

C.4	Coagulation factors for haemophilia – review of square box alternatives – EML and EMLc
Draft recommendation	<input type="checkbox"/> Recommended <input checked="" type="checkbox"/> Not recommended Justification: I think an appropriate application for recombinant coagulation factors (as treatment, prophylaxis, and bypassing factors) should be developed as current guidelines recommend that recombinant products should be used in preference to plasma-derived products. Same consideration for coagulation factor IX complex, emicizumab (bispecific monoclonal antibody FVIII mimetic)
Does the proposed medicine address a relevant public health need?	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not applicable Comments: Hemophilia affects more than 1.2 million individuals (mostly males) worldwide. <ul style="list-style-type: none"> • Hemophilia A – Incidence is around 1 in 4000 to 1 in 5000 live male births. Approximately ½ to 2/3 have severe disease (factor VIII activity <1% of normal). • Hemophilia B – Incidence is around 1 in 15,000 to 1 in 30,000 live male births. Approximately 1/3 to ½ have severe disease (factor IX activity <1% of normal).
Does adequate evidence exist for the efficacy/effectiveness of the medicine for the proposed indication? (this may be evidence included in the application, and/or additional evidence identified during the review process)	<input type="checkbox"/> Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> Not applicable Comments: Not reported in the application
Does adequate evidence exist for the safety/harms associated with the proposed medicine? (this may be evidence included in the application, and/or additional evidence identified during the review process)	<input type="checkbox"/> Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> Not applicable Comments: Not reported in the application

<p>Are there any adverse effects of concern, or that may require special monitoring?</p>	<p><input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not applicable Comments: Some of the factors mentioned can be associated with thromboembolism between others</p>
<p>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)</p>	<p><input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not applicable Comments: Involvements of a hematologists is required. Additionally, careful management and testing of blood derived products is required.</p>
<p>Are there any issues regarding cost, cost-effectiveness, affordability and/or access for the medicine in different settings?</p>	<p><input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not applicable Comments:</p>
<p>Are there any issues regarding the registration of the medicine by national regulatory authorities? (e.g. accelerated approval, lack of regulatory approval, off-label indication)</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> Not applicable Comments: Not reported in the application</p>
<p>Is the proposed medicine recommended for use in a current WHO guideline? (refer to: https://www.who.int/publications/who-guidelines)</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> Not applicable Comments:</p>

Iorio A, Stonebraker JS, Chambost H, et al. Establishing the Prevalence and Prevalence at Birth of Hemophilia in Males: A Meta-analytic Approach Using National Registries. Ann Intern Med 2019; 171:540.