Dear Committee Members:

We are pleased to submit this application requesting that misoprostol be listed for its postpartum hemorrhage prevention indication on the WHO’s Model List of Essential Medicines (EML) in section 22.01.00.00 “Oxytocics”. Postpartum hemorrhage (PPH) remains one of the largest contributors to maternal morbidity and mortality in low-resource settings; accounting for nearly one quarter of all maternal deaths worldwide. Prevention of PPH is paramount to reducing the overall burden of PPH globally and, in turn, to contributing to efforts aimed at achieving the United Nation’s Millennium Development Goal (#5) to reduce maternal mortality by 15% by the year 2015. Misoprostol is an evidence-based alternative to the standard uterotonicics, such as oxytocin and ergometrine, administered to women post-partum to prevent bleeding. Unlike these standard uterotonicics, which require a cold chain and skilled administration, misoprostol is stable at room temperature and its simple tablet form facilitates its use by providers at all levels of the health care system. The drug’s ease of use and low-cost makes it ideally suited for delivery in low resource settings and, thus, enhances the full package of interventions available to prevent PPH.

Several medical bodies, including The International Federation of Gynecologists and Obstetricians (FIGO), The Royal College of Obstetricians and Gynecologists (RCOG) and the International Consortium of Midwives (ICM) endorse the use of misoprostol in the prevention of PPH in various circumstances. Furthermore, in its 2007 document entitled “Recommendations for the Prevention of Postpartum Haemorrhage” the World Health Organization acknowledges that misoprostol may be used as PPH prevention in the absence of active management of the third stage of labor. In its 2006 policy statement on the management of the third stage of labor to prevent postpartum hemorrhage, FIGO and ICM recommend the use of misoprostol for PPH prevention when oxytocin is not available and/or birth attendant’s skills are limited.

In early 2009, a previous request for misoprostol to be listed for the prevention of postpartum hemorrhage on the Model List of Essential Medicines (EML) was declined. At that time, the Committee cited a need for more evidence and indicated a willingness to reexamine this application following the publication of ongoing/completed studies. Building on existing evidence presented in the previous proposal, this revised proposal presents new evidence that strengthens justification for inclusion of misoprostol on the EML. These new data, from a randomized controlled trial comparing misoprostol to placebo in a home birth setting in rural Pakistan, show that 600 mcg oral misoprostol reduced the rate of PPH (≥500 mL) by 24%, compared with placebo (Mobeen et al, in press BJOG). These findings corroborate the findings...
of Derman et al (Lancet 2006) showing the efficacy of misoprostol for the prevention of postpartum hemorrhage and highlight the drugs usefulness and appropriate use at the community-level. In total, four randomized controlled trials have tested misoprostol as PPH prevention at the community level. In these trials, the trained providers – either auxiliary nurse midwives, midwives or trained birth attendants – were able to safely administer misoprostol after delivery, identify need for referral, and recognize and manage any side effects occurring following misoprostol administration.

Please note that grade tables showing comparative safety and efficacy are included in the “WHO Recommendations for the Prevention of Postpartum Hemorrhage” (WHO 2007). We have included a PDF copy of those tables to this application. If the Committee would like, we would be happy to update the tables as appropriate to include findings from the Mobeen et al. publication. A copy of that manuscript is attached for the Committee’s review. Please do not post the manuscript on the WHO’s website as it is still in press. We will notify the Committee when the paper appears in print.

We thank you for reconsidering the addition of this medication to the Model List of Essential Medicines for the prevention of postpartum hemorrhage. We hope you agree that the full body of evidence supports the inclusion of misoprostol for this important women’s health indication.

Sincerely,

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