

**7.09 PEGCETACOPLAN,
Solution for subcutaneous infusion 1,080 mg in
20 mL,
Empaveli[®],
Swedish Orphan Biovitrum Australia Pty Ltd**

1 Purpose

- 1.1 The early re-entry resubmission sought a Section 100, Authority Required (Written) listing for pegcetacoplan for the treatment of adults with paroxysmal nocturnal haemoglobinuria (PNH) who have inadequate clinical response or are intolerant to C5 inhibitor treatment.
- 1.2 The resubmission was based on the PBAC recommendation from March 2022. This resubmission addressed the issues raised by PBAC; see table below.

Table 1: Summary of key matters to be addressed

Matter of concern	Response	Addressed?
The economic model provided was not reliable for decision-making (para 7.1). With ravulizumab and eculizumab considered appropriate comparators, the PBAC considered a cost-minimisation analysis (CMA) likely an appropriate way forward (para 7.8)	A CMA for one year of pegcetacoplan maintenance therapy compared to one year of maintenance therapy with ravulizumab.	Y
The CMA versus ravulizumab should (para 7.12):		
i. use dosing for ravulizumab accepted by the Committee in July 2021	3,288 mg x 6.5 administrations per year (total dose 21,375 mg) used for ravulizumab as accepted by the PBAC in the July 2021 ravulizumab PSD.	Y
ii. base pegcetacoplan dosing on that reported over 48-weeks in the PEGASUS trial;	Proportion of patients receiving dosing frequency escalation based on 48-week PEGASUS trial data (19.5% receive more frequent dose).	Y
iii. not include cost offsets for pegcetacoplan	Cost offsets have not been included.	Y
iv. include the sponsor proposed % price rebate for pegcetacoplan for the initial 4-week treatment phase	Not included in the CMA calculations as advised in the post-PBAC meeting. Proposed in principle and estimated using pegcetacoplan AEMP from the CMA.	Y
v. incorporate the costs of vaccination against pneumococcal disease and HIB	Vaccination acquisition and administration for pneumococcal disease and HIB included in the annual cost of pegcetacoplan maintenance therapy.	Y
vi. use approved ex-manufacturer price (AEMP)	Published ravulizumab AEMP used in CMA: - \$6,877.57 for 300 mg/3 mL vial - \$25,217.76 for 1.1 g/11 mL vial	Y
Revised financial estimates incorporating revised pricing for the CMA and concerns regarding overestimation of cost offsets addressed (para 7.12)	Financial estimates updated as follows: - removed PBS and MBS cost of iron chelation therapies - removed PBS and MBS costs of blood transfusions - removed MBS cost of treatment administration - updated MBS services to align with proposed vaccine regimen - incorporated revised pricing from the CMA	Y

Source: paragraphs 7.1, 7.8, 7.12, pegcetacoplan March 2022 PBAC Public Summary Document (PSD)

1.3 The equi-effective doses over a 52-week maintenance period for the cost-minimisation approach were:

- Pegcetacoplan 116,365 mg (1,080 mg x 107.7 injections) is equivalent to ravulizumab 21,375 mg (3,288 mg x 6.5 infusions).

1.4 The results of the cost-minimisation are presented in the table below.

Table 2: Results of the cost-minimisation analysis

	Pegcetacoplan	Ravulizumab
Drug cost	\$489,648.55	\$489,958.15 ^a
Vaccination costs	\$309.60 ^b	\$0.00
Total cost per patient per 52-week maintenance period	\$489,958.15	\$489,958.15

Source: Table 3.4 of the resubmission

^a Published ravulizumab AEMP \$25,217.76 for the 1.1 g/11 mL vial. Ravulizumab cost per day of \$1,341.43 = AEMP \$25,217.76 x vials required 2.99 / Frequency (days) 56.2. Drug cost = \$1,341.43 x 365.25

^b *S.pneumoniae* 13vPCV administered once over patient lifetime (unit price \$85.46 + administration cost \$39.10 = \$124.56) plus *S.pneumoniae* 23PPV administered twice over patient lifetime ($[\$38.93 \times 2] + [\$39.10 \times 2] = \$156.06$) plus *H. influenzae* Type B administered once over patients lifetime ($\$28.98 + \$0.00 = \$28.98$). The resubmission stated that although vaccinations are a one-off cost incurred over an abbreviated time horizon for a lifelong therapy the sponsor is willing to incur this cost on a yearly time horizon in the interest of simplicity and expediting the evaluation of this CMA.

- 1.5 Using the equi-effective dose of pegcetacoplan and proposed treatment regimen (1 x 1,080 mg vial x 107.7 injections), the approved ex-manufacturer price of pegcetacoplan is calculated to be \$4,544.50 per 1,080 mg vial.
- 1.6 The estimated drug cost/patient/year would be \$489,958.15, based on a 52-week maintenance period.
- 1.7 In March 2022, the PBAC considered that as ravulizumab is dosed every 8 weeks it would be the C5 inhibitor most likely to be replaced in clinical practice now that it is PBS listed (paragraph 7.9, pegcetacoplan PBAC Public Summary Document (PSD), March 2022 PBAC meeting). The resubmission stated that, in line with this advice and the cost-minimisation approach, only the replacement of ravulizumab in the financial implications was considered.
- 1.8 The resubmission estimated a net cost saving to the PBS in Year 6 of listing, with a total net cost saving to the PBS; see table below. The PBAC noted the net save to the PBS will reduce once the effective price of ravulizumab is applied.

Table 3: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Total treated patients	1	1	1	1	1	1
Total initiating scripts	1	1	1	1	1	1
Total continuing scripts	1	1	1	1	4	4
Total PBS scripts ^a	1	1	1	1	4	4
Total treated patients March 2022	1	1	1	1	1	1
Total PBS scripts March 2022 ^b	1	1	1	1	4	4
Estimated financial implications of pegcetacoplan						
Cost to PBS less co-pay	\$ 2	\$ 2	\$ 2	\$ 2	\$ 5	\$ 5
Cost to PBS less co-pay	\$ 2	\$ 2	\$ 2	\$ 2	\$ 2	\$ 2
Change in utilisation of other medicines						
PBS cost of displaced ravulizumab less co-pay ^c	\$ 2	\$ 2	\$ 2	\$ 2	\$ 5	\$ 5
PBS cost of displaced ravulizumab less co-pay March 2022 ^d	\$ 2	\$ 2	\$ 2	\$ 2	\$ 2	\$ 2
PBS cost of displaced iron chelation therapies less co-pay March 2022	\$ 3	\$ 3	\$ 3	\$ 3	\$ 3	\$ 3
Net financial implications						
Net cost to PBS/RPBS	-\$ 3	-\$ 3	-\$ 3	-\$ 3	-\$ 3	-\$ 3
Net cost to MBS	-\$ 3	-\$ 3	-\$ 3	-\$ 3	-\$ 3	-\$ 3
Net cost to Government	-\$ 3	-\$ 3	-\$ 3	-\$ 3	-\$ 3	-\$ 3
Net cost to PBS March 2022	-\$ 3	-\$ 3	-\$ 3	-\$ 3	-\$ 3	-\$ 3
Net cost to MBS March 2022 ^e	-\$ 3	-\$ 3	-\$ 3	-\$ 3	-\$ 3	-\$ 3
Net cost to Government March 2022	-\$ 3	-\$ 3	-\$ 3	-\$ 3	-\$ 3	-\$ 3

Source: Attachment A4.1 – July22 - Pegcetacoplan Section 4 Model Tab '3b. Impact – proposed (pub)', Table 13 pegcetacoplan March 2022 PBAC PSD

^a Assuming 13.04 scripts per patient per year as estimated by the resubmission. In March 2022, the PBAC Secretariat suggest that flexible quantities would be appropriate, to align with the PBS listings of eculizumab and ravulizumab. The resubmission stated that using the proposed flexible dosing, the total number of scripts per year was calculated to be 13.04

^b Assuming 13.15 scripts per patient per year as estimated by the March 2022 submission.

^c Ravulizumab AEMP \$6,877.57 per 300mg/30mL vial or AEMP \$25,217.76 per 1.1gm/11mL vial

^d Ravulizumab AEMP \$6,154.77 per 300mg/30mL vial

^e Includes cost offsets due to displaced intravenous administrations of ravulizumab, cost offsets due to reduced blood transfusions, additional cost of therapeutic venesections for treatment of iron overload and additional cost of vaccine administrations.

The redacted values correspond to the following ranges:

¹ < 500

² \$10 million to < \$20 million

³ \$0 to < \$10 million

⁴ 500 to < 5000

⁵ \$20 million to < \$30 million

1.9 In March 2022, the PBAC noted that no risk sharing arrangement was proposed in the submission. The PBAC considered it would likely be appropriate for pegcetacoplan to be included in the current risk sharing arrangement for eculizumab and ravulizumab (paragraph 7.11, pegcetacoplan PBAC PSD, March 2022 PBAC meeting). The resubmission proposed the PBS listing include patients who are intolerant to C5

inhibitors to align with the TGA indication (see paragraph 3.3). The resubmission considered it was unclear if these patients would be captured in the existing C5 inhibitor risk share arrangement. In the absence of robust evidence to inform the epidemiology and utilisation estimates for patients included in this expanded indication, the resubmission stated an increase in the existing risk sharing arrangement was not requested at this stage.

- 1.10 In line with the March 2022 PBAC submission, the resubmission proposed a [REDACTED] % rebate of the initial pegcetacoplan script to mitigate the financial impact of concomitant administration as patients switch therapies. In the initial phase of treatment, patients are administered 1,080 mg doses of pegcetacoplan twice weekly while receiving their current C5 inhibitor, as per the pegcetacoplan TGA product information¹. It is estimated therefore that patients will receive eight doses of pegcetacoplan in the first four weeks of treatment (28 days / 3.5 days). Using a pegcetacoplan AEMP of \$4,544.50, the estimated total rebate amount for the initial script is \$[REDACTED].

For more detail on PBAC's view, see section 5 PBAC outcome.

2 Background

- 2.1 Pegcetacoplan was TGA registered on 28 January 2022 for the treatment of adult patients with PNH who have an inadequate response to, or are intolerant of, a C5 inhibitor.
- 2.2 The PICO from the March 2022 submission is presented below.

¹ Dosing frequency may be increased to 1,080 mg every third day if a patient's lactate dehydrogenase (LDH) level is greater than 2 x upper limit of normal (ULN).

Table 4: Key components of the clinical issue addressed in the submission

Component	Description
Population	Patients with paroxysmal nocturnal haemoglobinuria (PNH) and inadequate clinical response to C5 inhibitor treatment (haemoglobin level <10.5 g/dL after ≥3 months of stable treatment)
Intervention	Pegcetacoplan 1,080 mg in 20 mL twice weekly subcutaneous infusion via a commercially available infusion pump ^a
Comparators	Eculizumab 900 mg every 2 weeks intravenous infusion (maintenance dose) and ravulizumab 3,300 mg every 8 weeks intravenous infusion (maintenance dose)
Outcomes	Improved haemoglobin level and transfusion avoidance, leading to improvements in quality of life
Clinical claim	Pegcetacoplan is superior in terms of improvements in haemoglobin level and at least non-inferior in terms of efficacy and safety compared to eculizumab and ravulizumab

Source: Table 1, pegcetacoplan March 2022 PBAC meeting PSD

^a Dosing frequency may be increased to 1,080 mg every third day if a patient's lactate dehydrogenase (LDH) level is greater than 2 x upper limit of normal (ULN)

2.3 The product information indicates that pegcetacoplan is to be included in the Black Triangle Scheme and includes a boxed warning regarding the risk of serious infections caused by encapsulated bacteria, such as *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type B, with recommendations to vaccinate against these bacteria prior to initiation of pegcetacoplan treatment. The PBAC noted ATAGI advice dated 3 March 2022 which stated it would be reasonable to recommend vaccination prior to pegcetacoplan including against *S. pneumoniae*; *N. meningitidis* A, C, W, Y, and B; and *H. influenzae*. The advice stated that if the therapy with pegcetacoplan is ongoing, noting some treatment courses can be months/years, this will lead to persistent complement deficiency, so ongoing vaccination will be required to provide ongoing protection from these encapsulated bacteria. The ATAGI advice stated the required number of vaccines would be:

- HIB – single dose
- Conjugate pneumococcal vaccine (PCV13) single dose
 - PPV23 max 2 doses (1st at min 8-weeks following PCV13); 2nd min 4 years later
- Men ACWY- single dose with a booster recommended every 5 years
- Men B vaccine: 2 doses minimum 8-weeks apart
 - Booster dose 3-years after the previous dose if aged ≤6 years at completion of primary course and at 5 years after the previous dose if aged ≥7 years at completion of primary (paragraph 2.3, pegcetacoplan PBAC PSD, March 2022 PBAC meeting).

For more detail on PBAC's view, see section 5 PBAC outcome.

3 Requested listing

3.1 The resubmission requested a SPA with a rebate on the published AEMP to achieve a price consistent with the cost-minimisation claim once the effective ravulizumab price is incorporated.

Public Summary Document – July 2022 PBAC Meeting

3.2 The resubmission accepted with amendments the March 2022 Secretariat suggestions, as presented in the March 2022 PBAC PSD (paragraph 3.1, pegcetacoplan PBAC PSD, March 2022 PBAC meeting). Key amendments proposed by the resubmission included changes to the clinical criteria to incorporate patients intolerant to C5 inhibitors (see paragraph 3.3) and the provision of a returning from PBS-subsidised eculizumab restriction to allow resumption of treatment post pregnancy (see paragraph 3.5).

Add new medicinal product as follows:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Dispensed price for maximum quantity	Available brands
PEGCETACOPLAN						
Pegcetacoplan <i>injection</i> 1,080 mg/20 mL; 20 mL <i>vial</i>	NEW	1	1	0	\$4,544.50 published price	Empaveli SOBI AU
Restriction Summary [new1]/ Treatment of Concept: [new1]						
Category / Program: Section 100 – Highly Specialised Drugs Program (Public and Private)						
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners						
Restriction type: <input checked="" type="checkbox"/> Authority Required – non-immediate/delayed assessment by Services Australia (In-writing only via mail/postal service or electronic submission)						
Administrative Advice: Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001						
Administrative Advice: No increase in the maximum number of repeats may be authorised.						
Administrative Advice: <i>Special Pricing Arrangements apply.</i>						
CAUTION: WARNING: This drug increases the risk of encapsulated bacterial infections. Consult the approved PI for information about vaccination against meningococcal, pneumococcal and <i>Haemophilus influenzae</i> type B (Hib) infection.						
Indication: Paroxysmal nocturnal haemoglobinuria (PNH)						
Treatment Phase Initial treatment						
Clinical criteria: Patient must not have received prior treatment with this drug for this condition within 6 months.						
AND						
Clinical criteria: Patient must have <i>experienced an inadequate response to a complement 5 (C5) inhibitor demonstrated by a haemoglobin level of less than 10.5 g/dL. OR</i>						
Patient is <i>must be</i> intolerant to C5 inhibitors as determined by the treating physician clinician.						

Public Summary Document – July 2022 PBAC Meeting

	AND
	Clinical criteria:
	Patient must have received treatment with <i>at least one</i> C5 inhibitor for at least 3 months before initiating treatment with this drug.
	AND
	Clinical criteria:
	The treatment must be in combination with <i>one a</i> PBS-subsidised C5 inhibitor for a period of 4 weeks during initiation of therapy.
	Treatment criteria:
	Must be treated by a haematologist; OR
	Must be treated by a non-specialist medical physician who has consulted a haematologist on the patient's drug treatment details
	Population criteria:
	Patient must be at least 18 years of age.
	Administrative Advice: <i>Complement 5 (C5) inhibitors are defined as eculizumab or ravulizumab</i>
	Prescribing Instructions: At the time of the authority application, medical practitioners <i>must should</i> request the appropriate number of vials for 4 weeks supply <i>per dispensing</i> as per the Product Information.
	Prescribing Instructions: <i>The authority application must be made in writing and must include:</i> (1) <i>a completed authority prescription form; and</i> (2) <i>a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice).</i>
	Prescribing Instructions: At the time of the authority application, details (result and date of result) of the following monitoring requirements must be provided: (i) Haemoglobin (g/L) (ii) Platelets (x10 ⁹ /L) (iii) White Cell Count (x10 ⁹ /L) (iv) Reticulocytes (x10 ⁹ /L) (v) Neutrophils (x10 ⁹ /L) (vi) Granulocyte clone size (%) (vii) Lactate Dehydrogenase (LDH) and the upper limit of normal (ULN) for the reporting laboratory (viii) Multiple of LDH, ULN
Restriction Summary [new2]/ Treatment of Concept: [new2]	
	Category / Program: Section 100 – Highly Specialised Drugs Program (Public and Private)
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
	Restriction type: <input checked="" type="checkbox"/> Authority Required – non-immediate/delayed assessment by Services Australia (In-writing only via mail/postal service or electronic submission)
	Indication: Paroxysmal nocturnal haemoglobinuria (PNH)
	Treatment Phase: Return from PBS-subsidised eculizumab
	Clinical criteria:
	Patient must have received prior PBS-subsidised treatment with this drug for this condition,
	AND
	Clinical criteria:

Public Summary Document – July 2022 PBAC Meeting

	Patient must have <i>experienced an inadequate response to a complement 5 (C5) inhibitor demonstrated by a haemoglobin level of less than 10.5 g/dL</i> OR
	Patient must be is intolerant to C5 inhibitors as determined by the treating physician <i>clinician</i>
	AND
	Clinical criteria:
	Patient must have received prior PBS-subsidised treatment with eculizumab through the 'Initial treatment – Initial 2 (switching from PBS-subsidised <i>ravulizumab/pegcetacoplan</i> for pregnancy)' criteria,
	AND
	Clinical criteria:
	The treatment must not be in combination with eculizumab. <i>The treatment must be in combination with one PBS-subsidised C5 inhibitor for a period of 4 weeks during initiation of therapy.</i>
	Treatment criteria:
	Must be treated by a haematologist; OR
	Must be treated by a non-specialist medical physician who has consulted a haematologist on the patient's drug treatment details
	Population criteria:
	Patients must be at least 18 years of age.
	Administrative Advice: <i>Complement 5 (C5) inhibitors are defined as eculizumab or ravulizumab</i>
	Prescribing Instructions: At the time of the authority application, medical practitioners must <i>should</i> request the appropriate number of vials for 4 weeks one month <i>the supply per dispensing</i> as per the Product Information.
	Prescribing Instructions: At the time of the authority application, details (result and date of result) of the following monitoring requirements must be provided: <ul style="list-style-type: none"> (i) Haemoglobin (g/L) (ii) Platelets (x10⁹/L) (iii) White Cell Count (x10⁹/L) (iv) Reticulocytes (x10⁹/L) (v) Neutrophils (x10⁹/L) (vi) Granulocyte clone size (%) (vii) Lactate Dehydrogenase (LDH) and the upper limit of normal (ULN) for the reporting laboratory (viii) Multiple of LDH ULN
	Prescribing Instructions: Patient may qualify under this treatment phase more than once for the purposes of family planning. Where long-term continuing PBS-subsidised treatment with this drug is planned, a 'Returning' patient may proceed under the Continuing Treatment' criteria.

Public Summary Document – July 2022 PBAC Meeting

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Dispensed price for maximum quantity	Available brands
PEGCETACOPLAN						
Pegcetacoplan <i>injection</i> 1,080 mg/20 mL; 20 mL <i>vial</i>	NEW	1	1	5	\$4,544.50 published price	Empaveli SOBI AU
Restriction Summary [new3] / Treatment of Concept: [new3]						
Category / Program: Section 100 – Highly Specialised Drugs Program (Public and Private)						
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners						
Restriction type: <input checked="" type="checkbox"/> Authority Required – non-immediate/delayed assessment by Services Australia (In-writing only via mail/postal service or electronic submission)						
<p>Administrative Advice: Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>						
<p>Administrative Advice: No increase in the maximum number of repeats may be authorised</p>						
<p>Administrative Advice: Special Pricing Arrangements apply.</p>						
<p>CAUTION: WARNING: This drug increases the risk of encapsulated bacterial infections. Consult the approved PI for information about vaccination against meningococcal, pneumococcal and Haemophilus influenzae type B (Hib) infection.</p>						
Indication: Paroxysmal nocturnal haemoglobinuria (PNH)						
Treatment Phase: Continuing treatment						
Clinical criteria:						
Patient must have received had PBS-subsidised treatment with this drug for this condition under the 'initial' or 'Grandfather' treatment criteria phase.						
AND						
Clinical criteria:						
Patient must have demonstrated clinical improvement or stabilisation of condition.						
AND						
Clinical criteria:						
The treatment must not be in combination with a PBS-subsidised C5 inhibitor.						
Treatment criteria:						
Must be treated by a haematologist; OR						

Public Summary Document – July 2022 PBAC Meeting

	Must be treated by a non-specialist medical physician who has consulted a haematologist on the patient's drug treatment details.
	Population criteria:
	Patients must be <i>at least 18 years of age</i> .
	Prescribing Instructions: At the time of the authority application, medical practitioners must <i>should</i> request the appropriate number of vials for 4 weeks one month <i>supply per dispensing</i> as per the Product Information
	Administrative advice: Complement 5 (C5) inhibitors are defined as eculizumab or ravulizumab
	Prescribing Instructions: <i>The authority application must be made in writing and must include:</i> (1) a completed authority prescription form; and (2) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice).
	Prescribing Instructions: At the time of the authority application, details (result and date of result) of the following monitoring requirements must be provided: (i) Haemoglobin (g/L) (ii) Platelets (x10 ⁹ /L) (iii) White Cell Count (x10 ⁹ /L) (iv) Reticulocytes (x10 ⁹ /L) (v) Neutrophils (x10 ⁹ /L) (vi) Granulocyte clone size (%) (vii) Lactate Dehydrogenase (LDH) and the upper limit of normal (ULN) for the reporting laboratory (viii) Multiple of LDH ULN
	Category / Program: Section 100 – Highly Specialised Drugs Program (Public and Private)
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
	Restriction type: <input checked="" type="checkbox"/> Authority Required – non-immediate/delayed assessment by Services Australia (In-writing only via mail/postal service or electronic submission)
	Indication: Paroxysmal nocturnal haemoglobinuria (PNH)
	Treatment Phase: Grandfathered Treatment (<i>transition from non-PBS-subsidised treatment</i>)
	Clinical criteria:
	Patient must have received non-PBS-subsidised treatment with this drug for this condition prior to [listing date]
	AND
	Clinical criteria:
	Patient must have had <i>experienced an inadequate response to a complement 5 (C5) inhibitor demonstrated by a haemoglobin level of less than 10.5 g/dL prior to initiating non-PBS-subsidised treatment with this drug. OR</i>
	Patient must be <i>is</i> intolerant to C5 inhibitors as determined by the treating physician <i>clinician</i> .
	AND
	Clinical criteria:
	Patient must have been receiving treatment with <i>at least one</i> a C5 inhibitor for at least 3 months <i>prior to initiating non-PBS-subsidised treatment with this drug before initiating treatment with this drug</i>
	AND
	Clinical criteria:
	Patient must have demonstrated clinical improvement or stabilisation of condition while receiving treatment with this drug for this condition.

Public Summary Document – July 2022 PBAC Meeting

	AND
	Clinical criteria:
	<i>The treatment must; (i) not be in combination with a PBS-subsidised C5 inhibitor, (ii) the patient has had at least the first 4 weeks of pegcetacoplan treatment, (iii) has demonstrated clinical improvement/stabilisation of the condition while receiving treatment with this drug Or</i>
	<i>The treatment must be in combination with one PBS-subsidised C5 inhibitor for a period of 4 weeks during initiation of therapy.</i>
	Treatment criteria:
	Must be treated by a haematologist; OR
	Must be treated by a non-specialist medical physician who has consulted a haematologist on the patient's drug treatment details
	Population criteria:
	Patients must be <i>at least 18 years of age</i>
	Administrative Advice: <i>Complement 5 (C5) inhibitors are defined as eculizumab or ravulizumab</i>
	Prescribing Instructions: At the time of the authority application, medical practitioners must request the appropriate number of vials for 4 weeks supply per dispensing as per the Product Information.
	Prescribing Instructions: <i>The authority application must be made in writing and must include:</i> <i>(1) a completed authority prescription form; and</i> <i>(2) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice).</i>
	Prescribing Instructions: At the time of the authority application, details (result and date of result) of the following monitoring requirements must be provided: (i) Haemoglobin (g/L) (ii) Platelets (x10 ⁹ /L) (iii) White Cell Count (x10 ⁹ /L) (iv) Reticulocytes (x10 ⁹ /L) (v) Neutrophils (x10 ⁹ /L) (vi) Granulocyte clone size (%) (vii) Lactate Dehydrogenase (LDH) and the upper limit of normal (ULN) for the reporting laboratory (viii) Multiple of LDH ULN
	Note Patients may qualify for PBS-subsidised treatment under this restriction once only. For continuing PBS-subsidised treatment, a 'Grandfathered' patient must qualify under the 'Continuing Treatment' criteria.
	<i>This grandfather restriction will cease to operate from 5 years after the date specified in the clinical criteria.</i>

3.3 In March 2022, the ESC considered it would be reasonable for the PBS listing to include patients who are intolerant to C5 inhibitors to align with the TGA indication (paragraph 3.7, pegcetacoplan PBAC PSD, March 2022 PBAC meeting). In response, the resubmission has added the clinical criterion 'Patient is intolerant to C5 inhibitors as determined by treating clinician' to the initial, grandfathering and the return from PBS-subsidised eculizumab treatment restrictions. The PBAC considered this addition was appropriate. In addition, the PBAC advised that patients considered intolerant to

C5 inhibitors could switch at any time to pegcetacoplan (i.e. pegcetacoplan is another option to eculizumab and ravulizumab in case of intolerance). As such, the PBAC considered modification of a clinical criterion to state ‘Patient must have received treatment with at least one C5 inhibitor for at least 3 months before initiating treatment with this drug unless intolerance of severity necessitating permanent treatment withdrawal had occurred’ was appropriate.

- 3.4 A second change to the initial treatment restriction was the application of a ‘within 6 month’ time frame to the requirement that a patient must not have received prior treatment with this drug for this condition. The resubmission stated that if treatment discontinuation was related to non-response then the patient should not be eligible for re-initiation with pegcetacoplan. The resubmission stated the sponsor is willing to work with the Department to determine appropriate criteria for defining ‘non-response’. However, the resubmission argued that if discontinuation is due to other clinical or lifestyle factors then the patient should be allowed to re-initiate treatment. The PBAC advised that re-initiation of pegcetacoplan treatment for reasons other than post pregnancy were rare but may occur (e.g. a patient with fluctuating haemolysis may need to switch therapies over time or for travel). The PBAC considered that reference to a ‘within 6 month’ time frame was not required in the initial treatment restriction. Instead, the PBAC considered a restriction that included reference to a return from PBS subsidised eculizumab or ravulizumab for reasons other than pregnancy would be appropriate.
- 3.5 In March 2022, the PBAC advised that pegcetacoplan patients would need to be able go back onto a C5 inhibitor if they were non-responders (a one-off) and for pregnancy (with the option to return pegcetacoplan postpartum, unless they were a non-responder). Multiple switches for pregnancy should be allowed (paragraph 3.11, pegcetacoplan PBAC PSD, March 2022 PBAC meeting). Consistent with the ravulizumab listing for PNH the resubmission proposed a return from PBS-subsidised eculizumab restriction to allow for switching for pregnancy. The PBAC noted that patients returning to pegcetacoplan post pregnancy are required to receive additional C5 inhibitor treatment over the first 4 weeks of therapy to minimise the risk of haemolysis with abrupt discontinuation. As such, the PBAC considered it appropriate that the clinical criterion stating ‘must not be used in combination with eculizumab’ be replaced with the need for use in combination with C5 inhibitor therapy over the first 4 weeks. The PBAC considered that haemoglobin levels are not required in the restriction for patients returning to pegcetacoplan post pregnancy (i.e. patients do not need to requalify for treatment).
- 3.6 The PBAC noted that allowing switching from pegcetacoplan to eculizumab for pregnancy will require flow on changes to the current eculizumab Initial treatment listings.
- 3.7 In addition to pregnancy, in March 2022 the PBAC advised that pegcetacoplan patients would need to be able to go back onto a C5 inhibitor if they were non-responders (a one-off) (paragraph 3.11, pegcetacoplan PBAC PSD, March 2022 PBAC meeting).

Hence, the PBAC considered that flow on changes will be required to the current eculizumab and ravulizumab initial treatment listings to allow patients to switch back to one of the C5 inhibitors if they do not respond to pegcetacoplan.

- 3.8 The current listings of both eculizumab and ravulizumab have first continuing treatment and subsequent continuing treatment restrictions. The first continuing treatment restriction requires the monitoring of the same eight measures outlined in the prescribing instructions of the pegcetacoplan continuing restriction. The PBAC considered that the pegcetacoplan restriction should be consistent with the eculizumab and ravulizumab restrictions in that only the result and date of result need to be submitted with the authority application. In addition, the PBAC considered the pegcetacoplan continuing treatment restriction should be separated into first and subsequent continuing treatment listings (like those for eculizumab and ravulizumab) as test results do not need to be resupplied with each authority application.
- 3.9 In March 2022, the submission stated that there were < 500 patients currently receiving pegcetacoplan, and up to < 500 patients would require grandfathering at the time of PBS listing. At that time, the PBAC considered the inclusion of a grandfathering restriction was appropriate (paragraph 3.13, pegcetacoplan PBAC PSD, March 2022 PBAC meeting). The PBAC considered a grandfathering restriction remained appropriate and noted that clinical criteria have been added by the Secretariat to the grandfathering restriction to account for patients moving from non-PBS subsidised therapy at different treatment phases. The PBAC also considered it appropriate that the grandfathering restriction contain criterion that direct that the restriction will cease to operate 12 months from the date specified in the clinical criteria.
- 3.10 The PBAC noted that administrative advice reflecting the request for a SPA have been added to the proposed restriction.

For more detail on PBAC's view, see section 5 PBAC outcome.

4 Consideration of the evidence

Sponsor hearing

- 4.1 There was no hearing for this item.

Consumer comments

- 4.2 The PBAC noted that no consumer comments were received for this item.

Clinical trials

- 4.3 Clinical data was not presented in this early re-entry resubmission.

Clinical claim

- 4.4 In March 2022, the PBAC considered that the evidence presented demonstrated a benefit in short-term haematological outcomes. In addition, while uncertain, the claim

of non-inferior comparative effectiveness to the known benefits of eculizumab treatment in this population was reasonable (paragraph 7.5, pegcetacoplan PBAC PSD, March 2022 PBAC meeting).

- 4.5 In March 2022, the PBAC considered that the claim of non-inferior comparative safety was uncertain but reasonable (paragraph 7.6, pegcetacoplan PBAC PSD, March 2022 PBAC meeting).

5 PBAC Outcome

- 5.1 The PBAC recommended the Section 100, Authority Required (Written) listing for pegcetacoplan for the treatment of adults with paroxysmal nocturnal haemoglobinuria (PNH) who have inadequate clinical response or are intolerant to treatment with eculizumab or ravulizumab. The PBAC considered the resubmission adequately addressed the previous issues raised, providing a cost-minimisation approach for pegcetacoplan compared to ravulizumab and revised financial estimates.

- 5.2 The PBAC's recommendation for listing was based on, among other matters, its assessment, as described above, that the cost-effectiveness of pegcetacoplan would be acceptable if it were cost-minimised against ravulizumab, and if the following measures were implemented to contain risks associated with the cost of the drug to the PBS:

- pegcetacoplan to be included in the current risk sharing arrangement for eculizumab and ravulizumab.
- % price rebate for pegcetacoplan for the initial 4-week treatment phase.

- 5.3 With regard to the requested listing and restriction, the PBAC advised that:

- A PBS listing that includes patients who are intolerant C5 inhibitors was appropriate (see paragraph 3.3).
- Patients returning to pegcetacoplan post pregnancy do not need to requalify for treatment (see paragraph 3.5).
- A listing that allows return from PBS subsidised eculizumab or ravulizumab for reasons other than pregnancy was appropriate (see paragraph 3.4).
- The pegcetacoplan continuing treatment restriction should be separated into first continuing and subsequent continuing listings (see paragraph 3.8).
- The inclusion of a grandfathering restriction was appropriate (see paragraph 3.9).
- Flow on changes to the current eculizumab and ravulizumab restriction would be required as outlined in paragraphs 3.6 and 3.7.

- 5.4 The PBAC recalled that in March 2022, it had considered that while uncertain, the claim of non-inferior comparative effectiveness to the known benefits of eculizumab treatment in this population was reasonable (paragraph 7.5, pegcetacoplan PBAC PSD,

March 2022 PBAC meeting). The PBAC also recalled that it had considered that the claim of non-inferior comparative safety was uncertain but reasonable (paragraph 7.6, pegcetacoplan PBAC PSD, March 2022 PBAC meeting).

- 5.5 In March 2022, the PBAC had advised that an appropriate way forward would likely be a cost-minimisation versus ravulizumab that: i) uses dosing for ravulizumab accepted by the Committee in July 2021; ii) bases pegcetacoplan dosing on that reported over 48-weeks in the PEGASUS trial; iii) does not include cost offsets for pegcetacoplan; iv) includes the sponsor proposed 1% price rebate for pegcetacoplan for the initial 4-week treatment phase; v) incorporates the costs of vaccination against pneumococcal disease and HIB; and vi) uses AEMP in the cost-minimisation calculations (paragraph 7.12, pegcetacoplan PBAC PSD, March 2022 PBAC meeting). The PBAC noted that the submission presented a cost-minimisation between pegcetacoplan and ravulizumab and considered the analysis inputs and assumptions were consistent with its March 2022 recommendations (see Table 1). The PBAC considered the equi-effective doses over a 52-week maintenance period were:
- Pegcetacoplan 116,365 mg (1,080 mg x 107.7 injections) is equivalent to ravulizumab 21,375 mg (3,288 mg x 6.5 infusions).
- 5.6 The PBAC noted the resubmission provided revised financial estimates which incorporated the pegcetacoplan pricing from the cost-minimisation and addressed previous concerns regarding the overestimation of cost offsets (see Table 1).
- 5.7 The PBAC considered it would be appropriate for pegcetacoplan to be included in the current risk sharing arrangement for eculizumab and ravulizumab for PNH to manage any residual uncertainty associated with the cost to government. The PBAC noted that grandfathered patients were included within the prevalent population estimates. The PBAC considered that an increase in the patient numbers informing the current financial caps was not required as these patients were adequately accounted for in the existing agreement. The PBAC also considered the proposed 1% price rebate for pegcetacoplan for the initial 4-week treatment phase to be appropriate to mitigate the financial impact of concomitant administration as patients switch therapies (see paragraph 1.10).
- 5.8 The PBAC noted ATAGI advice which stated it would be reasonable to recommend vaccination prior to pegcetacoplan against *Streptococcus pneumoniae*; *Neisseria meningitidis* A, C, W, Y, and B; and *Haemophilus influenzae* type B. The PBAC considered it would be appropriate to extend access on the National Immunisation Program for the vaccinations recommended by ATAGI as outlined in paragraph 2.3.
- 5.9 The PBAC recommended that pegcetacoplan should not be treated as interchangeable with any drugs.
- 5.10 The PBAC advised that pegcetacoplan is not suitable for prescribing by nurse practitioners.
- 5.11 The PBAC recommended that the Early Supply Rule should not apply.

- 5.12 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, while the evidence presented in March 2022 demonstrated a benefit in short-term haematological outcomes (see paragraph 4.4), because pegcetacoplan is not expected to provide a substantial and clinically relevant improvement in efficacy over the known benefits of eculizumab or ravulizumab, the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022* for Pricing Pathway A were not met.
- 5.13 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:

Recommended

6 Recommended listing

6.1 Add new medicinal product as follows:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
PEGCETACOPLAN					
Pegcetacoplan injection 1,080 mg/20 mL; 20 mL vial	NEW (Public) NEW (Private)	1	1	0	Empaveli SOBI AU
Restriction Summary [new 1]/ Treatment of Concept: [new 1]					
Category / Program: Section 100 – Highly Specialised Drugs Program (Public and Private)					
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners					
Restriction type: <input checked="" type="checkbox"/> Authority Required – non-immediate/delayed assessment by Services Australia (In-writing only via mail/postal service or electronic submission)					
Administrative Advice: Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001					
Administrative Advice: No increase in the maximum number of repeats may be authorised.					
Administrative Advice: Special Pricing Arrangements apply.					
CAUTION: WARNING: This drug increases the risk of encapsulated bacterial infections. Consult the approved Product Information (PI) for information about vaccination against meningococcal, pneumococcal and <i>Haemophilus influenzae</i> type B (Hib) infection.					
Indication: Paroxysmal nocturnal haemoglobinuria (PNH)					
Treatment Phase Initial treatment (New patient)					
Clinical criteria:					

Public Summary Document – July 2022 PBAC Meeting

	Patient must not have received prior treatment with this drug for this condition.
	AND
	Clinical criteria:
	Patient must have a PNH granulocyte clone size equal to or greater than 10% within the last 3 months.
	AND
	Clinical criteria:
	Patient must have experienced an inadequate response to a complement 5 (C5) inhibitor demonstrated by a haemoglobin level of less than 105 g/L. OR
	Patient must be intolerant to C5 inhibitors as determined by the treating physician.
	AND
	Clinical criteria:
	Patient must have received treatment with at least one C5 inhibitor for at least 3 months before initiating treatment with this drug unless intolerance of severity necessitating permanent treatment withdrawal had occurred.
	AND
	Clinical criteria:
	The treatment must be in combination with one PBS-subsidised C5 inhibitor for a period of 4 weeks during initiation of therapy.
	Treatment criteria:
	Must be treated by a haematologist; OR
	Must be treated by a non-specialist medical physician who has consulted a haematologist on the patient's drug treatment details
	Population criteria:
	Patient must be at least 18 years of age.
	Administrative Advice: Complement 5 (C5) inhibitors are defined as eculizumab or ravulizumab
	Prescribing Instructions: The authority application must be made in writing and must include: (1) a completed authority prescription form; and (2) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice).
	Prescribing Instructions: At the time of the authority application, medical practitioners must request the appropriate number of vials for 4 weeks supply per dispensing as per the Product Information.
	Prescribing Instructions: At the time of the authority application, details (result and date of result) of the following monitoring requirements must be provided: (viii) Haemoglobin (g/L) (ix) Platelets (x10 ⁹ /L) (x) White Cell Count (x10 ⁹ /L) (xi) Reticulocytes (x10 ⁹ /L) (xii) Neutrophils (x10 ⁹ /L) (xiii) Granulocyte clone size (%) (xiv) Lactate Dehydrogenase (LDH) and the upper limit of normal (ULN) for the reporting laboratory (viii) Multiple of LDH, ULN
Restriction Summary [new 2]/ Treatment of Concept: [new 2]	
	Category / Program: Section 100 – Highly Specialised Drugs Program (Public and Private)
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
	Restriction type: <input checked="" type="checkbox"/> Authority Required – non-immediate/delayed assessment by Services Australia (In-writing only via mail/postal service or electronic submission)
	Indication: Paroxysmal nocturnal haemoglobinuria (PNH)

Public Summary Document – July 2022 PBAC Meeting

	Treatment Phase: Return from PBS-subsidised eculizumab post pregnancy or from PBS-subsidised C5 inhibitor for reasons other than post pregnancy.
	Clinical criteria:
	Patient must have received prior PBS-subsidised treatment with this drug for this condition.
	AND
	Clinical criteria:
	Patient must have received prior PBS-subsidised treatment with eculizumab through the 'Initial treatment – Initial 3 (switching from PBS-subsidised pegcetacoplan for pregnancy)' criteria OR
	Patient must have received prior PBS-subsidised treatment with at least one C5 inhibitor and returning to pegcetacoplan treatment for reasons other than post pregnancy.
	AND
	Clinical criteria:
	Patient must have demonstrated clinical improvement / stabilisation of condition when the patient was receiving pegcetacoplan.
	AND
	Clinical criteria:
	The treatment must be in combination with one PBS-subsidised C5 inhibitor for a period of 4 weeks during initiation of therapy.
	Treatment criteria:
	Must be treated by a haematologist; OR
	Must be treated by a non-specialist medical physician who has consulted a haematologist on the patient's drug treatment details.
	Population criteria:
	Patients must be at least 18 years of age.
	Administrative Advice: Complement 5 (C5) inhibitors are defined as eculizumab or ravulizumab
	Prescribing Instructions: The authority application must be made in writing and must include: (1) a completed authority prescription form; and (2) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice).
	Prescribing Instructions: At the time of the authority application, medical practitioners must request the appropriate number of vials for 4 weeks supply per dispensing as per the Product Information.
	Prescribing Instructions: At the time of the authority application, details (result and date of result) of the following monitoring requirements must be provided: (ix) Haemoglobin (g/L) (x) Platelets ($\times 10^9/L$) (xi) White Cell Count ($\times 10^9/L$) (xii) Reticulocytes ($\times 10^9/L$) (xiii) Neutrophils ($\times 10^9/L$) (xiv) Granulocyte clone size (%) (xv) Lactate Dehydrogenase (LDH) and the upper limit of normal (ULN) for the reporting laboratory (xvi) Multiple of LDH ULN
	Prescribing Instructions: For the purposes of family planning, patient may qualify under this treatment phase more than once. To return to pegcetacoplan treatment for reasons other than post pregnancy, patient may qualify under this treatment phase only once in any 12 consecutive months. Where long-term continuing PBS-subsidised treatment with this drug is planned, a 'Returning' patient may proceed under the 'Subsequent Continuing Treatment' criteria.

Public Summary Document – July 2022 PBAC Meeting

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
PEGCETACOPLAN					
Pegcetacoplan injection 1,080 mg/20 mL; 20 mL vial	NEW (Public) NEW (Private)	1	1	5	Empaveli SOBI AU
Restriction Summary [new 4] / Treatment of Concept: [new 4]					
Category / Program: Section 100 – Highly Specialised Drugs Program (Public and Private)					
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners					
Restriction type: <input checked="" type="checkbox"/> Authority Required – non-immediate/delayed assessment by Services Australia (In-writing only via mail/postal service or electronic submission)					
Administrative Advice: Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001					
Administrative Advice: No increase in the maximum number of repeats may be authorised					
Administrative Advice: Special Pricing Arrangements apply.					
CAUTION: WARNING: This drug increases the risk of encapsulated bacterial infections. Consult the approved PI for information about vaccination against meningococcal, pneumococcal and <i>Haemophilus influenzae</i> type B (Hib) infection.					
Category / Program: Section 100 – Highly Specialised Drugs Program (Public and Private)					
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners					
Restriction type: <input checked="" type="checkbox"/> Authority Required – non-immediate/delayed assessment by Services Australia (In-writing only via mail/postal service or electronic submission)					
Indication: Paroxysmal nocturnal haemoglobinuria (PNH)					
Treatment Phase: Grandfathered Treatment (transition from non-PBS-subsidised treatment)					
Clinical criteria: Patient must have received non-PBS-subsidised treatment with this drug for this condition prior to [listing date]					
AND					
Clinical criteria: Patient must have a PNH granulocyte clone size equal to or greater than 10% within the 3 months prior to initiating non-PBS-subsidised treatment with this drug.					
AND					
Clinical criteria Patient must have had experienced an inadequate response to a complement 5 (C5) inhibitor demonstrated by a haemoglobin level of less than 105 g/L prior to initiating non-PBS-subsidised treatment with this drug. OR					
Patient must be intolerant to C5 inhibitors as determined by the treating physician.					
AND					
Clinical criteria:					

Public Summary Document – July 2022 PBAC Meeting

	Patient must have been receiving treatment with at least one C5 inhibitor for at least 3 months prior to initiating non-PBS-subsidised treatment with this drug unless intolerance of severity necessitating permanent treatment withdrawal had occurred.
	AND
	Clinical criteria:
	The treatment must; (i) not be in combination with a PBS-subsidised C5 inhibitor, (ii) the patient has had at least the first 4 weeks of pegcetacoplan treatment, (iii) has demonstrated clinical improvement / stabilisation of the condition while receiving treatment with this drug Or
	The treatment must be in combination with one PBS-subsidised C5 inhibitor for a period of 4 weeks during initiation of therapy.
	Treatment criteria:
	Must be treated by a haematologist; OR
	Must be treated by a non-specialist medical physician who has consulted a haematologist on the patient's drug treatment details.
	Population criteria:
	Patients must be at least 18 years of age
	Administrative Advice: Complement 5 (C5) inhibitors are defined as eculizumab or ravulizumab
	Prescribing Instructions: The authority application must be made in writing and must include: (1) a completed authority prescription form; and (2) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice).
	Prescribing Instructions: At the time of the authority application, medical practitioners must request the appropriate number of vials for 4 weeks supply per dispensing as per the Product Information. A maximum of 5 repeats may be requested.
	Prescribing Instructions: At the time of the authority application, details (result and date of result) of the following monitoring requirements must be provided: (ix) Haemoglobin (g/L) (x) Platelets (x10 ⁹ /L) (xi) White Cell Count (x10 ⁹ /L) (xii) Reticulocytes (x10 ⁹ /L) (xiii) Neutrophils (x10 ⁹ /L) (xiv) Granulocyte clone size (%) (xv) Lactate Dehydrogenase (LDH) and the upper limit of normal (ULN) for the reporting laboratory Multiple of LDH ULN
	Note Patients may qualify for PBS-subsidised treatment under this restriction once only. For continuing PBS-subsidised treatment, a 'Grandfathered' patient must qualify under the 'Continuing Treatment' criteria.
	This grandfather restriction will cease to operate from 12 months after the date specified in the clinical criteria.
Restriction Summary [new 5] / Treatment of Concept: [new 5]	
	Category / Program: Section 100 – Highly Specialised Drugs Program (Public and Private)
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
	Restriction type: <input checked="" type="checkbox"/> Authority Required – non-immediate/delayed assessment by Services Australia (In-writing only via mail/postal service or electronic submission)
	Indication: Paroxysmal nocturnal haemoglobinuria (PNH)
	Treatment Phase: First Continuing treatment
	Clinical criteria:

Public Summary Document – July 2022 PBAC Meeting

	Patient must have received PBS-subsidised treatment with this drug for this condition under the 'initial' or 'Grandfather' treatment criteria.
	AND
	Clinical criteria:
	The treatment must not be in combination with a PBS-subsidised C5 inhibitor.
	Treatment criteria:
	Must be treated by a haematologist; OR
	Must be treated by a non-specialist medical physician who has consulted a haematologist on the patient's drug treatment details.
	Population criteria:
	Patients must be at least 18 years of age.
	Administrative advice: Complement 5 (C5) inhibitors are defined as eculizumab or ravulizumab
	Prescribing Instructions: The authority application must be made in writing and must include: (1) a completed authority prescription form; and (2) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice).
	Prescribing Instructions: At the time of the authority application, medical practitioners must request the appropriate number of vials for 4 weeks supply per dispensing as per the Product Information. A maximum of 5 repeats may be requested.
	Prescribing Instructions: At the time of the authority application, details (result and date of result) of the following monitoring requirements must be provided: (ix) Haemoglobin (g/L) (x) Platelets (x10 ⁹ /L) (xi) White Cell Count (x10 ⁹ /L) (xii) Reticulocytes (x10 ⁹ /L) (xiii) Neutrophils (x10 ⁹ /L) (xiv) Granulocyte clone size (%) (xv) Lactate Dehydrogenase (LDH) and the upper limit of normal (ULN) for the reporting laboratory (xvi) Multiple of LDH ULN
Restriction Summary [new 6] / Treatment of Concept: [new 6]	
	Category / Program: Section 100 – Highly Specialised Drugs Program (Public and Private)
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
	Restriction type: <input checked="" type="checkbox"/> Authority Required – non-immediate/delayed assessment by Services Australia (In-writing only via mail/postal service or electronic submission)
	Indication: Paroxysmal nocturnal haemoglobinuria (PNH)
	Treatment Phase: Subsequent Continuing Treatment
	Clinical criteria:
	Patient must have previously received PBS-subsidised treatment with this drug for this condition under the First Continuing Treatment; or Return criteria
	AND
	Clinical criteria:
	Patient must have demonstrated clinical improvement or stabilisation of condition.
	AND
	Clinical criteria:
	The treatment must not be in combination with a PBS-subsidised C5 inhibitor.

Public Summary Document – July 2022 PBAC Meeting

	Treatment criteria:
	Must be treated by a haematologist; OR
	Must be treated by a non-specialist medical physician who has consulted a haematologist on the patient's drug treatment details
	Population criteria:
	Patients must be at least 18 years of age
	Administrative Advice: Complement 5 (C5) inhibitors are defined as eculizumab or ravulizumab
	Prescribing Instructions: The authority application must be made in writing and must include: (1) a completed authority prescription form; and (2) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice).
	Prescribing Instructions: At the time of the authority application, medical practitioners must request the appropriate number of vials for 4 weeks supply per dispensing as per the Product Information.

6.2 Flow on changes to ravulizumab and eculizumab to allow:

- 1-switching from PBS subsidised pegcetacoplan to eculizumab for pregnancy (induction doses)
- 2-return to one of C5 inhibitors (induction doses) for patients who are intolerant/resistant to pegcetacoplan

Addition of new listing of eculizumab to switch from pegcetacoplan for pregnancy (induction doses)					
MEDICINAL PRODUCT Medicinal Product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
ECULIZUMAB					
eculizumab 300 mg/30 mL injection, 30 mL vial	New (Public) New (Private)	8	8	0	Soliris®
Restriction Summary [New 7]/ ToC [New 7]:					
	Indication: Paroxysmal nocturnal haemoglobinuria (PNH)				
	Treatment Phase: Initial treatment - (initial 3) switching from PBS-subsidised pegcetacoplan for pregnancy (induction doses)				
	Clinical criteria:				
	Patient must be planning pregnancy; or				
	Patient must be pregnant				
	AND				
	Clinical criteria:				
	Patient must have received PBS-subsidised treatment with pegcetacoplan for this condition				
	AND				
	Clinical criteria:				
	The treatment must not be in combination with either of (i) ravulizumab, (ii) pegcetacoplan				
	AND				
	Treatment criteria:				
	Must be treated by a haematologist; or				
	Must be treated by a non-specialist medical physician who has consulted a haematologist on the patient's drug treatment details				

Public Summary Document – July 2022 PBAC Meeting

<p>Prescribing Instructions: The authority application must be made in writing and must include: (1) a completed authority prescription form; and (2) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice).</p>						
<p>Prescribing Instructions: Patient may qualify under this treatment phase more than once. In the event of miscarriage, patient may continue on eculizumab if patient is stable, and/or is planning a subsequent pregnancy. For continuing PBS-subsidised treatment, a 'Switching' patient must proceed under the 'Subsequent Continuing Treatment' criteria.</p>						
<p>Addition of new restriction to allow return to one of C5 inhibitors for patients who are intolerant/resistant to pegcetacoplan</p>						
MEDICINAL PRODUCT		PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
Medicinal Product pack						
ECULIZUMAB						
eculizumab 300 mg/30 mL injection, 30 mL vial		New (Public) New (Private)	8	8	0	Soliris®
Add Restriction Summary [New 8] / ToC: [New 8]						
Indication: Paroxysmal nocturnal haemoglobinuria (PNH)						
Treatment Phase: Return from PBS subsidised pegcetacoplan - induction doses						
Clinical criteria: Patient must have received PBS-subsidised treatment with at least one Complement 5 (C5) inhibitor for this condition						
AND						
Clinical criteria: Patient must have received PBS-subsidised treatment with pegcetacoplan for this condition						
AND						
Clinical criteria: Patient must have developed resistance / intolerance to pegcetacoplan						
AND						
Clinical criteria: The treatment must not be in combination with either of (i) ravulizumab, (ii) pegcetacoplan						
AND						
Treatment criteria: Must be treated by a haematologist; or Must be treated by a non-specialist medical physician who has consulted a haematologist on the patient's drug treatment details						
Administrative Advice: Complement 5 (C5) inhibitors are defined as eculizumab or ravulizumab						
<p>Prescribing Instructions: The authority application must be made in writing and must include: (1) a completed authority prescription form; and (2) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice).</p>						
<p>Prescribing Instructions: Where long-term continuing PBS-subsidised treatment with this drug is planned, a 'Returning' patient may proceed under the 'Subsequent Continuing Treatment' criteria.</p>						

Public Summary Document – July 2022 PBAC Meeting

Addition of new restriction to allow return to one of C5 inhibitor for patients who are intolerant/resistant to pegcetacoplan					
MEDICINAL PRODUCT Medicinal Product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
RAVULIZUMAB					
ravulizumab 1.1 g/11 mL injection, 11 mL vial	New (Public) New (Private)	1	1	0	Ultomiris®
ravulizumab 300 mg/3 mL injection, 3 mL vial					
Add Restriction Summary [New 9] / ToC: [New 9]					
Indication: Paroxysmal nocturnal haemoglobinuria (PNH)					
Treatment Phase: Return from PBS subsidised pegcetacoplan – induction dose					
Clinical criteria: Patient must have received PBS-subsidised treatment with at least one Complement 5 (C5) inhibitor for this condition					
AND					
Clinical criteria: Patient must have received PBS-subsidised treatment with pegcetacoplan for this condition					
AND					
Clinical criteria: Patient must have developed resistance / intolerance to pegcetacoplan					
AND					
Clinical criteria: The treatment must not be in combination with either of (i) eculizumab, (ii) pegcetacoplan					
AND					
Treatment criteria: Must be treated by a haematologist; or Must be treated by a non-specialist medical physician who has consulted a haematologist on the patient's drug treatment details					
Administrative Advice: Complement 5 (C5) inhibitors are defined as eculizumab or ravulizumab					
Prescribing Instructions: The authority application must be made in writing and must include: (1) a completed authority prescription form; and (2) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice).					
Prescribing Instructions: Where long-term continuing PBS-subsidised treatment with this drug is planned, a 'Returning' patient may proceed under the 'Subsequent Continuing Treatment' criteria.					

This restriction may be subject to further review. Should there be any changes made to the restriction the sponsor will be informed.

7 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS

listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

8 Sponsor's Comment

Sobi welcomes the positive recommendation made by the PBAC which will provide Australian PNH patients with access to an additional treatment option via a different mechanism of action to those already available.