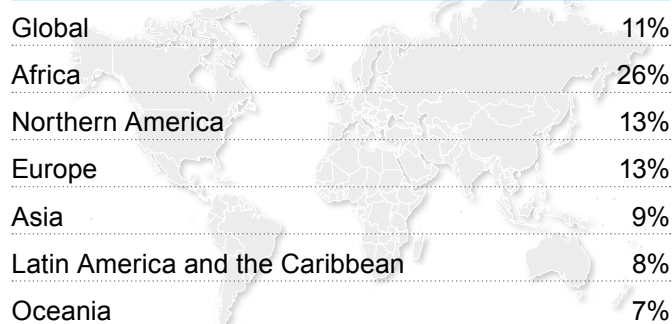


The role of heat-stable carbetocin in preventing postpartum haemorrhage (PPH)

PPH is the leading direct cause of maternal mortality worldwide¹

PPH is excessive bleeding after childbirth, and is generally defined as blood loss greater than or equal to 500 ml within 24 hours of vaginal birth.² Severe PPH is defined as blood loss greater than or equal to 1000 ml within 24 hours.² 14 million mothers are affected by PPH each year.³

Prevalence of PPH^{4*}



Global	11%
Africa	26%
Northern America	13%
Europe	13%
Asia	9%
Latin America and the Caribbean	8%
Oceania	7%

99% of deaths from PPH occur in low- and lower-middle income countries.³

The most common cause of PPH is uterine atony which is when the uterus fails to contract adequately after the delivery of the baby.⁵ PPH prevention and treatment involves medicines, called uterotonics, which help the uterus to contract, stopping the bleeding.^{3,6}

Global guidelines from the World Health Organization (WHO) currently recommend the uterotonic oxytocin as the standard of care for the prevention of PPH.² Oxytocin requires sustained cold-chain transport and storage at 2-8°C, typically in a refrigerator, to maintain its effectiveness.^{7,8} However, in many low- and lower-middle income countries access to cold chain storage is not readily available.^{7,8}

Heat-stable carbetocin: history and development

Ferring scientists developed a uterotonic medicine called carbetocin that has been approved since 1997 for the prevention of uterine atony following caesarean section.⁹ Carbetocin is now approved in more than 80 countries worldwide and is listed in numerous guidelines.⁹ Carbetocin is also approved in around 10 countries for the prevention of uterine atony following vaginal delivery.⁹

The treatment is marketed under the brand names Pabal[®], Duratocin[®], Lonactene[®] and Duratobal[®].⁹

*in women giving birth

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A heat-stable formulation of carbetocin is now approved in the EU and some additional countries for use after caesarean section.⁹ Data show that heat-stable carbetocin maintains effectiveness for at least three years at 30°C, six months at 40°C, three months at 50°C; it is not sensitive to light or freezing.¹⁰ By removing the need for refrigeration, heat-stable carbetocin could potentially reduce the incidence of PPH in areas where cold storage is difficult to achieve and maintain.⁷

How does carbetocin prevent PPH?

Both carbetocin and oxytocin selectively bind to oxytocin receptors in the smooth muscle of the uterus. This stimulates rhythmic contractions of the uterus, increases the frequency of existing contractions, and raises the tone of the uterine musculature.¹¹ Uterine contraction closes the vessels carrying blood to the placenta.¹²

Following birth, carbetocin is capable of increasing the rate and force of spontaneous uterine contractions. This action prevents uterine atony which leads to excessive bleeding following delivery by caesarean section.¹¹ Carbetocin has a longer duration of action than oxytocin.^{11,13}

In addition, a *Cochrane* network meta-analysis of 137 studies (N=87,466) demonstrated that carbetocin was consistently amongst the top three uterotonics in terms of preventing PPH, and had the fewest side effects of all uterotonics reviewed.¹⁴

CHAMPION trial

The CHAMPION (Carbetocin Haemorrhage Prevention) trial was conducted by the WHO Department of Reproductive Health and Research including the UNDP-UNFPA-UNICEF-WHO-World Bank Special Programme of Research, Development and Research Training in Human Reproduction, using Ferring's proprietary heat-stable carbetocin, and was funded by *MSD for Mothers*. Involving nearly 30,000 women in 10 countries, CHAMPION is the largest clinical trial conducted in PPH. The trial compared the effectiveness and safety of heat-stable carbetocin to oxytocin in the prevention of PPH after vaginal births, exploring a new option that isn't compromised when exposed to heat in countries where cold storage is a barrier.^{7,15}

