Misoprostol

Essential medicine status

Section: 22. Medicines for reproductive health and perinatal care > 22.3. Uterotonics

ATC codes: G02AD06

Indication	Spontaneous abortion, incomplete, without complication ICD11 code: JA00.04
INN	Misoprostol
Medicine type	Chemical agent
List type	Complementary
Additional notes	For management of incomplete abortion and miscarriage.
Formulations	Oral > Solid: 200 µg
EML status history	First added in 2009 (TRS 958)
Sex	Female
Age	Adolescents and adults
Therapeutic alternatives	The recommendation is for this specific medicine
Patent information	Patents have expired in most jurisdictions Read more about patents.
Wikipedia	Misoprostol
DrugBank	Misoprostol

Summary of evidence and Expert Committee recommendations

Applications for the inclusion of misoprostol 100- and 200-microgram tablets were submitted by Gynuity Health Projects and Venture Strategies for Health, for the prevention of postpartum haemorrhage (PPH) and by Gynuity Health Projects, for the treatment of first trimester incomplete abortion. Misoprostol is currently included on the Model List as: — a 25 microgram vaginal tablet, for use in induction of labour, on the Complementary List (added in 2005); — in combination with mifepristone as a 200 microgram tablet, for termination of pregnancy (where legally permitted and culturally acceptable), on the Complementary List (added in 2005). The public health relevance of treatments for both indications (PPH and incomplete abortion) had been accepted previously by the Expert Committee and is documented in the applications. It is further supported in the many letters received by the Secretariat in support of the proposals from organizations and individuals. In brief, PPH remains the major cause of maternal death (25% of mortality, WHO World Health Report 2005), and the risk of death from PPH is much higher in developing than in developed countries. In addition, atonic uterus is the main cause of PPH (1). The Committee also noted one letter against the proposals, on the grounds of the potential for use of misoprostol as an abortifacient. Prevention of postpartum haemorrhage: The Committee noted the systematic review of seven trials (2) comparing 600 micrograms misoprostol with other uterotonics. In the context of active management of labour by a skilled birth attendant, in comparison with oxytocin, misoprostol appears to be less effective and is associated with more adverse effects. The major argument made in the application is that misoprostol should be an option in situations where oxytocin is NOT available. The evidence for this claim is based on three published trials (3-5). The estimates of efficacy of misoprostol compared with placebo are not consistent across the trials which took place in settings mostl likely to be similar to those where it is used; there is a significant risk of increased shivering and fever, and an unresolved concern about increased mortality. Furthermore, the Committee is aware of a completed, but not yet reported, large trial assessing the effect of misoprostol on maternal blood loss and mortality. Treatment of incomplete abortion in the first trimester: The application identified 22 relevant studies that directly compare the use of misoprostol with surgery for the treatment of incomplete first trimester abortion. Based on these data, there is no statistically significant difference between surgery and oral misoprostol in terms of uterine clearance up to 14 days after administration. Comparison of adverse effects showed that while misoprostol administration was associated with predictable adverse effects (such as bleeding and pyrexia) due to the pharmacological actions of the medicine, these effects generally did not require further interventions (such as blood transfusion) and were reported as acceptable by the women. The adverse effect profile of misoprostol needs to be compared with the potential risks of surgery in unsafe settings. The application cites one unpublished study to support the proposal that 400 micrograms orally may be equivalent to 600 micrograms orally, but the data are not provided in detail. The application presents current prices of misoprostol and a brief summary of some published cost-effectiveness data. With respect to use of misoprostol for the treatment of incomplete abortion, the Committee decided that the evidence showed that misoprostol is as effective as surgery and, in some settings, may be safer as well as cheaper and therefore recommended inclusion of the 200 microgram tablet on the Complementary List with a note indicating the appropriate use, for management of incomplete abortion and miscarriage. For prevention of PPH, the Committee decided that the data presented in the application did not establish sufficient evidence of comparative effectiveness, safety or cost-effectiveness and therefore the Committee did not include misoprostol for this indication. The Committee will review this decision after the results of the large trial become available. 1. WHO recommendations for the prevention of postpartum haemorrhage. Geneva, World Health Organization, 2006. 2. Gülmezoglu AM et al. Prostaglandins for preventing post partum haemorrhage. Cochrane Database of Systematic Reviews, 2007 (3):CD000494. 3. Høj L et al. Effect of sublingual misoprostol on severe postpartum haemorrhage in a primary health centre in Guinea-Bissau: randomised double blind clinical trial. British Medical Journal, 2005, 331:723–727. 4. Walraven G et al. Misoprostol in the management of the third stage of labour in the home delivery setting in rural Gambia: a randomised controlled trial. BJOG: an International Journal of Obstetrics and Gynaecology, 2005, 112:1277–1283. 5. Derman RJ et al. Oral misoprostol in preventing postpartum hemorrhage in a community setting. Lancet, 2006, 368:1248–1253.