A.12 Emicizumab – EML and EMLc

Reviewer summary	☒ Supportive of the proposal (at least in part) ☐ Not supportive of the proposal Justification (based on considerations of the dimensions described below): <u>Patients with FVIII inhibitors</u> There is robust clinical trial and real-world evidence supporting the contention that emicizumab is a major advance in care for patients with Hemophilia A who have a history for Factor VIII (FVIII) inhibitors. That case is well presented in the application before the committee and also clearly summarised in other reports eg the 2018 ICER report. For people with FVIII inhibitors, emicizumab reduces bleeds by 90%, reduces bypass agent use, increases the chances of being bleed-free, maintains joint function, reduces surgical risks and reduces caregiver burden. When compared with bypass agents as prophylaxis, emicizumab is both more effective and cost-saving in many country-specific economic analyses. Where analyses comparing emicizumab versus "on demand" bypass agent use have been performed, it is more effective while more expensive, but remains cost-effective. The totality of the data makes a compelling case that emicizumab prophylaxis is the management of choice for patients with FVIII inhibitors. This view will remain unchanged regardless of whether recombinant FVIII products are included on the core or complementary EML and EMLc after deliberation on that issue by the Expert Committee. <u>Patients without FVIII inhibitors</u> Again, the trial and real-world data indicate that emicizumab is superior to FVIII prophylaxis in patients with severe Hemophilia A. Whether it is superior to newer extended half-life and ultra-extended half-life recombinant FVIII products which are available in some countries is not established. Depending on country/jurisdiction, cost-effectiveness analyses have reported emicizumab to be cost-effective versus alternatives in the USA, but not in Europe, UK, etc. The acquisition costs of emicizumab are the major determinant of value for money for this product in this clinical situation. Emicizumab is a desirable alternative to FVIII products. However, the case for essentiality in patients without inhibitors is not as strong as it is in people with FVIII inhibitors when alternatives (such as blood-derived FVIII or recombinant FVIII) are both available and substantially cheaper.
Does the EML and/or EMLc currently recommend alternative medicines for the proposed indication that can be considered therapeutic alternatives? (**https://list.essentialmeds.org/**)	☒ Yes ☐ No ☐ Not applicable
Does adequate evidence exist for the efficacy/effectiveness of the medicine for the proposed indication? (e.g., evidence originating from multiple high-quality studies with sufficient follow up. This may be evidence included in the application, and/or additional evidence identified during the review process;)	☒ Yes ☐ No ☐ Not applicable
Does adequate evidence exist for the safety/harms associated with the proposed medicine? (e.g., evidence originating from multiple high-quality studies with sufficient follow up. This may be evidence included in the application, and/or additional evidence identified during the review process;)	☒ Yes ☐ No ☐ Not applicable
Overall, does the proposed medicine have a favourable and meaningful balance of benefits to harms?	☒ Yes ☐ No ☐ Not applicable

Are there any special requirements for the safe, effective and appropriate use of the medicines? (e.g. laboratory diagnostic and/or monitoring tests, specialized training for health providers, etc)	☒ Yes ☐ No ☐ Not applicable
Are there any issues regarding price, cost-effectiveness and budget implications in different settings?	☒ Yes ☐ No ☐ Not applicable
Is the medicine available and accessible across countries? (e.g. shortages, generics and biosimilars, pooled procurement programmes, access programmes)	☒ Yes ☐ No ☐ Not applicable
Does the medicine have wide regulatory approval?	☒ Yes, for the proposed indication ☐ Yes, but only for other indications (off-label for proposed indication) ☐ No ☐ Not applicable