WHO/MCA Department inputs and comments on selection and use of essential medicines for discussion at the 25th expert committee, 5-9 May 2025

Dear EML Secretariat,

Thanks for the request to provide inputs and comments on selection and use of essential medicines. The WHO/MCA department has reviewed the relevant applications submitted and proposed changes on EMLc, specifically, F.2 Phytomenadione, new formulation – mixed micelle solution, I.8 Prednisolone for Adrenal insufficiency, C.2 Medicines for haemoglobinopathies, and A.24 Risdiplam for Spinal muscular atrophy.

Our input and recommendations are as follows:

1. Regarding the application to include Phytomenadione (Vitamin K1) mixed micelle (MM) solution on the WHO EMLc, WHO/MCA recommends the inclusion of Phytomenadione MM solution EMLc for prevention and treatment haemorrhagic disease of the newborn. (***See details attached***).

2. Regarding the application to include, WHO/MCA recommends inclusion of prednisolone on adult EML and not on the EMLc due to its long-acting nature and the potential for adverse impacts on growth. This approach ensures that the medication is available for those who can benefit from it while minimizing the risks for younger patients. (***See details attached***)

3. Changes to listings 10.3.1 Medicines for sickle-cell disease, WHO/MCA recommends that hydroxyurea (hydroxycarbamide) is included in the EMLc as "**10.3 Medicine for haemoglobinopathies**", rather than "other," and not as a “complementary list” but as a main essential treatment. Hydroxyurea (hydroxycarbamide) is currently recommended by WHO as a disease modifying agent for treatment of all children over 9 months of age with sickle cell disease regardless of clinical severity.

4. Regarding the application to include Risdiplam for treatment of Spinal muscular atrophy (SMA)on the WHO EMLc, although WHO/MCA does not have the specific expertise in this area, Risdiplam being the only oral disease-modifying therapy available today for the treatment of SMA, and may be the best choice for the LMICs. Therefore, WHO/MCA proposes that it be included on the EMLc.

For any further clarifications, please feel free to contact Dr Wilson Were, at werew@who.int.

Best regards,

Dr Anshu Banerjee
Director, WHO Department of Maternal, Newborn, Child and Adolescent Health and Ageing

Application to include Phytomenadione mixed micelle solution on the WHO Model List of Essential Medicines

Dear EML Secretariat,

Regarding the application to include Phytomenadione (Vitamin K1) mixed micelle (MM) solution on the WHO essential Medicine List for Children (WHO EMLc) for prevention and treatment of haemorrhagic disease of the newborn (VKDB), WHO/MCA considers inclusion of Phytomenadione MM will ensure availability and access Vitamin K prevention and treatment. The different formulations of Phytomenadione MM solution will provide alternative formulation in view of the ongoing scarcity we have experienced in the last two years.

Vitamin K Deficiency Bleeding is a serious condition in newborns caused by insufficient vitamin K, leading to uncontrolled internal or external bleeding. This can result in severe complications, including brain and organ damage, or even death. WHO recommends a single vitamin K shot at birth to prevent VKDB, significantly reducing the risk of life-threatening bleeds. Despite being preventable, VKDB remains a critical health issue, highlighting the need for effective prophylactic measures and widespread availability of vitamin K formulations.

This proposal is supported based on the evidence provided on the efficacy of Phytomenadione MM which has been shown to be highly effective in preventing and treating VKDB. Studies have demonstrated that this formulation is absorbed faster and more efficiently than other formulations, leading to higher plasma vitamin K1 levels and lower PIVKA-II concentrations. This indicates superior bioavailability and faster pharmacodynamic response, making it a reliable option for prophylaxis and treatment.

In addition, Phytomenadione MM can be administered orally, intramuscularly, or intravenously, providing flexibility in treatment options. The oral administration is particularly beneficial for routine prophylaxis, while intramuscular and intravenous routes are essential in life-threatening situations where rapid increase in plasma levels is required.

In terms of the cost, Phytomenadione MM is relatively low, with prices ranging from $0.26 to $3.00 per ampoule for the 2 mg/0.2 mL formulation and $0.35 to $4.00 per ampoule for the 10 mg/1 mL formulation. This makes it a cost-effective option for both prophylaxis and treatment.

The evidence supports its efficacy, safety, and economic benefits, making it a valuable addition to essential medicine lists globally. The inclusion of Phytomenadione MM solution in the WHO EMLc would widen the choice of options for vitamin K formulations, and hence improve access to prevention and treatment.

Conclusion

In view of the above, WHO/MCA recommends inclusion of Phytomenadione MM in the WHO Model List of Essential Medicines for children to ensure broader availability and access to effective, flexible, and cost-effective treatment for VKDB and other conditions requiring vitamin K.

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