patients with hepatic impairment.

Paediatric population
The safety and efficacy of Soliris in children with refractory gMG aged less than 6 years old have not been established.
The safety and efficacy of Soliris in children with NMOSD aged less than 18 years old have not been established.

1.4 Route of Administration

Intravenous infusion.

1.5 Pharmacological Aspects

Pharmacotherapeutic group: Selective immunosuppressants, ATC code: L04AJ01

Pharmacodynamic properties

Eculizumab, the active ingredient in Soliris, 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. Eculizumab preserves the early components of complement activation that are essential for opsonization of microorganisms and clearance of immune complexes.

Pharmacokinetic Properties:

Biotransformation

Human antibodies undergo endocytotic digestion in the cells of the reticuloendothelial system. Eculizumab contains only naturally occurring amino acids and has no known active metabolites. Human antibodies are predominately catabolized by lysosomal enzymes to small peptides and amino acids.

Elimination

No specific studies have been performed to evaluate the hepatic, renal, lung, or gastrointestinal routes of excretion/elimination for Soliris. In normal kidneys, antibodies are not excreted and are excluded from filtration by their size.

Pharmacokinetic/pharmacodynamic relationship(s)

In 40 patients with PNH, a 1-compartmental model was used to estimate pharmacokinetic parameters after multiple doses. Mean clearance was 0.31 ± 0.12 mL/hr/kg, mean volume of distribution was 110.3 ± 17.9 mL/kg, and mean elimination half-life was 11.3 ± 3.4 days. The steady state is achieved by 4 weeks using the PNH adult dosing regimen.

In PNH patients, pharmacodynamic activity correlates directly with eculizumab serum concentrations and maintenance of trough levels above ≥ 35 microgram/mL results in essentially complete blockade of haemolytic activity in the majority of PNH patients.

A second population PK analysis with a standard 1 compartmental model was conducted on the multiple dose PK data from 37 aHUS patients receiving the recommended Soliris regimen in studies C08-002A/B and C08-003A/B. In this model, the clearance of Soliris for a typical aHUS patient weighing 70 kg was 0.0139 L/hr and the volume of distribution was 5.6 L. The elimination half-life was 297 h (approximately 12.4 days).

The second population PK model was applied to the multiple dose PK data from 22 paediatric aHUS patients receiving the recommended Soliris regimen in aHUS C10-003. The clearance and volume of distribution of Soliris are weight dependent, which forms the basis for a weight categorical based dose regimen in paediatric patients. Clearance values of Soliris in paediatric aHUS patients were 10.4, 5.3, and 2.2 mL/hr with body weight of 70, 30, and 10 kg, respectively; and the corresponding volume of distribution values were 5.23, 2.76, and 1.21 L, respectively. The corresponding elimination half-life remained almost unchanged within a range of 349 to 378 h (approximately 14.5 to 15.8 days).

The clearance and half-life of eculizumab were also evaluated during plasma exchange interventions. Plasma exchange resulted in an approximately 50% decline in eculizumab concentrations following a 1 hour intervention and the elimination half-life of eculizumab was reduced to 1.3 hours. Supplemental dosing is recommended when Soliris is administered to aHUS patients receiving plasma infusion or exchange.

All aHUS patients treated with Soliris when administered as recommended demonstrated rapid and sustained reduction in terminal complement activity. In aHUS patients, pharmacodynamic activity correlates directly with eculizumab serum concentrations and maintenance of trough levels of approximately 50-100 microgram/ml results in essentially complete blockade of terminal complement activity in all aHUS patients.

PK parameters are consistent across PNH, aHUS, refractory gMG and NMOSD patient populations. Pharmacodynamic activity measured by free C5 concentrations of <0.5 ug/mL, is correlated with essentially complete blockade of terminal complement activity in PNH, aHUS, refractory gMG and NMOSD patients.

Special Populations
Dedicated studies have not been conducted to evaluate the pharmacokinetics of Soliris in special patient populations identified by gender, race, age (geriatric), or the presence of renal or hepatic impairment. Population PK analysis on data collected across studies in PNH, aHUS, gMG and NMOSD patients showed that gender, race, age (geriatric), or the presence of renal or hepatic impairment function do not influence the PK of eculizumab. Body weight was a significant covariate resulting in a lower eculizumab clearance in paediatric patients requiring body weight based dosing in paediatric patients.

Paediatric population
The pharmacokinetics of eculizumab was evaluated in Study M07-005 in PNH paediatric patients (aged from 11 to less than 18 years), in Studies C08-002, C08-003, C09-001r and C10-003 in aHUS paediatric patients (aged 2 months to less than 18 years), and in Study ECU-MG-303 paediatric patients with refractory gMG (aged from 12 years to less than 18 years) with body-weight based dose regimen.

Weight was a significant covariate resulting in a lower eculizumab clearance 0.0105 L/h in the adolescent PNH patients.

2.0 SUMMARY REPORT

2.1 Quality

2.1.1 Active Substance

- Eculizumab is a humanized IgG2/4 kappa antibody, consisting of two 448 amino acid heavy chains and two 214 amino acid light chains.
- There are 3 drug substance (DS) manufacturers i.e. Lonza Biologics Tuas, Singapore (LBT, 20, 000L bioreactor), Lonza Biologics Porrino (LBP) SL, Spain (LBP, 10, 000L bioreactor) and Alexion Pharma International Operations Limited, Ireland (ADMF, 22,000L bioreactor). The process validation study for 3 consecutive batches at each site demonstrated that the eculizumab manufacturing process at the three DS manufacturing sites can be repeatedly and robustly operated within the established process limits. Comparability study were conducted and showed that the DS manufactured by all 3 DS manufacturers produce comparable drug substance.
- Stability data had been submitted for 3 batches respectively from LBP, LBT and ADMF at long term and accelerated storage condition and support the proposed shelf life at 2-8^{o}C for 18 months.
- The GMP certificate for DS manufacturer were issued by the relevant authority as follows:

a) LBT: Health Sciences Authority, Singapore
b) LBP: Competent Regional Authority, Spain
c) ADMF: Health Products Regulatory Authority, Ireland

2.1.2 Finished Product

- There are 2 drug product (DP) manufacturers i.e. Alexion Pharma International Operations Limited, Ireland (AAMF) and Patheon Italia S.p.A., Italy. Process validation had been submitted for 3 batches respectively from AAMF and Patheon Italia site.
- Stability data had also been submitted for 3 batches respectively from AAMF and Patheon Italia at 2-8ºC for 30 months and at 23-27ºC for 12 months. The data support a proposed shelf life of 30 months at 2-8°C. Soliris vials in the original package may be removed from refrigerated storage for only one single period of up to 3 days. At the end of this period, the product can be put back in the refrigerator and this is supported by the data provided.
- Soliris needs to be diluted to a final concentration of 5mg/ml with sodium chloride 9 mg/ml (0.9%) solution for injection, sodium chloride 4.5 mg/ml (0.45%) solution for injection, or 5% dextrose in water. After dilution, the medicinal product should be used immediately. However, chemical and physical stability has been demonstrated for 24 hours at 2°C to 8°C.
- Soliris is a clear, colorless liquid. It is supplied as a 30mL aqueous solution filled into Type 1 glass vials.
- GMP certificate for DP manufacturer was issued by Health Products Regulatory Authority, Ireland for the AAMF site while it was issued by Italian Medicines Agency for Patheon Italia.
- The protocol of analysis and validation data have been evaluated and were found satisfactory based on the documentation submitted.

2.2 Non-Clinical

- There are no new non-clinical studies compared to the previous DCA approved Soliris.

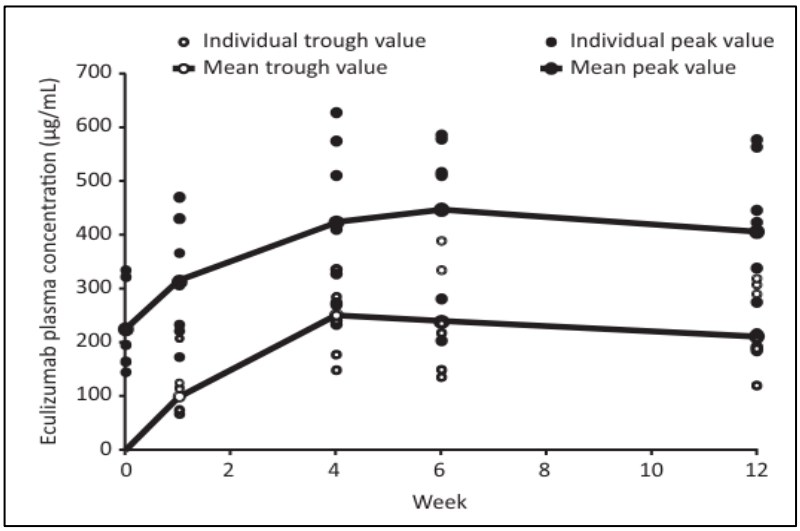
2.3 Clinical

2.3.1 Efficacy

- Previously, DCA has approved Soliris for the treatment of PNH in adults and aHUS in adults and paediatrics. The results presented here focus on the new indications and populations: paediatric PNH, gMG and adult NMOSD.

Study Type & Design	**Objective**	**Results**
PNH		
Study M07-005 (Paeds) Phase 1/2, open-label, single-arm, multicentre. N=7	To evaluate the PK and PD parameters of eculizumab in order to confirm the proposed dose regimens for pediatric patients with PNH.	**Primary endpoint: PK/PD**

<table>
<tr><th>Study Type & Design</th><th>Objective</th><th>Results</th></tr>
<tr><td>Eculizumab was administered via intravenous infusion and dosed according to pre-established weight-based cohorts.</td><td></td><td>Figure 1: Peak and trough plasma concentration over the 12-week treatment period (n=7)

Peak and trough eculizumab concentrations increased gradually and
 

reached a plateau by week 4. At week 12, median trough eculizumab levels were 192.5 mg/ml (mean [SD] 214.5 [68.33]; range 124.2–321.1) and median peak levels were 425.4 mg/ml (403.9 [131.19]; 220.5–556.1). The maximum and minimum concentration of eculizumab, and area under the concentration versus time curve (AUC) were significantly associated with the change from baseline in LDH at the various follow-up visits (P = 0.0273, P = 0.0250, and P = 0.0263, respectively). Increasing eculizumab levels resulted in decreasing hemolysis.

Conclusion
The findings indicate the dosing regimen resulted in rapid and high cessation of intravascular hemolysis in children with PNH.</td></tr>
<tr><td>Patient Registry Study
The use in PNH patients without history of transfusion is supported by a study of patient registry data

Data from the 145 patients from the PNH Registry without a history of transfusion was analysed.</td><td></td><td>Change in Hemoglobin in PNH Registry Patients without History of Transfusion
<table><tr><th></th><th>PNH Registry Eculizumab No transfusion</th><th>PNH Registry No Eculizumab No transfusion</th></tr><tr><td></td><td>N=39</td><td>N=106</td></tr><tr><td>Baseline value (g/L), median (min, max)</td><td>100 (59, 160)</td><td>116 (13, 214)</td></tr><tr><td>Hemoglobin value (g/L) at Month 6, median (min, max)</td><td>112 (73, 148)</td><td>123 (10, 161)</td></tr><tr><td>Change in haemoglobin at Month 6, median (min, max)</td><td>9 (-30, 34)</td><td>1 (-82, 115)</td></tr></table>
Conclusion
Results demonstrate the benefit of eculizumab over standard of care (No Eculizumab) among others in terms of haemoglobin level improvement in patients without history of transfusion.</td></tr>
<tr><td colspan="3">Refractory gMG</td></tr>
</table>

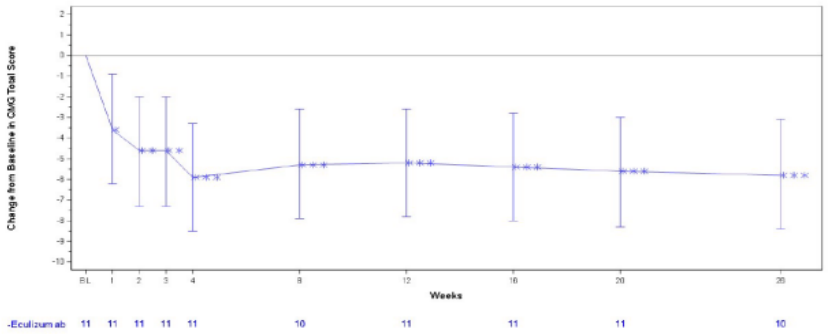
<table>
<tr><th>Study Type & Design</th><th>Objective</th><th>Results</th></tr>
<tr><td>Study ECU-MG-301 (Adults)
Phase 3 randomized, double-blind, placebo-controlled, multicentre

N = 125
(62 eculizumab, 63 placebo)</td><td>To assess the efficacy of eculizumab as compared with placebo in the treatment of refractory gMG with antiacetylcholine receptor (AChR) antibody-positive based on the improvement in the Myasthenia Gravis-specific Activities of Daily Living profile (MG-ADL).</td><td>Primary endpoint: Change from Baseline in the MG-ADL total score at Week 26 of the Study Period for eculizumab compared with placebo: ANCOVA Worst-Rank Analysis.
<table>
<tr><th>Variable</th><th>Statistic</th><th>Placebo (N=63)</th><th>Eculizumab (N=62)</th><th>Difference in LS Means and 95% CI</th><th>p-value</th></tr>
<tr><td>Worst-Rank change from Baseline</td><td>Ranked Score LS Mean (95% CI)</td><td>68.3 (59.43, 77.20)</td><td>56.6 (47.66, 65.61)</td><td>-11.7 (-24.33, 0.96)</td><td>0.0698</td></tr>
</table>
In the primary analysis of changes in MG-ADL score at Week 26 (Worst-Rank ANCOVA) no statistically significant difference was shown for the eculizumab treatment regimen when compared against placebo (p=0.0698).

However, statistically significant differences were achieved in the pre-specified sensitivity analyses (ANCOVA and Repeated-Measured), though the magnitude of the effect remains modest.

Sensitivity Analyses
<table>
<tr><th>Sensitivity Analysis</th><th>Statistic</th><th>Placebo (N=63)</th><th>Eculizumab (N=62)</th><th>Difference in LS Means and 95% CI</th><th>p-value</th></tr>
<tr><td>Analysis of Covariance for MG-ADL</td><td>LS Mean (95% CI)</td><td>-2.6 (-3.52, -1.63)</td><td>-4.0 (-4.96, -3.04)</td><td>-1.4 (-2.77, -0.07)</td><td>0.039</td></tr>
</table>
<table>
<tr><th>Sensitivity Analysis</th><th>Statistic</th><th>Placebo (N=60)</th><th>Eculizumab (N=57)</th><th>Difference in LS Means and 95% CI</th><th>p-value</th></tr>
<tr><td>Repeated-Measures Model for MG-ADL</td><td>LS Mean (95% CI)</td><td>-2.3 (-3.2, -1.4)</td><td>-4.2 (-5.2, -3.3)</td><td>-1.9 (-3.3, -0.6)</td><td>0.0058</td></tr>
</table>
Conclusion
Although statistically significant differences over placebo have not been formally demonstrated for the primary endpoint based on mean change in MG-ADL score from baseline to week 26 (Worst-Rank ANCOVA), sensitivity analysis conducted reached statistical significant differences in favour of eculizumab.</td></tr>
<tr><td>Study ECU-MG-303 (Paeds)
Phase 3, open-label, single-arm, multicentre</td><td>To evaluate the efficacy of eculizumab in the treatment of pediatric patients aged 6 to < 18 years with AChR-Ab + refractory</td><td>Primary endpoint: Change from Baseline in the QMG total score at Week 26.
<table>
<tr><th>Variable</th><th>LS Mean Difference (95% CI)</th><th>p-value</th></tr>
<tr><td>QMG</td><td>-5.8 (-8.4, -3.13)</td><td>0.0004</td></tr>
</table></td></tr>
</table>

<table>
<tr><th>Study Type & Design</th><th>Objective</th><th>Results</th></tr>
<tr><td>N=11

Eculizumab was administered via intravenous infusion and dosed according to pre-established weight-based cohorts.</td><td>gMG based on change from Baseline in the Quantitative Myasthenia Gravis (QMG) total score for disease severity.</td><td>Figure 2: Change from Baseline in QMG Total Score (LS Mean and 95% CI) During the Primary Evaluation Treatment Period Using a Repeated Measures Model (Modified Full Analysis Set)
 
Note: Baseline is defined as the last available assessment value prior to first study drug infusion. Estimates are based on MMRM that included terms of visit and baseline value. *, **, and *** represent two-sided nominal p-value is less than 0.05, 0.01, and 0.001 for testing whether the LS mean is equal to 0. A compound symmetry covariance structure was used.
Abbreviations: BL = baseline; CI = confidence interval; LS = least square; MMRM = mixed model for repeated measures; QMG = Quantitative Myasthenia Gravis

Conclusion
Statistically significant improvements from Baseline were observed as early as Week 1 and were maintained throughout the Primary Evaluation Treatment Period (Week 26). This supports a clinically meaningful benefit of eculizumab in children with refractory gMG.</td></tr>
<tr><td colspan="3">NMOSD</td></tr>
<tr><td>Study ECU-NMO-301
Phase 3 randomized, double-blind, placebo-controlled, multicentre

N = 143
(96 eculizumab, 47 placebo)</td><td>To assess the efficacy of eculizumab treatment as compared with placebo in relapsing neuromyelitis optica spectrum disorder (NMOSD) patients with Anti-aquaporin 4 antibody seropositive</td><td>Primary endpoint: Time to First Adjudicated On-trial Relapse

<table>
<tr><th>Variable</th><th>Statistic</th><th>Placebo (N=47)</th><th>Eculizumab (N=96)</th></tr>
<tr><td>Patient with a relapse (Time to First Adjudicated On-trial Relapse Rate)</td><td>n (%)</td><td>20 (42.6)</td><td>3 (3.1)</td></tr>
<tr><td rowspan="3">Treatment effect</td><td>p-value</td><td colspan="2"><0.001</td></tr>
<tr><td>HR (95% CI)</td><td colspan="2">0.058 (0.017, 0.197)</td></tr>
<tr><td>% reduction (95% CI)</td><td colspan="2">94.2 (80.3, 98.3)</td></tr>
</table>

Conclusion
A significant effect on the time to first adjudicated On-trial Relapse was observed for eculizumab compared with placebo (p<0.0001), confirming that the primary endpoint of the study was met. The hazard ratio (95% CI) for eculizumab compared with placebo was 0.058 (0.017, 0.197), representing a 94.2% reduction in the risk of relapse.</td></tr>
</table>

2.3.2 SAFETY

- Eculizumab has been well tolerated by adult and pediatric patients with PNH, refractory gMG and NMOSD.
- No major/new safety concerns arose from this small pediatric PNH and gMG cohorts. The results are consistent with observations in adult patients for previously-approved indications.
- Overall, there are no changes to its well-characterized safety profile.

3.0 CONCLUSION

The Drug Control Authority (DCA) in their 400th meeting on 5th September 2024 has decided to approve the registration of this product with the following indication:

Soliris is indicated in adults and children for the treatment of:

- Paroxysmal nocturnal haemoglobinuria (PNH).
  Evidence of clinical benefit is demonstrated in patients with haemolysis with clinical symptom(s) indicative of high disease activity, regardless of transfusion history
- Atypical haemolytic uremic syndrome (aHUS)
- Refractory generalized myasthenia gravis (gMG) in patients aged 6 years and above who are anti-acetylcholine receptor (AChR) antibody-positive

Soliris is indicated in adults for the treatment of:

- Neuromyelitis optica spectrum disorder (NMOSD) in patients who are anti-aquaporin-4 (AQP4) antibody-positive with a relapsing course of the disease