NICE National Institute for Health and Care Excellence

PART 1

Slides for all - contain no ACIC data

Pegcetacoplan for treating paroxysmal nocturnal haemoglobinuria

Chair: Peter Selby
Lead team: Mudasar Mushtaq, Richard Nicholas, Stella O'Brien
ERG: Liverpool Reviews & Implementation Group (LRiG)
Technical team: Anita Sangha, Hannah Nicholas, Linda Landells
Company: Swedish Orphan Biovitrum (Sobi)
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Fast track appraisals: low ICER appraisal

This topic is a low ICER FTA

- FTAs are appraisals in which less-detailed discussion is sufficient.
- Low ICER FTA considered if:
  - the company's deterministic and probabilistic base-case ICER are less than £10,000 per QALY gained
  - it is likely that the most plausible ICER for a technology is less than £20,000 per QALY gained, and it is highly unlikely that it is greater than £30,000 per QALY gained.

Possible recommendations in a low ICER FTA include:

✓ The committee will recommended the technology as an option.

✓ The ICER is higher than £20,000 but the technology can be recommended.

X The ICER is higher than £30,000 or uncertain so the technology cannot be recommended.

? Request for further exploratory analyses from the company and a critique of these from the ERG, to be discussed at a subsequent committee meeting.

Disease background summary

- Paroxysmal nocturnal haemoglobinuria (PNH) is a rare blood condition in which red blood cells are attacked by the body's immune system.
- It is characterised by intravascular haemolysis (rupturing of red blood cells) with resultant anaemia often leading to transfusion dependence, severe disabling symptoms of haemolysis and, frequently, thrombosis (blood clotting).
- PNH can also lead to extravascular haemolysis (haemolysis taking place in the liver, spleen, bone marrow, and lymph nodes).
- It is estimated that there are about 650 to 900 people in England with PNH.
- Current treatments include complement C5 inhibitors: eculizumab and ravulizumab.

Company's description of pegcetacoplan compared to current treatments:

- C5 inhibitors target underlying intravascular haemolysis (IVH), but do not address extravascular haemolysis (EVH).
- Pegcetacoplan is a complement C3 inhibitor which prevents both IVH and EVH by targeting the complement cascade earlier than C5 inhibitors.

Summary of key considerations

Considerations for committee	Risk level
• The assumption of equal efficacy between ravulizumab and eculizumab in the PEGASUS trial population is reasonable.	Low
• The ERG considers that the company's model is well built and satisfactorily reflects the treatment pathway for PNH.	
• All scenario and sensitivity analyses carried out by the company and ERG show that pegcetacoplan dominates both eculizumab and ravulizumab.	
• The ERG considers that the most plausible ICERs for pegcetacoplan versus eculizumab and pegcetacoplan versus ravulizumab are below £20,000 per QALY gained.	
• Risk to NHS is low: small eligible population and high comparator costs.	

Based on the above, there are no critical issues for consideration by the committee, therefore is the committee satisfied that:

- ***the most plausible ICERs for pegcetacoplan compared with eculizumab and ravulizumab are less than £20,000 per QALY gained? And therefore,***
- ***pegcetacoplan should be recommended via the low ICER FTA route?***

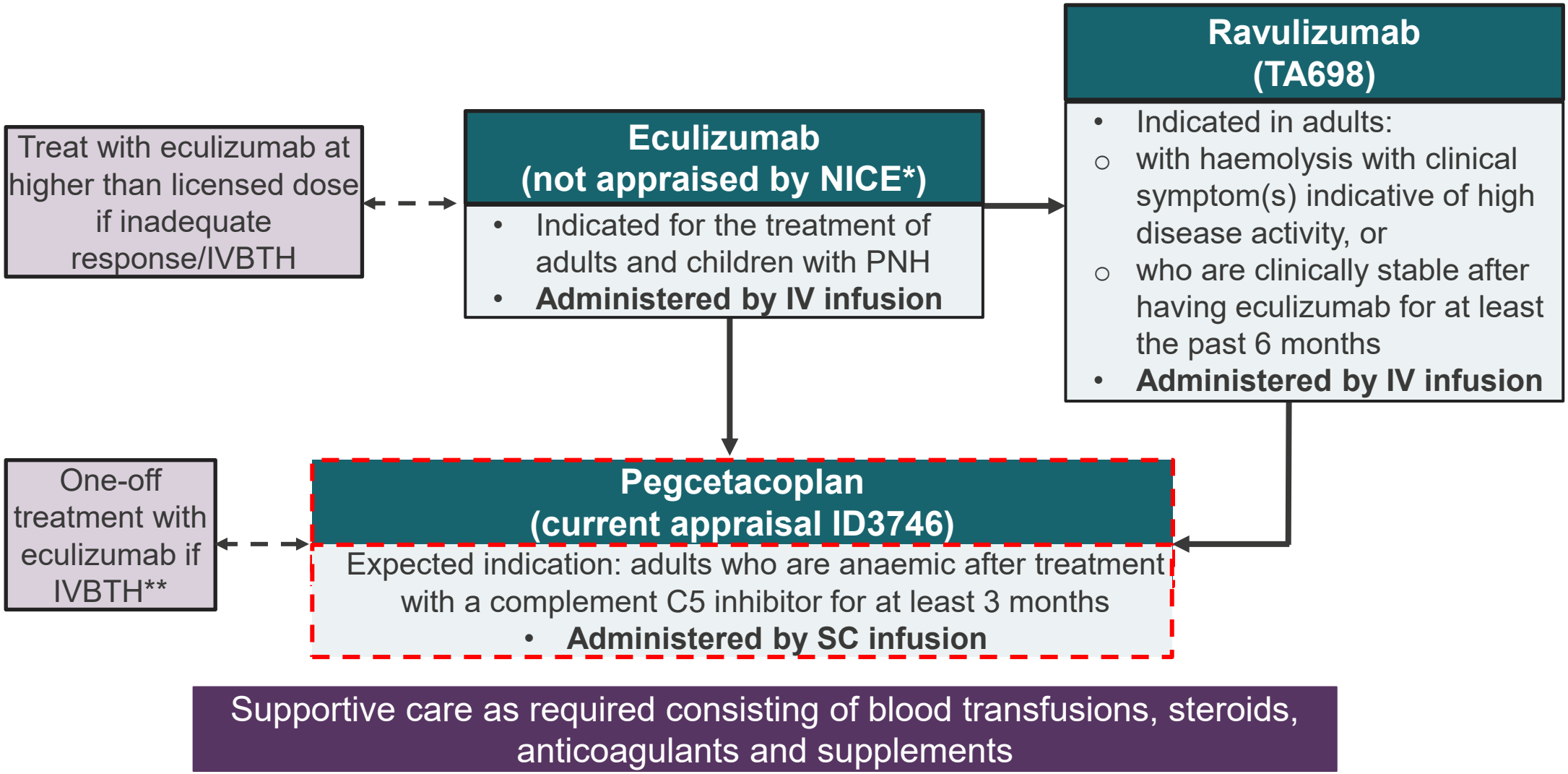
Patient, carer and clinician perspectives

Pegcetacoplan offers benefits to people with PNH

- C5 inhibitors have significantly reduced the burden of PNH, however some people still experience EVH and anaemia requiring blood transfusions whilst on treatment. This population has the potential to benefit significantly from pegcetacoplan.
- Current treatment can be inconvenient for some people because a healthcare professional is needed to administer the intravenous infusion at a person's home and frequent canulation can be difficult if venous access is poor.
- Pegcetacoplan is self-administered via the subcutaneous route which is more convenient. However, it is administered more frequently than existing treatments and this may increase the likelihood of injection-site reactions.
- Pegcetacoplan offers many benefits including:
  - improvement of symptoms including fatigue and energy levels
  - reduced need for blood transfusions as a result of anaemia, which together with self-administration results in a decreased burden on the NHS
  - improved quality of life, including a positive impact on a person's mental health, social and family life and ability to work.

Submissions from 2 patient experts, 1 patient organisation (PNH support) and 1 clinical expert

Company's positioning of pegcetacoplan



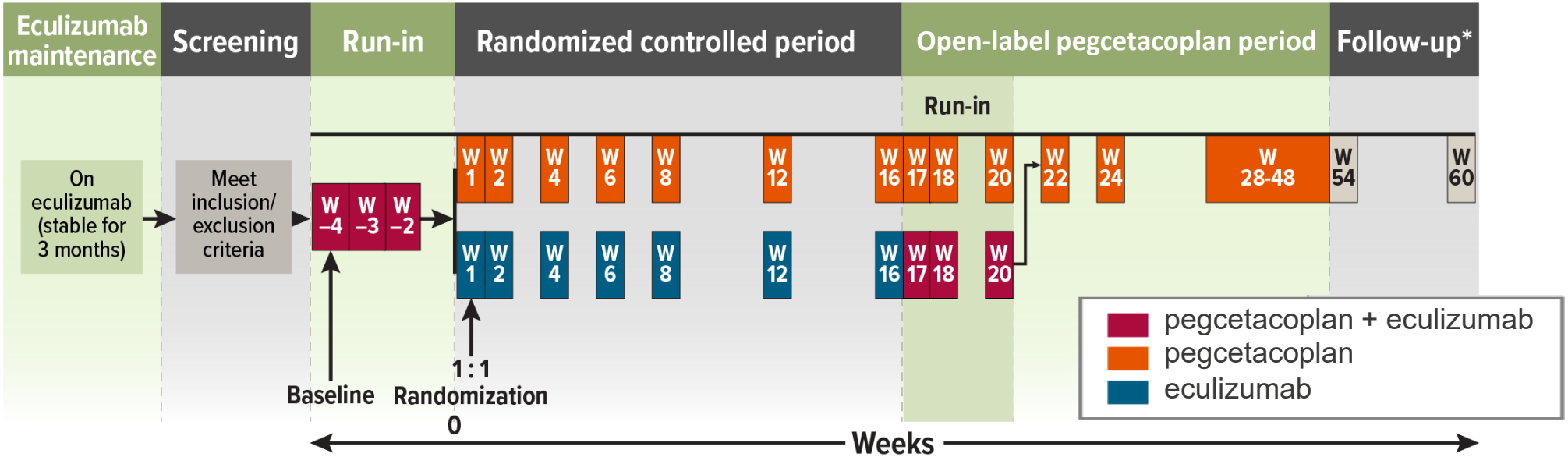
IV = intravenous; IVBTH = intravascular breakthrough haemolysis, SC = subcutaneous

* Eculizumab has not been appraised by NICE for PNH, but is available through a highly specialised service.

** Clinical advice to the company is that IVBTH would be treated in people having pegcetacoplan with a one-off 900 mg dose of eculizumab.

Summary of clinical effectiveness evidence (1)

PEGASUS trial: phase 3, multicentre, open-label, active-comparator, randomised controlled trial comparing pegcetacoplan (n=41) with eculizumab (n=39) in adults with PNH who had haemoglobin levels <105 g/L despite treatment with eculizumab



Source: company submission Figure 4.

- ERG considers that trial was well-designed, well-conducted and appropriate statistical techniques were used to analyse the data.
- **Primary outcome: change from baseline in haemoglobin level at week 16 was statistically significantly higher in the pegcetacoplan arm compared to the eculizumab arm.**
- Clinical advice to the company and ERG suggests that the PEGASUS trial results are generalisable to the population who would receive pegcetacoplan in NHS clinical practice.

Summary of clinical effectiveness evidence (2)

Assumption of equal efficacy between ravulizumab and eculizumab

- In the absence of robust evidence comparing treatment efficacy of pegcetacoplan and ravulizumab, the company assumed equal efficacy between ravulizumab and eculizumab in the PEGASUS trial population:
  - ravulizumab is a re-engineered form of eculizumab (over 99% homology)
  - the committee concluded in TA698 that ravulizumab and eculizumab were similarly effective and had a similar safety profile
  - clinical advice to the ERG is that ravulizumab and eculizumab are biologically very similar and the efficacy of the 2 treatments is likely to be equal in any population.

Summary of cost effectiveness evidence

Model and cost effectiveness results

- ERG considers that the company's model is largely well built and the model structure reflects the PNH treatment pathway. It made 2 minor revisions to the company's base case which did not change the cost effectiveness conclusions.

Base case results	Deterministic		Probabilistic	
	Company	ERG	Company	ERG
Pegcetacoplan versus eculizumab [a]	Pegcetacoplan dominates		Pegcetacoplan dominates	
Pegcetacoplan versus ravulizumab [b]	Pegcetacoplan dominates		Pegcetacoplan dominates	

[a] ICERs include PAS for pegcetacoplan; [b] ICERs include PAS for pegcetacoplan and cPAS for ravulizumab.

Sensitivity and scenario analyses

- Results from all scenario and sensitivity analyses carried out by the company and ERG show that pegcetacoplan dominates both eculizumab and ravulizumab.
- ERG is satisfied that the most plausible ICERs for comparisons of pegcetacoplan with both eculizumab and ravulizumab are below £20,000 per QALY gained.

Innovation

Comments raised by company, clinical/patient experts, patient organisation:

- Pegcetacoplan will be the first and only C3 inhibitor that can effectively control PNH by preventing both intravascular and extravascular haemolysis.
- Pegcetacoplan is the first self-administered subcutaneous infusion therapy in PNH.

Equality

Potential issues raised during scoping:

- Because pegcetacoplan is given by subcutaneous injection and can be self-administered at home, this may have implications for people who have physical or learning disabilities as they may struggle with the self-administration, especially if they have manual dexterity issues.*
- Age and pregnancy were highlighted as protected characteristics. Inequalities may arise if different recommendations are made for children and pregnant women.

- **Children and pregnant women were excluded from the PEGASUS trial. Clinical expert submission to NICE states that pegcetacoplan should not be used in pregnancy.**
- **The committee can only make recommendations within a technology's marketing authorisation.**

*Text has been amended after the committee meeting for clarity

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