



# Oxytocin

## Description

Oxytocin is a peptide hormone best known for its roles in childbirth and breastfeeding. It is released in large amounts from the body's pituitary gland during labor, causing contractions of the uterus to facilitate birth. It also stimulates contractions during the third stage of labor—separation of the placenta from the uterine wall and compression of maternal blood vessels after delivery of the placenta.<sup>1</sup> When uterine contractions are not strong enough to compress blood vessels, postpartum hemorrhage (PPH) can threaten a woman's life. In this situation, a woman will be given a uterotonic medicine, such as oxytocin, to stimulate contractions and stop the bleeding.

Obstetric hemorrhage is estimated to cause 25 percent of all maternal deaths and is the leading direct cause of maternal mortality worldwide.<sup>2</sup> In Africa and Asia, nearly a third of pregnancy-related deaths are associated with PPH.<sup>1</sup> The World Health Organization (WHO) and other international bodies recommend that all women giving birth should be offered uterotonics during the third stage of labor for the prevention of PPH.\*

According to the WHO, oxytocin is the preferred drug for prevention and initial treatment of PPH because it is effective in two to three minutes after injection, can be used in all women, and is more stable in storage than other uterotonics.<sup>3,4</sup> WHO, with the Partnership for Maternal, Newborn, and Child Health, lists oxytocin as a first-line drug for induction of labor and the prevention and management of PPH.<sup>5</sup> The United Nations Population Fund (UNFPA) and its partners have identified oxytocin as one of four priority medicines that can save mothers' lives during difficult pregnancies and childbirth.<sup>6</sup>

The standard dose of oxytocin for preventing PPH is 10 international units (IU) administered intramuscularly or intravenously (IV) within a few minutes after birth. If a woman is experiencing heavy bleeding after delivery, the WHO recommends intravenous oxytocin (10-IU initial dose) up to 40 IU. Oxytocin can be administered as an IV infusion of 20 IU in 1 liter of IV fluid at 60 drops per minute, and

continued at 20 IU in 1 liter of IV fluid at 40 drops per minute until hemorrhage stops.<sup>7</sup> Oxytocin is most commonly available in either 5- or 10-IU glass ampoules.

In 2012, the United Nations Commission on Life-Saving Commodities for Women and Children endorsed oxytocin as one of its 13 Life-Saving Commodities, catalyzing inter-organizational efforts to overcome several commodity-specific barriers currently inhibiting women in the developing world from benefiting from the drug.

## Efficacy

WHO has determined that, as a package, active management of the third stage of labor (administration of a uterotonic soon after birth of the baby, delayed cord clamping, and delivery of the placenta by controlled cord traction and uterine massage) can reduce PPH by as much as 60 percent.<sup>8</sup> WHO also reviewed the available evidence for using oxytocics for treatment of PPH, and while both oxytocin and ergometrine were similarly effective, ergometrine is associated with more adverse effects, especially vomiting and high blood pressure.<sup>8</sup>

## Current program/sector use

Oxytocin is used worldwide for several indications. As noted above, it is the WHO preferred uterotonic for prevention and treatment of PPH and it is also used to induce and augment labor. In some developed countries, it is used to initiate or increase breast-milk production.

In developing countries, oxytocin is commonly used in clinical environments where a skilled birth attendant and refrigeration are available. However, use of oxytocin for the indications noted previously is not universal and other drugs are also being used for induction and augmentation of labor, and for prevention or treatment of PPH.<sup>9</sup> This is for a variety of reasons, including changes in recommendations over time, differences in country-level protocols and

\* In settings where oxytocin is unavailable, the use of other injectable uterotonics, such as ergometrine, or oral misoprostol (600 µg) is recommended. Please see the Caucus product brief on misoprostol for more information.

guidelines, and differences in the availability, cost, and storage requirements for the various drugs.

Oxytocin in the Uniject™\* injection system (oxytocin in Uniject), a prefilled, single-dose injection system, has been used successfully by skilled providers in health facilities. Research on the use of oxytocin in Uniject for the prevention of PPH during home and community-level deliveries has been conducted in Ghana, India, Mali, Senegal, and Vietnam.<sup>10-14</sup>

Work is underway to increase access to oxytocin by making it more heat stable and easier to use, particularly for developing-country settings with limited access to skilled birth attendants and refrigeration. A number of organizations are investigating potential improvements to the heat stability of oxytocin, including a consortium made up of the WHO, the International Confederation of Midwives, and pharmaceutical companies, among others.<sup>15</sup> Some of these organizations are also seeking to make oxytocin easier to deliver through non-parenteral routes, such as dry powder inhalation.

### Manufacturer/supplier

Oxytocin is a generic drug no longer subject to patent protection and is widely produced and distributed around the world. Two oxytocin brand names are broadly recognized: Syntocinon,<sup>®</sup> which is marketed by Novartis, and Pitocin<sup>®</sup>, which is marketed by Pfizer in some countries and other producers in other countries. There are multiple generic manufacturers of oxytocin in almost all countries that have an active sterile injectables pharmaceutical manufacturing sector, including Argentina, Bangladesh, China, India, Indonesia, and Pakistan. One manufacturer, Instituto Biologico Argentino (BIOL) in Argentina, has the capacity to manufacture oxytocin in Uniject.

As noted above, oxytocin, whether packaged in ampoules or a prefilled injection device such as Uniject™, is a heat-sensitive product. Depending upon the manufacturer and regulatory agency specification, oxytocin products should be stored at either controlled room temperature (25°C or less) or refrigerated storage (2°–8°C) in order to ensure quality and comply with the labeled storage conditions. There is widespread inconsistency in the labeled storage conditions for oxytocin from various manufacturers, which can lead to confusion about proper storage practices.

### Registration status

Oxytocin is often registered for multiple obstetric indications, including prevention and treatment of PPH, as well as induction of labor. Due to the large number of manufacturers producing oxytocin globally, a complete listing of all manufacturers and their corresponding country registrations is beyond the scope of this brief; however, almost all countries have one or more registered oxytocin product.

Oxytocin in Uniject is currently registered for commercial sale in Argentina, Bolivia, Ecuador, Guatemala, Honduras, Nicaragua, Paraguay, and Uruguay by BIOL. Modest commercial sales of the product are underway in Argentina.

### Public-sector price agreements

According to the International Drug Price Indicator Guide for prices in 2011, the median cost to procurers of oxytocin (both nonprofits such as UNFPA and for-profit organizations that sell to charitable groups) was US\$0.15 per 10-IU ampoule.<sup>16</sup> The median cost for governments purchasing from agencies such as these is US\$0.22, but the cost can be as low as US\$0.04.

There are no known global public-sector price agreements for oxytocin. Governments can purchase oxytocin products that are registered in their country and can negotiate the price with the distributor that holds the market approval.

Oxytocin is one of the reproductive health commodities covered under the WHO prequalification system.

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\* Uniject is a trademark of BD.

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