A.22	Multiple Micronutrient supplements (MMS) – Pregnancy
Does the application adequately address the issue of the public health need for the medicine?	☒ Yes ☐ No ☐ Not applicable Comments: The application shows the elevated prevalence of micronutrient deficiency around the world in women of reproductive age while highlighting the role of micronutrients in foetal development; neonatal and maternal outcomes.
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.	A nutritional supplement specific for pregnant women is not included in the EML
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). A Cochrane review including 19 trials showed that MMS was associated with a lower rates of low birth weight (LBW) and small for gestational age (SGA) when compared to iron and folic acid (IFA) supplementation. Subgroup analysis showed that MMS was not associated with lower rates of SGA in women with BMI<20 and in women with a height <154.9 cm. On the other hand, women with BMI <20 who received MMS had lower rates of preterm birth. Individual patient meta-analysis showed statistically significant benefits of MMS over IFA in the following outcomes: stillbirth, LBW, early preterm birth, preterm birth, SGA. It also showed that MMS was associated with increased risk of LGA, with no increased risk of still birth and mortality (even in women <1.5m). Benefits were more significant among specific subgroups for some of the outcomes: Mother's with anaemia, mother who were underweight, female infants. Is there evidence of efficacy in diverse settings (e.g. low-resource settings) and/or populations (e.g. children, the elderly, pregnant patients)? Yes. Studies were developed in America, Asia and Africa, most of them in low resource settings. Also most of the studies in the systematic review did not exclude women with chronic on conditions and or/ pregnancy complications.

Does the application provide adequate evidence of the safety and adverse effects associated with the medicine?	☒ Yes ☐ No ☐ Not applicable Comments: No severe side effects have been reported with use. Also, doses included in the MMS are considered safe.
Are there any adverse effects of concern, or that may require special monitoring?	☐ Yes ☒ No ☐ Not applicable Comments:
Briefly summarize your assessment of the overall benefit to risk ratio of the medicine (e.g. favourable, uncertain, etc.)	Favourable. I consider MMS has shown clear benefits with minimal risks if any.
Briefly summarize your assessment of the overall quality of the evidence for the medicine(s) (e.g. high, moderate, low etc.)	Evidence is high to moderate quality considering there are 2 big well conducted systematic review supporting the benefits of MMS.
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: There is no consensus about the regulatory status. It is considered a nutritional supplement in some countries while others regulate it as drug. There are strategies in place to help with this issue.

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: It is recommended in the following guidelines: • Preventing and controlling micronutrient deficiencies in populations affected by an emergency • Micronutrient supplementation in individuals with active tuberculosis They are also recommended by the guidelines developed by UNICEF and The World Food Programme titled: *Protecting Maternal Diets and Nutrition Services and Practices in the Context of COVID-19*
Briefly summarize your assessment of any issues regarding access, cost and affordability of the medicine in different settings.	There are no major issues related to cost or access. Transitioning from IFA to MMS shows to be cost-effective according to 2 modelling analysis. Even when the cost is variable I consider that the potential benefits of MMS justify the cost. Additionally, there seems to be global capacity to manufacture enough product to supply current demands.
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. I consider there is enough evidence to include MMS in the EML as the results of 2 well conducted systematic reviews that adequately represent the population of interest showed clear benefits. MMS also seems as a safe option already available in a big part of the developing world with strategies in place to reach the target population.
References (if required)	