Expert peer review on application for intermittent iron and folic acid supplementation for prevention of anaemia in menstruating women and adolescent girls.

1. **Assessment of efficacy**
   a. Have all relevant studies on efficacy been included
      - Yes  No  (if no, please provide reference and information)

      b. Summarize the data on efficacy, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)

      Intermittent supplementation with iron (with or without folic acid) in menstruating women is effective in decreasing the risk of anaemia, and increasing haemoglobin and ferritin concentrations. Positive effects of intermittent supplementation were seen in patients receiving iron once or twice per week. Furthermore, the haematological responses were evaluated with supplements containing more or less than 60 mg of elemental iron per week for duration of 3 months or less or more than 3 months.

      c. Please provide any additional relevant information with reference

2. **Assessment of safety**
   a. Have all relevant studies on safety been included
      - Yes  No  (if no, please provide reference and information)

      b. Summarize the data on safety, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)

      The most common side-effects of iron supplementation include nausea, constipation, dark stools, and metallic taste. The current evidence suggests there is no significant difference in adverse side-effects between once weekly intermittent iron supplementation versus no intervention or placebo (RR 1.98, 95% CI 0.31 to 12.72) and between once weekly intermittent iron supplementation versus daily iron supplementation (RR 0.36, 95% CI 0.10 to 1.31).

      c. Please provide any additional relevant information with reference

3. **Assessment of cost and availability**
   a. Have all relevant data on safety provided
      - Yes  No  (if no, please provide reference and information)

      Yes
b. Summarize the data on cost and cost effectiveness, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)

Currently there are no available iron and folic acid supplements in the market for this intervention with the recommended composition. No Fe 60+FA 2.8 mg manufacturer found.

c. Please provide any additional relevant information with reference

d. Is the product available in several low and middle income countries?

Iron and Folic acid supplements are available in the majority of National Essential Medical Lists of Low and middle income countries.

None of the NEMLs surveyed contained a combination of 60 mg elemental iron with 2.8 Mg folic acid.

4. Assessment of public health need

a. Please provide the public health need for this product (1-2 sentences)

The world-wide prevalence of anaemia in non-pregnant women is estimated at 30.2%.

Anaemia impairs resistance to infection and reduces physical capacity and work performance among all age groups. In addition, women with anaemia who become pregnant are at higher risk of negative maternal and neonatal outcomes.

b. Do guidelines (especially WHO guidelines) recommend this product? If yes, which ones? List 1 or 2 international preferable


5. Are there special requirements for use or training needed for safe/effective use?

If yes, please provide details in 1-2 sentences

N/A

6. Is the proposed product registered by a stringent regulatory authority?

Yes    No

Both iron and folic acid supplements are currently on the WHO/EML for adults.

7. Any other comments

8. What is your recommendation to the committee (please provide the rationale)

There is sufficient evidence to show that intermittent supplementation with iron and folic acid is a feasible and effective public health policy to decrease the risk of anaemia in menstruating women and adolescent girls. The addition of folic acid can help prevent neural tube defect-affected pregnancies should a woman become pregnant.
The recommendations for changes to the EML Section 10.1 - Antanaemia Medicines, are as follows:

1. Add 60 mg elemental iron in a ferrous form plus 2.8 mg folic acid tablet/capsule formulation for the prevention of anaemia in menstruating women.
   a. Dose
      i. 60 mg of elemental iron equals 300 mg of ferrous sulfate heptahydrate, 180 mg of ferrous fumarate or 500 mg of ferrous gluconate.
   b. Frequency and duration of intermittent supplementation
      i. Once weekly for menstruating women for three months followed by 3 months of no supplementation, after which the provision of supplements should restart.
      ii. If feasible, intermittent supplements could be given throughout the school or calendar year.