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Summary of the risk management plan (RMP) for Hemoprostol (misoprostol)

Overview of disease epidemiology

Postpartum haemorrhage is significant bleeding occurring after a woman has given birth. Normally after childbirth, the muscles of the womb contract firmly, sealing off the blood vessels that supply the womb. If this fails to happen properly (uterine atony) the blood vessels can bleed, causing serious blood loss. Postpartum haemorrhage occurs in about 6% of all deliveries, and is severe in about 1.86%, although there is a wide variation across regions of the world. The risk of death from post-partum haemorrhage is 1 in 16 cases in Africa and 1 in 300 in Latin America, compared with 1 in 3,700 in the United States.

Summary of treatment benefits

The active ingredient in Hemoprostol is misoprostol, a medicine that has been used for several decades in the prevention and treatment of post-partum haemorrhage. Unlike the main treatment for postpartum haemorrhage, oxytocin, which has to be given by a drip into a vein (intravenous infusion) and which must be stored in cool conditions, misoprostol can be given as tablets that are placed under the tongue and allowed to melt.

The benefit of treatment was shown in a published study, involving 978 women who developed post-partum haemorrhage and had not been given treatment during labour that would help prevent bleeding (including previous oxytocin). Treatment with Hemoprostol was compared with an infusion of oxytocin and the main measures of effectiveness were that bleeding stopped within 20 minutes, and that less than 300 ml of further blood loss occurred after the treatment had been given. The study found that 90% of women given Hemoprostol and 96% of those given oxytocin had their bleeding controlled within 20 minutes; 30% of Hemoprostol-treated and 17% of oxytocin-treated women lost more than 300 ml of blood after treatment.

Unknowns relating to treatment benefits

The patients in the studies were given Hemoprostol in a hospital setting, so the benefits of giving the medicine outside hospital, particularly by non-medical staff, could not be assessed. Only limited information is available about the use of Hemoprostol in women aged under 18 years.

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Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Fever and related events (chills, shivering)	Shivering and fever may affect more than 1 in 10 women given Hemoprostol. They generally occur 60 to 90 minutes after the medicine is given.	The effects are not preventable, but are generally short-lived.

Important potential risks

Risk	What is known
Off-label use for labour induction	In some countries, medicines containing misoprostol are available for induction of labour. However, the dose supplied by a tablet of Hemoprostol (200 micrograms) is unsuitable and potentially dangerous when used to induce labour. The product information for Hemoprostol includes a warning against such use.
Off-label use for pregnancy termination	In some countries, medicines containing misoprostol are available for termination of pregnancy. However, the dose supplied by a tablet of Hemoprostol (200 micrograms) is unsuitable and potentially dangerous for such use. The product information contains a contraindication against use in ongoing pregnancy.
Incomplete abortion in the context of off-label use for pregnancy termination	In some countries, medicines containing misoprostol are available for termination of pregnancy. A known risk of such use is failure of the procedure, requiring surgical treatment. The product information contains a contraindication against use in ongoing pregnancy.
Congenital abnormalities in the context of off-label use in early pregnancy	A known risk of the use of misoprostol during pregnancy is effects on the development of the baby resulting in congenital (inborn) abnormalities. The product information contains a contraindication against use in ongoing pregnancy and warnings of the risk of fetal malformation.
Misuse for illegal purposes in case of "not subject to prescription "	Many misoprostol preparations are available without prescription in developing countries which can lead to misuse. Hemoprostol is recommended to be given only by medical prescription.
Cardiovascular events (effects on heart and circulation)	Cases of cardiovascular events associated with misoprostol have been reported. The product information for Hemoprostol includes a warning

Risk	What is known
	on the possibility of a cardiovascular event in women with pre-existing cardiovascular risk factors.
Breastfeeding	Misoprostol passes into breast milk in small amounts for a short period after a dose. The risk to a breast-fed baby after the mother has received Hemoprostol is not considered significant.
Prostaglandin class effects	Misoprostol is a synthetic medicine that acts like a substance naturally produced in the body, prostaglandin E_1, and might therefore have other effects similar to substances of the prostaglandin class. So far, the only known risks of the prostaglandin class that have been seen with the licensed use of Hemoprostol are cardiovascular effects (see above).

Missing information

Risk	What is known
Use in children	The studies that showed the efficacy of Hemoprostol included some participants from 14 years of age, but information in those aged below 18 years is limited.
Women who also have kidney or liver problems	No studies have been performed in women with kidney or liver problems.

Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SmPC) which provides physicians, pharmacists and other healthcare professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

The Summary of Product Characteristics and the package leaflet for Hemoprostol can be found in the Hemoprostol EPAR page.

This medicine has no additional risk minimisation measures.

This summary was last updated in 02-2014.