19th Expert Committee on The Selection and Use of Essential Medicines

April 8-12 2013

Expert peer review on application for addition of misoprostol for treatment of postpartum haemorrhage

1. Assessment of efficacy
   a. Have all relevant studies on efficacy been included
      Yes

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

      2 published RCTs compared misoprostol to placebo (Blum et al 2010, Winikoff et al 2010) and an “expert” review (Sheldon 2012)
      Winikoff: misoprostol compared to oxytocin: increased risk of blood loss above 300ml (RR 1.78 (1.4-2.26), blood transfusion 1.58 (.98-2.55)
      Blum: misoprostol compared to oxytocin: increased risk of blood loss above 300ml (RR 1.12 (.92-1.37), blood transfusion 1.32 (.73-2.39)

   c. Please provide any additional relevant information with reference

2. Assessment of safety
   a. Have all relevant studies on safety been included
      Yes

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

      Rates of fever and shivering dose related and dependent on route, greater than oxytocin shivering RR 2.8 (2.25-3.49), fever RR 8.07 (5.52-11.8)

   c. Please provide any additional relevant information with reference

3. Assessment of cost and availability
   a. Have all relevant data on cost provided
      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)

      off patent, affordable

   c. Please provide any additional relevant information with reference
d. Is the product available in several low and middle income countries?

Yes

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

Yes, about one fourth of maternal deaths due to PPH

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

yes, several, but recommend when oxytocin is not available or practical. From WHO 2012 recommendations for the prevention and treatment of PPH.

In settings where skilled birth attendants are not present and oxytocin is unavailable, the administration of misoprostol (600 μg PO) by community health care workers and lay health workers is recommended for the prevention of PPH.

If intravenous oxytocin is unavailable, or if the bleeding does not respond to oxytocin, the use of intravenous ergometrine, oxytocin-ergometrine fixed dose, or a prostaglandin drug (including sublingual misoprostol, 800 μg) is recommended.

5. Are there special requirements for use or training needed for safe/effective use?
   If yes, please provide details in 1-2 sentences

In contrast to the alternative oxytocin, there are less stringent requirements for transport, storage and administration

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

   Yes    No

7. Any other comments

Already in section 22.1 oxytocics for different indication

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

Maintain current listing of misoprostol in Section 22.1 with statement “, and for prevention of postpartum haemorrhage where oxytocin is not available or cannot be safely used”

This is consistent with current guidelines and supported by the two recent trials showing no benefit of misoprostol over oxytocin