A.12	Equine rabies immunoglobulin – rabies post-exposure prophylaxis
Does the application adequately address the issue of the public health need for the medicine?	☒ Yes ☐ No ☐ Not applicable Comments:
Briefly summarize the role of the proposed medicine(s) relative to other therapeutic agents currently included in the Model List, or available in the market.	Rabies immune globulin (RIG) products are used during post-exposure prophylaxis (PEP) to neutralize rabies virus locally at the wound site, while an active response to rabies vaccine is mounting. The RIG is derived from the plasma either of horses (eRIG) or humans (hRIG). Despite the extensive data that demonstrate both safety and efficacy, eRIG is not always used, even when available, due in part to prior medical concerns over the historical use of crude horse serum or unpurified eRIG.
Have all important studies and all relevant evidence been included in the application?	☒ Yes ☐ No ☐ Not applicable If no, please provide brief comments on any relevant studies or evidence that have not been included:
Does the application provide adequate evidence of efficacy/effectiveness of the medicine for the proposed indication?	☒ Yes ☐ No ☐ Not applicable Briefly summarize the reported benefits (e.g. hard clinical versus surrogate outcomes) and comment, where possible on the actual magnitude and clinical relevance of benefit associated with use of the medicine(s). There are no human clinical studies comparing efficacy of eRIG vs. hRIG. One study (Madhusudana et al., 2013) compared the neutralization effectiveness of reduced eRIG and hRIG in cell culture and in mice: in vitro, neutralization of rabies virus by eRIG and hRIG were identical, while in vivo, full protection was conferred by both (Madhusudana et al., 2013). Moreover, no vaccine was administered to those animals that received RIG, yet the experimental groups that received at least 0.025 IU/100 µl of either eRIG or hRIG had a 100% survival rate, compared to 100% morality in the control group. Is there evidence of efficacy in diverse settings (e.g. low-resource settings) and/or populations (e.g. children, the elderly, pregnant patients)? Not applicable as there are no human studies.
Does the application provide adequate evidence of the safety and adverse effects associated with the medicine?	☒ Yes ☐ No ☐ Not applicable Comments: Modern eRIG is highly purified and enzyme-refined and contains over 85% antigen-binding Ig fragments.

Are there any adverse effects of concern, or that may require special monitoring?	☐ Yes ☒ No ☐ Not applicable Comments: Very rarely serum sickness and anaphylaxis has been reported. Need to consider this.
Briefly summarize your assessment of the overall benefit to risk ratio of the medicine (e.g. favourable, uncertain, etc.)	Favourable. Considering the purified eRIG availability, similar efficacy as hRIG in animal experiments and rare side effects this drug should be included in EML and EMLc.
Briefly summarize your assessment of the overall quality of the evidence for the medicine(s) (e.g. high, moderate, low etc.)	As suggested that there are no comparative human studies with eRIG and hRIG however there is high evidence from human studies that post-exposure prophylaxis with RIG is highly effective in prevention of Rabies
Are there any special requirements for the safe, effective and appropriate use of the medicine(s)**?** (e.g. laboratory diagnostic and/or monitoring tests, specialized training for health providers, etc)	☐ Yes ☒ No ☐ Not applicable Comments:
Are you aware of any issues regarding the registration of the medicine by national regulatory authorities? (e.g. accelerated approval, lack of regulatory approval, off-label indication)	☐ Yes ☒ No ☐ Not applicable Comments:
Is the proposed medicine recommended for use in a current WHO Guideline approved by the Guidelines Review Committee? (refer to: https://www.who.int/publications/who-guidelines)	☒ Yes ☐ No ☐ Not applicable Comments: Rabies vaccines: WHO position paper – April 2018
Briefly summarize your assessment of any issues regarding access, cost and affordability of the medicine in different settings.	eRIG is less costly than hRIG which makes it more affordable.
Any additional comments	

Based on your assessment of the application, and any additional evidence / relevant information identified during the review process, briefly summarize your proposed recommendation to the Expert Committee, including the supporting rationale for your conclusions, and any doubts/concerns in relation to the listing proposal.	Include EML and EMLc for rabies post-exposure prophylaxis. Considering the purified eRIG availability, similar efficacy as hRIG in animal experiments and rare side effects this drug should be included in EML and EMLc.
References (if required)	