GENERAL PRODUCT INFORMATION

Postpartum hemorrhage (PPH) refers to excessive bleeding after childbirth. Left untreated, it can lead to anemia, shock, and also death. PPH is the leading cause of maternal death in low- and middle-income countries. Proper screening, prevention, and treatment of PPH can save women’s lives and reduce global burden of maternal mortality.

Prevention and treatment for most cases of PPH require the use of a uterotonic medicine to increase muscle contractions in the uterus that compress the blood vessels. In settings where multiple uterotonic options are available, WHO recommends oxytocin as the uterotonic agent for the prevention and treatment of PPH for all births. In settings where oxytocin is unavailable (or its quality cannot be guaranteed), the use of other uterotonics injectable ergometrine or oral misoprostol is recommended for the prevention and treatment of PPH. It is also prioritized as an essential medicine by the UN Commission on Life-Saving Commodities for Women and Children.

Other uterotonic medicines, such as misoprostol, carbetocin, ergotamine and ergometrine, have some drawbacks. Misoprostol is recommended by WHO for the prevention and treatment of PPH where oxytocin is unavailable (or its quality cannot be guaranteed). It is recommended for use in women giving birth outside of a health facility for PPH prevention (e.g., home deliveries), as it is administered as a pill rather than by injection. Carbetocin has a heat-stable formulation that does not require cold-chain storage and transportation and it is recommended by the WHO for the prevention of PPH in settings and contexts where its cost is comparable to other effective uterotonics. Unlike oxytocin, carbetocin is not indicated for treatment of PPH and is contraindicated for induction or augmentation of labor. Ergotamine and ergometrine have more side effects, should only be given after the birth of the placenta, must be kept in the cold chain...

and out of light and are contraindicated for many conditions, including hypertension and pre-eclampsia.

Oxytocin is the safest and most effective uterotonic medicine for the prevention and treatment of PPH, which should be procured over other uterotonic medicines and made available in all health facilities to help lower maternal death rates and improve overall maternal health.

According to the WHO recommendations on routes of oxytocin administration for the prevention of PPH, the use of oxytocin (10 IU, intramuscular/intravenous) is recommended for all births. In situations where women giving birth vaginally already have intravenous access, the slow intravenous administration of 10 IU oxytocin is recommended in preference to intramuscular administration.

KEY CONSIDERATIONS IN PROCUREMENT

1. Procurement should be made from trusted sources. This includes manufacturers prequalified by WHO, approved by an SRA, or recommended by the ERP and with a proven record of quality products.

2. Procurers need to focus on product quality to ensure the product is sterile and safe for patient use as oxytocin is an injectable medicine.

3. As per the WHO/UNICEF/UNFPA joint statement, procurers and distributors of oxytocin should ensure that specifications clearly reference appropriate quality standards and requirements, including appropriate labeling for storage at 2–8°C (35–46°F), and supply chains managers should ensure that oxytocin is maintained at 2–8°C (35–46°F).

KEY QUALITY CONSIDERATIONS

Product specification

Oxytocin injection products must comply with the quality specifications as detailed in “Product Specifications” section below.

Packaging and labeling

The container-closure system (ampoule/vial) must be sufficient to preserve sterility during the shelf life of the product. Additional information about oxytocin injection packaging and labeling can be found in the Annex.

Storage, transportation, and distribution

Oxytocin that is procured should be labeled and stored between 2°C and 8°C from the point of manufacture to the point of use to maintain the product quality.

Although some manufacturers state the product can be stored at controlled room temperature, between 20°C and 25°C, it should be noted that room temperatures in health facilities in tropical countries often exceed the controlled room temperature, which can put oxytocin quality at risk.

Oxytocin is temperature-sensitive and loses effectiveness after three months of storage at temperatures above 30°C. Significant quality issues can stem from inappropriate transport and storage, which may expose the product to high temperatures that can degrade it and result in low potency.

Detailed records of all stages of transport from the date the oxytocin product leaves the FPP manufacturer to its arrival at the procurer facility should be provided to assure the product has not been subject to adverse temperatures for a potentially harmful length of time. The procurer should reach agreement with the FPP manufacturer and/or distributor to use the most suitable transport and handling to protect the product from exposure to high temperatures. Data loggers or suitable temperature-time integrators can be used to alert procurers of any excursions during transportation and be alert to possible degradation of oxytocin.

Name of the Medicinal Product

Oxytocin injection

Chemical Name

Oxytocin (L-cysteinyl-L-tyrosyl-L-isoleucyl-L-glutamyl-L-asparaginyl-L-cysteinyl-L-proyl-L-leucylglycinamide cyclic (1→6)-disulfide)

Oxytocin is a synthetic cyclic nonapeptide having the structure of the hormone produced by the posterior lobe of the pituitary gland that stimulates contraction of the uterus and milk ejection in receptive mammals. Being wholly synthetic, it does not contain vasopressin and has a constant and reliable effect.

Chemical Structure

\[ C_{43}H_{66}N_{12}O_{12}S_2 \]

\[ H - Cys - Tyr - Ile - Gln - Asn - Cys - Pro - Leu - Gly - NH_2 \]
Pharmaceutical Form
A clear, colorless solution

Qualitative and Quantitative Composition
Oxytocin injection is a sterile solution of oxytocin or a sterile dilution of oxytocin concentrated solution in water for injection. It contains 10 IU of oxytocin per mL.
List of typical excipients:
- Acetic acid
- Chlorobutanol
- Ethanol
- Sodium acetate trihydrate
- Water for injection

Packaging and Presentation
The WHO Essential Medicines List states “oxytocin injection 10 IU in 1-mL,” which does not preclude procurement of any particular presentation of injectable oxytocin. Oxytocin injection is generally packed in glass ampoules. However, some manufacturers provide the product in glass or plastic vial.

SUPPLY
Generally, products prequalified by the WHO PQP and/or approved by an SRA are considered quality-assured and highly recommended for procurement. In the absence of WHO-prequalified, SRA-approved, or ERP-recommended products, medicines from trusted sources, such as manufacturers approved by UN agencies, can be considered for procurement. Alternatively, the procurement agency may conduct its own quality assessment as described in Module II.

WHO-prequalified products
As of June 2022, four oxytocin injections are prequalified by the WHO PQP, as shown below. It is recommended to check the updated information at the time of procurement, by going to https://extranet.who.int/pqweb/medicines/prequalified-lists/finished-pharmaceutical-products.

3 Based on the formulation of an innovator product, Syntocinon®.
<table>
<thead>
<tr>
<th>WHO REF. NUMBER</th>
<th>MARKETING AUTHORIZATION HOLDER</th>
<th>MANUFACTURING SITE</th>
<th>DOSAGE FORM AND STRENGTH</th>
<th>PACKAGING AND PRESENTATION</th>
<th>DATE OF PREQUALIFICATION</th>
<th>SHELF LIFE</th>
<th>STORAGE CONDITION</th>
</tr>
</thead>
<tbody>
<tr>
<td>RH050</td>
<td>PT Sanbe Farma, Jl. Taman Sari no. 10, Bandung, 40116, Indonesia</td>
<td>FPP manuf. site: PT Sanbe Farma, Sterile Preparation Plant, Unit 3, Jl. Industri Cimarene No. 8, Desa Cimarene, Kecamatan Ngamprah, Kabupaten Bandung Barat, 40553, Indonesia</td>
<td>Solution for injection 10 IU/mL</td>
<td>Ampoule; Type I glass 1 mL x 10's</td>
<td>30-Jun-17</td>
<td>18 months</td>
<td>Store in refrigerator (2–8°C), do not freeze, protect from light.</td>
</tr>
<tr>
<td>RH079</td>
<td>JSC Grindeks, 53 Krustpils Street, Riga, LV-1057, Latvia</td>
<td>FPP manuf. site: - HBM Pharma s.r.o., Sklabinska 30, Martin, 036 80, Slovakia - UAB Santonika, Veiveriu str. 134B, Kaunas, LT- 46353, Lithuania</td>
<td>Solution for injection 10 IU/mL</td>
<td>Ampoule, Type I glass 1 mL x 5's 1 mL x 10's 1 mL x 100's</td>
<td>14-Oct-19</td>
<td>36 months</td>
<td>Store in a refrigerator (2°C to 8°C), do not freeze.</td>
</tr>
<tr>
<td>RH083</td>
<td>Steril-Gene Life Sciences (P) Ltd, No.15, Gopalakrishna Road, T. Nagar, Chennai, 600 017, India</td>
<td>FPP manuf. site: Steril-Gene Life Sciences (P) Ltd., 45, Mangalam Main Road, Mangalam Village, Villianur Commune, Puducherry, 605 110, India</td>
<td>Solution for injection 10 IU/mL</td>
<td>Ampoule, USP Type I glass 1 mL x 5's 1 mL x 10's 1 mL x 100's</td>
<td>14-Oct-19</td>
<td>24 months</td>
<td>Store in a refrigerator (2°C to 8°C), do not freeze, protect from light.</td>
</tr>
<tr>
<td>RH097(a)</td>
<td>Panpharma Laboratories, ZI du Clairay, Luitre, 35133, France</td>
<td>FPP manuf. site: - PANPHARMA GmbH, Bunsenstrasse 4, Tittau, D-22946, Germany - Haupt Pharma Livron SAS, 1 rue Comte de Sinard, Livron sur Drôme, 26250, France</td>
<td>Concentrate for solution for infusion 10 IU/mL</td>
<td>Ampoule, Type I glass 1 mL ampoule x 10's</td>
<td>1-Jul-2021</td>
<td>36 months</td>
<td>Store in a refrigerator (2°C to 8°C), protect from light.</td>
</tr>
</tbody>
</table>
(a) Indicates SRA-approved product that has been prequalified based on abbreviated assessment.

### SRA-approved products

Table O-2. Examples of SRA-Approved Oxytocin Injection 10 IU/mL in 1-mL

<table>
<thead>
<tr>
<th>PRODUCT NAME</th>
<th>SRA</th>
<th>MARKETING AUTHORIZATION HOLDER</th>
<th>REGISTRATION NUMBER</th>
<th>PACKAGING AND PRESENTATION</th>
<th>SHELF LIFE</th>
<th>STORAGE CONDITION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Syntocinon® 10 IU/mL concentrate for solution for infusion</td>
<td>UK MHRA</td>
<td>Mylan Products Ltd, UK</td>
<td>PL 46302/0063</td>
<td>Clear glass 1-mL ampoule</td>
<td>5 years</td>
<td>Store between 2°C and 8°C. May be stored up to 30°C for 3 months, but must then be discarded.</td>
</tr>
<tr>
<td>Oxytocin 10 IU/mL concentrate for solution for infusion</td>
<td>UK MHRA</td>
<td>Hameln Pharmaceuticals Ltd, UK</td>
<td>PL 01502/0097, PL 01502/0102</td>
<td>Clear glass 1-mL ampoule</td>
<td>5 years</td>
<td>Store between 2°C and 8°C.</td>
</tr>
<tr>
<td>Oxytocin 10 IU/mL concentrate for solution for infusion</td>
<td>UK MHRA</td>
<td>Wockhardt UK Ltd, UK</td>
<td>PL 29831/0625</td>
<td>Clear, type I, neutral glass, 1-mL ampoule</td>
<td>3 years</td>
<td>Store between 2°C and 8°C. May be stored up to 30°C for 3 months, but must then be discarded. Store in the original package in order to protect from light.</td>
</tr>
<tr>
<td>Oxytocin 10 IU solution for injection</td>
<td>UK MHRA</td>
<td>EVER Neuro Pharma GmbH, Austria</td>
<td>PL 40369/0006</td>
<td>Colorless glass (type I) 1-mL ampoule</td>
<td>3 years</td>
<td>Store in refrigerator (2–8°C). May be stored below 25°C for 6 months, but then must be discarded.</td>
</tr>
<tr>
<td>Oxytocin 10 IU/mL solution for infusion</td>
<td>UK MHRA</td>
<td>Intrapharm Laboratories Ltd, UK</td>
<td>PL 17509/0089</td>
<td>Transparent 1 ml Ph.Eur. type I glass ampoules</td>
<td>4 years</td>
<td>Store in a refrigerator (2–8°C). May be stored up to 30°C for 3 months, but must then be discarded. Keep the ampoules in the outer carton in order to protect from light.</td>
</tr>
<tr>
<td>Oxytocin PANPHARMA 10 IU/mL concentrate for solution for infusion</td>
<td>UK MHRA</td>
<td>PANPHARMA, France</td>
<td>PL 44124/0024</td>
<td>1-mL clear glass ampoules</td>
<td>3 years</td>
<td>Store in a refrigerator (2–8°C). Keep the ampoules in outer carton in order to protect from light.</td>
</tr>
<tr>
<td>Oxytocin injection, USP (synthetic)</td>
<td>US FDA</td>
<td>West-Ward Pharmaceutical, USA</td>
<td>NDA #018243</td>
<td>1-mL single-dose vial</td>
<td>Not specified</td>
<td>Store at 25°C; excursions permitted to 15–30°C [See USP Controlled Room Temperature.] Do not freeze.</td>
</tr>
<tr>
<td>PRODUCT NAME</td>
<td>SRA</td>
<td>MARKETING AUTHORIZATION HOLDER</td>
<td>REGISTRATION NUMBER</td>
<td>PACKAGING AND PRESENTATION</td>
<td>SHELF LIFE</td>
<td>STORAGE CONDITION</td>
</tr>
<tr>
<td>------------------------------------------------</td>
<td>------</td>
<td>------------------------------------------</td>
<td>--------------------</td>
<td>-----------------------------</td>
<td>------------</td>
<td>-----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Oxytocin injection USP</td>
<td>US FDA</td>
<td>Fresenius Kabi, USA</td>
<td>NDA #018248</td>
<td>1-mL single-dose vial</td>
<td>Not specified</td>
<td>Store at 20°–25°C [See USP Controlled Room Temperature.]* Do not permit to freeze.</td>
</tr>
<tr>
<td>Pitocin® (oxytocin injection, USP)</td>
<td>US FDA</td>
<td>Par Sterile Products LLC, USA</td>
<td>NDA #018261</td>
<td>1-mL single-dose vial</td>
<td>Not specified</td>
<td>Store between 20° and 25°C [See USP Controlled Room Temperature.]*</td>
</tr>
<tr>
<td>Oxytocin injection, USP</td>
<td>US FDA</td>
<td>Hikma Farmaceutica, USA</td>
<td>ANDA #200219</td>
<td>1-mL single-dose vial</td>
<td>Not specified</td>
<td>Store at 20°–25°C [See USP Controlled Room Temperature.]* Do not permit to freeze.</td>
</tr>
<tr>
<td>Syntocinon® oxytocin 10 IU/mL injection ampoule</td>
<td>TGA Australia</td>
<td>Viatris Pty Ltd, Australia</td>
<td>AUST R 13383</td>
<td>Clear glass 1-mL ampoule</td>
<td>5 years</td>
<td>Store at 2° to 8°C. Refrigerate. Do not freeze.</td>
</tr>
<tr>
<td>Viatocinon oxytocin 10 IU/mL injection ampoule</td>
<td>TGA Australia</td>
<td>Viatris Pty Ltd, Australia</td>
<td>AUST R 164131</td>
<td>Clear glass 1-mL ampoule</td>
<td>3 years</td>
<td>Store at 2°C to 8°C. Refrigerate. Protect from light. Once removed from refrigerator the ampoules may be stored below 25°C for up to 4 weeks only, provided that the product is used before printed expiry date. Thereafter, ampoules must be discarded.</td>
</tr>
<tr>
<td>Oxytocin GH solution for injection 10 IU/mL ampoule</td>
<td>TGA Australia</td>
<td>Generic Health Pty Ltd</td>
<td>AUST R 207986</td>
<td>Clear glass 1-mL ampoule</td>
<td>3 years</td>
<td>Store at 2°C–8°C. Refrigerate. Do not freeze. Protect from light.</td>
</tr>
<tr>
<td>Oxytocin APX oxytocin 10 IU/mL solution for injection ampoule</td>
<td>TGA Australia</td>
<td>Arrotex Pharmaceuticals Pty Ltd, Australia</td>
<td>AUST R 225656</td>
<td>Clear glass 1-mL ampoule</td>
<td>3 years</td>
<td>Store at 2–8°C (Refrigerate. Do not freeze). Protect from light.</td>
</tr>
</tbody>
</table>

* Please note that this is the storage condition as approved for the US market. Since the room temperatures in low- and middle-income countries often exceed such controlled room temperature, it is recommended oxytocin supplied to those countries be included in the cold chain between 2°C and 8°C and be labeled as such.
It should be noted that the list of SRA-approved products provided in the table above is not exhaustive. The list may be changed over time. When a manufacturer claims that its product is approved by an SRA, they should provide the following information/documents to prove the SRA approval:

- A copy of the marketing authorization issued by the reference SRA
- The approved product information (e.g., Summary of Product Characteristics, product information leaflet, and the labeling by the reference SRA).
- A statement confirming the FPP—including but not limited to composition/formulation, strength, manufacturing, specifications, packaging, and product information—will in all respects be the same as the product approved by the reference SRA
- Product sample

The procurer may cross-check the submitted information with the corresponding NMRA websites:

- UK MHRA: https://products.mhra.gov.uk/
- EU regulatory authorities: https://ec.europa.eu/health/documents/community-register/regca_en
- Swissmedic: https://www.swissmedicinfo.ch/

**Related products**

Other presentations of oxytocin injection on the market include:

- Oxytocin injection 5 IU/mL in 1-mL ampoule
- Oxytocin injection 10 IU/mL in 10-mL multidose vial
- Oxytocin injection 2 IU/2mL in 2-mL ampoule

They are used for the same indications, dosage, and administration. However, it is important to note that the WHO EML recommends oxytocin injection 10 IU in 1-mL presentation for convenient use in prevention and treatment of PPH. According to the WHO recommendations for the prevention and treatment of PPH, for PPH prevention 10 IU is administered as intramuscular or slow intravenous injection and for PPH treatment, 10–40 IU is administered as an intravenous (IV) infusion.

In certain markets, the price of the 5 IU/mL product may be attractive to meet local needs. However, as most dosing regimens for PPH are likely to require more ampoules of 5 IU/mL than 10 IU/mL, the cumulative costs may be substantively higher. It is therefore recommended to procure only oxytocin injection 10 IU/mL.
Oxytocin degrades when exposed to prolonged heat. It is therefore recommended that oxytocin products be kept refrigerated at 2–8˚C. Procurers and health facilities should have adequate cold-chain infrastructure for the transportation and storage of quality oxytocin.

Shelf life: 18–60 months, depending on the manufacturer. It is recommended to check the product label before use.

Storage condition: Store in a refrigerator (2–8˚C). Do not freeze. Protect from light.

The shelf life and storage condition of each WHO-prequalified and SRA-approved product can be found in Table O-1 and Table O-2 above.

PRODUCT SPECIFICATIONS

The product must meet pharmacopeial specifications, such as those of the International Pharmacopeia (IP), US Pharmacopeia (USP), and British Pharmacopeia (BP), depending on the quality assurance policy of the procurement agency, or the equivalent thereof. The testing parameters and acceptance criteria of the three pharmacopeias are similar, except the pH, related substances, and/or bacterial endotoxin limits.

Table O-3. International Pharmacopeia Specifications for Oxytocin Injection

<table>
<thead>
<tr>
<th>TEST</th>
<th>ACCEPTANCE CRITERIA</th>
<th>ANALYTICAL METHOD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>Clear, colorless solution, free from visible particulate matter</td>
<td>Visual inspection</td>
</tr>
<tr>
<td>Identification</td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) TLC</td>
<td>The principal spot obtained with solution A corresponds in position, appearance and intensity with that obtained with solution B.</td>
<td>1.14.1 TLC</td>
</tr>
<tr>
<td>b) HPLC</td>
<td>The principal peak in the chromatogram obtained with the test solution is similar in retention time to the principal peak in the chromatogram obtained with the reference solution.</td>
<td>1.14.4 HPLC</td>
</tr>
<tr>
<td>pH</td>
<td>pH of the injection, 3.0 – 5.0</td>
<td>1.13 pH value</td>
</tr>
<tr>
<td>Assay</td>
<td>90.0–110.0%</td>
<td>1.14.4 HPLC</td>
</tr>
<tr>
<td>Related substances</td>
<td>In the chromatogram obtained with solution (1), the area of not more than one peak, other than the principal peak, is greater than the area of the principal peak obtained with solution (2) (2%). No such peak, other than the principal peak, is greater than 2.5 times the area of the principal peak obtained with solution (2) (5%).</td>
<td>1.14.4 HPLC</td>
</tr>
<tr>
<td>Bacterial endotoxins</td>
<td>Less than 0.5 IU of endotoxin per IU of oxytocin</td>
<td>3.4 Test for bacterial endotoxins</td>
</tr>
<tr>
<td>Sterility</td>
<td>Sterile</td>
<td>3.2 Test for sterility</td>
</tr>
<tr>
<td>Extractable volume</td>
<td>Comply</td>
<td>5.6 Extractable volume for parenteral preparations</td>
</tr>
</tbody>
</table>
### Table O-4. US Pharmacopeia Specifications for Oxytocin Injection

<table>
<thead>
<tr>
<th>TEST</th>
<th>ACCEPTANCE CRITERIA</th>
<th>ANALYTICAL METHOD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Particulate matter</td>
<td>Comply</td>
<td>5.7 Tests for particulate contamination: subvisible particles</td>
</tr>
</tbody>
</table>

#### Particulate matter
- **Comply**: Meet the requirements for small-volume injections

### Table O-5. British Pharmacopeia Specifications for Oxytocin Injection

<table>
<thead>
<tr>
<th>TEST</th>
<th>ACCEPTANCE CRITERIA</th>
<th>ANALYTICAL METHOD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>Clear, colorless solution, free from visible particulate matter</td>
<td>Visual inspection</td>
</tr>
</tbody>
</table>

#### Appearance
- **Clear, colorless solution, free from visible particulate matter**: Visual inspection

#### Identification
- **a) TLC**: The principal spot in the chromatogram obtained with solution (1) corresponds in position, size, and intensity to that in the chromatogram obtained with solution (2).
- **b) HPLC**: The chromatogram obtained with solution (1) exhibits a peak with the same retention time as the principal peak in the chromatogram obtained with solution (2).

#### Related substances
- **In the chromatogram obtained with solution (1), the area of any secondary peak is not greater than 0.75 times the area of the principal peak obtained with solution (2)**: HPLC, as in Appendix III D

#### Assay
- **90.0–110.0%**: HPLC, as in Appendix III D

#### Assay
- **90.0–110.0%**: HPLC, USP<621>

#### Sterility
- **Sterile**: USP<71>

#### Extractable volume
- **Comply**: USP<1>

#### Particulate matter
- **Meet the requirements for small-volume injections**: USP<788>
Oxytocin

<table>
<thead>
<tr>
<th>TEST</th>
<th>ACCEPTANCE CRITERIA</th>
<th>ANALYTICAL METHOD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(1.5%). The sum of the areas of any secondary peaks is not greater than 2.5 times the principal peak obtained with solution (2) (5%).</td>
<td></td>
</tr>
<tr>
<td>Bacterial endotoxins</td>
<td>Comply</td>
<td>Appendix XIV C</td>
</tr>
<tr>
<td>Sterility</td>
<td>Sterile</td>
<td>Appendix XVI A</td>
</tr>
<tr>
<td>Extractable volume</td>
<td>Comply</td>
<td>Appendix XII C5</td>
</tr>
<tr>
<td>Particulate matter</td>
<td>Comply</td>
<td>Appendix XIII A</td>
</tr>
</tbody>
</table>
OXYTOCIN ANNEX
PART 1: CLINICAL PARTICULARS

Therapeutic indications

Antepartum

- Induction of labor for medical reasons—for example, in cases of post-term gestation, premature rupture of the membranes, pregnancy-induced hypertension (pre-eclampsia)
- Stimulation of labor in hypotonic uterine inertia
- Early stages of pregnancy as adjunctive therapy for the management of incomplete, inevitable, or missed abortion

Postpartum

- During cesarean section, but following delivery of the child
- Prevention and treatment of postpartum uterine atony and hemorrhage.

Posology, method, and duration of administration

Oxytocin should be administered as an intravenous infusion or, preferably, by means of a variable-speed infusion pump. It can also be given by intramuscular injection, (although intravenous use can produce a more rapid onset of action and allow for better control of dosing). Attention should be paid to the oxytocin cold chain (i.e. the requirements of a temperature-controlled supply chain).

Induction or enhancement of labor

If vaginal prostaglandins have been used, oxytocin should be started at least 6 hours after use of vaginal prostaglandins. Oxytocin should be administered as an intravenous drip infusion or, preferably, by means of a variable-speed infusion pump. For drip infusion, it is recommended that 5 units of oxytocin be added to 500 mL of a physiological electrolyte solution (such as sodium chloride 0.9%). For patients in whom infusion of sodium chloride must be avoided, 5% glucose solution may be used as the infusion fluid (see “Special warnings and precautions for use” section below).

To ensure even mixing, the infusion bottle or bag must be turned upside down several times before use. The initial infusion rate should be set at 1 to 4 milliunits/minute (2 to 8 drops/minute).

The infusion rate may be gradually increased at intervals of at least 20 minutes and increments of not more than 1–2 milliunits/minute, until a contraction pattern similar to that of normal labor is established. In pregnancy near term, this can often be achieved with an infusion rate of less than 10 milliunits/minute (20 drops/minute), and the recommended maximum rate is 20 milliunits/minute (40 drops/minute). In the unusual event that higher rates are required, as may occur in the management of fetal death or for induction of labor at an earlier stage of pregnancy when the uterus is less sensitive to oxytocin, it is advisable to use a more concentrated oxytocin solution, e.g. 10 units in 500 mL.
When using a motor-driven infusion pump, which delivers smaller volumes than with drip infusion, the concentration suitable for infusion must be calculated according to the specifications of the pump.

With either method of infusion, the frequency, strength, and duration of contractions as well as the fetal heart rate must be carefully monitored throughout the infusion. Once the level of uterine activity is adequate, aiming for 3 to 4 contractions every 10 minutes, the infusion rate can often be reduced. In the event of uterine hyperactivity or fetal distress, the infusion must be discontinued immediately.

If, in women who are at term or near term, regular contractions are not established after a total dose of 5 units, it is recommended that the attempt to induce labor be ceased; it may be repeated on the following day, starting again at an infusion rate of 1 to 4 milliunits/minute.

**Incomplete, inevitable or missed abortion**

The usual dose is 5 units by intravenous infusion (diluted in physiological electrolyte solution and administered as a drip infusion or, preferably, by means of a variable-speed infusion pump) over 5 minutes, followed if necessary by an intravenous infusion at a rate of 20 to 40 milliunits/minute.

**Caesarean section**

The usual dose is 5 units by intravenous infusion (diluted in physiological electrolyte solution and administered as a drip infusion or, preferably, by means of a variable-speed infusion pump) over 5 minutes immediately after delivery.

**Prevention of postpartum uterine hemorrhage**

The usual dose is 10 units by intramuscular or intravenous injection. Alternatively, 5 units can be given by intravenous infusion (diluted in physiological electrolyte solution and administered as a drip infusion or, preferably, by means of a variable-speed infusion pump) over 5 minutes after delivery of the placenta. In women given oxytocin for induction or enhancement of labor, the infusion should be continued at an increased rate during the third stage of labor and for the next few hours.

**Treatment of postpartum uterine hemorrhage**

The usual dose is 10 units by intramuscular or intravenous injection. Alternatively, 5 units can be given by intravenous infusion (diluted in physiological electrolyte solution and administered as a drip infusion or, preferably, by means of a variable-speed infusion pump) over 5 minutes, followed in severe cases by infusion of a solution containing 5 to 20 units of oxytocin in 500 mL of an electrolyte-containing diluent, run at the rate necessary to control uterine atony.

**Contraindications**

- Hypersensitivity to the active substance or to any of the excipients of the product
- Hypertonic uterine contractions, mechanical obstruction to delivery, fetal distress

Any condition in which, for fetal or maternal reasons, spontaneous labor is advisable and/or vaginal delivery is contraindicated, such as:

- Significant cephalopelvic disproportion
- Fetal malpresentation
- Placenta previa and vasa previa
- Placental abruption
- Cord presentation or prolapse
- Overdistension or impaired resistance of the uterus to rupture as in multiple pregnancy
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- Polyhydramnios
- Grand multiparity
- In the presence of a uterine scar resulting from major surgery, including classical cesarean section.

Oxytocin should not be used for prolonged periods in patients with oxytocin-resistant uterine inertia, severe pre-eclampsia or severe cardiovascular disorders.

Oxytocin must not be administered within 6 hours after vaginal prostaglandins have been given (see “Interaction with other medicinal products and other forms of interaction” section below).

**Special warnings and precautions for use**

Attention should be paid to the oxytocin cold chain (i.e. the requirements of a temperature-controlled supply chain).

Oxytocin via intravenous infusion is preferred, as intravenous bolus injection may cause short-lasting hypotension accompanied by flushing and reflex tachycardia.

**Induction of labor**

The induction of labor by means of oxytocin should be attempted only when strictly indicated for medical reasons. Administration should only be under hospital conditions and qualified medical supervision.

Oxytocin should not be infused via the same apparatus as blood or plasma, because it is rapidly inactivated by oxytocin-inactivating enzymes.

**Cardiovascular disorders**

Oxytocin should be used with caution in patients who have a predisposition to myocardial ischemia due to preexisting cardiovascular disease (such as hypertrophic cardiomyopathy, valvular heart disease, and/or ischemic heart disease, including coronary artery vasospasm), to avoid significant changes in blood pressure and heart rate in these patients.

**QT syndrome**

Oxytocin should be given with caution to patients with known “long QT syndrome” or related symptoms and to patients taking medicines that are known to prolong the QTc interval (see “Interaction with other medicinal products and other forms of interaction” section below).

**Use for induction and enhancement of labour**

- Fetal distress and fetal death: Excessive doses of oxytocin can result in uterine overstimulation, which may cause fetal distress, asphyxia, and death, or may lead to hypertonicity, tetanic contractions, or rupture of the uterus. Careful monitoring of fetal heart rate and uterine motility (frequency, strength, and duration of contractions) is essential, so that the dosage may be adjusted to individual response.

- Particular caution is required in the presence of borderline cephalopelvic disproportion, secondary uterine inertia, mild or moderate pregnancy-induced hypertension or cardiac disease, and in patients above 35 years of age or with a history of lower-uterine-segment caesarean section.

- Disseminated intravascular coagulation: Rarely, the pharmacological induction of labor using uterotonic agents, including oxytocin, increases the risk of postpartum disseminated intravascular coagulation (DIC). The pharmacological induction itself and
not a particular agent is linked to such risk. This risk is increased in particular if the woman has additional risk factors for DIC, such as being 35 years of age or over, complications during pregnancy, and gestational age of more than 40 weeks. In these women, oxytocin or any other alternative medicine should be used with care, and the practitioner should be alerted by signs of DIC, such as bleeding from multiple sites, internal bleeding, purpura of extremities, severe malaise and fever.

**Intrauterine death**

In the case of fetal death in utero or in the presence of meconium-stained amniotic fluid, tumultuous labor must be avoided, as it may cause amniotic fluid embolism.

**Water intoxication**

Because oxytocin has mild antidiuretic activity, water intoxication associated with hyponatraemia may result from prolonged intravenous infusion at high doses with large volumes of fluid (e.g. in the treatment of inevitable or missed abortion or in the management of postpartum haemorrhage).

The combined antidiuretic effect of oxytocin and the intravenous fluid administration may cause fluid overload leading to a hemodynamic form of acute pulmonary edema without hyponatremia.

Features of water intoxication include:

- Headache, anorexia, nausea, vomiting and abdominal pain.
- Lethargy, drowsiness, unconsciousness and grand-mal type seizures.

To avoid this rare complication, the following precautions must be observed whenever high doses of oxytocin are administered over a long time:

- an electrolyte-containing diluent must be used (not glucose);
- the volume of infused fluid should be kept low (by infusing oxytocin at a higher concentration than recommended for the induction or enhancement of labor at term);
- fluid intake by mouth must be restricted and a fluid balance chart should be kept, and
- serum electrolytes should be measured when electrolyte imbalance is suspected.

**Renal impairment**

Caution should be exercised in patients with severe renal impairment because of possible water retention and possible accumulation of oxytocin.

**Anaphylaxis in women with latex allergy**

There have been reports of anaphylaxis following administration of oxytocin in women with a known latex allergy. Due to the existing structural homology between oxytocin and latex, latex allergy/intolerance may be an important predisposing risk factor for anaphylaxis following oxytocin administration.

**Interaction with other medicinal products and other forms of interaction**

**Concomitant use not recommended**

**Prostaglandins and their analogues**

Prostaglandins and their analogues facilitate contraction of the myometrium. They should not be used concomitantly with oxytocin because oxytocin can potentiate the uterine action of prostaglandins and analogues and vice versa (see “Contraindications” section above).
Note: Misoprostol may be used with oxytocin for the prevention and treatment of postpartum hemorrhage.

Medicines prolonging the QT interval
Oxytocin is potentially arrhythmogenic; concomitant drugs which prolong the QT interval should be used with caution (see “Special warnings and precautions for use” section above).

Other interactions
Inhalation anesthetics
Inhalation anesthetics (e.g., cyclopropane, halothane, sevoflurane, desflurane) have a relaxing effect on the uterus and produce a notable inhibition of uterine tone, which may in turn diminish the uterotonic effect of oxytocin. Their concurrent use with oxytocin has also been reported to cause cardiac rhythm disturbances.

Vasoconstrictors and sympathomimetics
Oxytocin may enhance the vasopressor effects of vasoconstrictors and sympathomimetics, even those contained in local anesthetics.

Caudal anesthetics
When given during or after caudal block anesthesia, oxytocin may potentiate the pressor effect of sympathomimetic vasoconstrictor agents.

Fertility, pregnancy and lactation
Pregnancy
The induction of labor by means of oxytocin should be attempted only when strictly indicated for medical reasons (see “Special warnings and precautions for use” section above).

Animal reproduction studies have not been conducted with oxytocin. Based on the wide experience with this medicine and its chemical structure and pharmacological properties, it is not expected to present a risk of fetal abnormalities when used as indicated.

Breastfeeding
Oxytocin may be found in small quantities in mother’s breast milk. However, oxytocin is not expected to cause harmful effects in the newborn because it passes into the alimentary tract where it undergoes rapid inactivation.

Fertility
Animal reproduction studies have not been conducted with oxytocin. The effects of oxytocin on fertility are unknown.

Effects on ability to drive and use machines
Oxytocin can induce labor. Women with uterine contractions should not drive or use machines.

Undesirable effects
As there is wide variation in uterine sensitivity, uterine spasm may be caused in some instances by what are normally considered to be low doses. When oxytocin is used by intravenous infusion for the induction or enhancement of labor, administration at too high a dose may result in uterine overstimulation, which may cause fetal distress, asphyxia, and death, or may lead to hypertonicity, tetanic contractions, soft tissue damage, or rupture of the uterus.
Undesirable effects in the tables below are ranked under heading of frequency, the most frequent first, using the following convention: very common (≥ 1/10); common (≥ 1/100, < 1/10); uncommon (≥ 1/1,000, < 1/100); rare (≥ 1/10,000, < 1/1,000); very rare (< 1/10,000), including isolated reports; frequency not known (cannot be estimated from the available data). The adverse drug reactions (ADRs) tabulated below are based on clinical trial results as well as post-marketing reports.

The ADRs related to post-marketing experience with oxytocin come from spontaneous case reports and literature cases. Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency—which is therefore categorized as not known. Within each system organ class, adverse reactions are presented in order of decreasing seriousness.

Table O-6. Adverse Reactions in Mother

<table>
<thead>
<tr>
<th>SYSTEM ORGAN CLASS</th>
<th>ADVERSE REACTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immune system disorders</td>
<td>Rare: anaphylactic/anaphylactoid reaction associated with dyspnoea, hypotension, or anaphylactic/anaphylactoid shock</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>Common: headache</td>
</tr>
</tbody>
</table>
| Cardiac disorders                          | Common: tachycardia, bradycardia  
Uncommon: arrhythmia  
Frequency not known: myocardial ischemia, electrocardiogram QTc prolongation |
| Vascular disorders                         | Frequency not known: hypotension, hemorrhage, angioedema                          |
| Gastrointestinal disorders                 | Common: nausea, vomiting                                                         |
| Skin and subcutaneous tissue disorders     | Rare: rash                                                                        |
| Pregnancy, puerperium, and perinatal conditions | Frequency not known: uterine hypertonus, tetanic contractions of uterus, rupture of the uterus |
| Metabolism and nutrition disorders         | Frequency not known: water intoxication, maternal hyponatremia                    |
| Respiratory, thoracic, and mediastinal disorders | Frequency not known: acute pulmonary edema                                        |
| General disorders and administration site conditions | Frequency not known: flushing                                                   |
| Blood and lymphatic system disorders       | Frequency not known: disseminated intravascular coagulation                      |

Table O-7. Adverse Reactions in Fetus/Neonate

<table>
<thead>
<tr>
<th>SYSTEM ORGAN CLASS</th>
<th>ADVERSE REACTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy, puerperium, and perinatal conditions</td>
<td>Frequency not known: fetal distress, asphyxia, death</td>
</tr>
<tr>
<td>Metabolism and nutrition disorders</td>
<td>Frequency not known: neonatal hyponatremia</td>
</tr>
</tbody>
</table>

**Overdose**

The fatal dose of oxytocin has not been established. Oxytocin is inactivated by proteolytic enzymes of the alimentary tract. Therefore, it is not absorbed from the intestine and is not likely to have toxic effects when ingested.

The symptoms and consequences of overdosage are those mentioned under the “Special warnings and precautions for use” and “Undesirable effects” sections above. In addition, as a result of uterine overstimulation, placental abruption, and/or amniotic fluid embolism have been reported.
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Treatment: When signs or symptoms of overdosage occur during continuous intravenous administration of oxytocin, the infusion must be discontinued at once and oxygen should be given to the mother. In cases of water intoxication, it is essential to restrict fluid intake, promote diuresis, correct electrolyte imbalance, and control convulsions that may eventually occur. In the case of coma, a free airway should be maintained with routine measures normally employed in the nursing of the unconscious patient.
PART 2: SPECIAL CONSIDERATIONS IN QUALITY ASSESSMENT

Information contained in this annex is intended to assist procurement agencies who plan to perform a full prequalification of oxytocin injection products. When assessing the complete quality/chemical, manufacturing and control (CMC) documentation, assessors should consider the following particular information on oxytocin injection.

API

As of June 2022, there is one oxytocin API prequalified by the WHO PQP.

Table O-8. Manufacturer of WHO-Prequalified Oxytocin API

<table>
<thead>
<tr>
<th>WHO REF. NUMBER</th>
<th>APPLICANT</th>
<th>API MANUFACTURING SITE</th>
<th>STORAGE CONDITION</th>
<th>RETEST PERIOD OR SHELF LIFE</th>
<th>DATE OF PRE-QUALIFICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>WHOAPI-361</td>
<td>Hemmo Pharmaceuticals Pvt. Ltd</td>
<td>Hemmo Pharmaceuticals Pvt. Ltd C-43, MIDC, Off Thane Belapur Road, TTC Industrial Area, Turbhe Navi, Mumbai Dist: Thane Maharashtra 400 613, India</td>
<td>Store in a refrigerator (2°C to 8°C), protect from moisture</td>
<td>36 months</td>
<td>9/25/2019</td>
</tr>
</tbody>
</table>

There are six manufacturers of oxytocin API that have obtained the certificate of suitability to monographs of the European Pharmacopoeia (CEP), confirming its suitable quality for use in medicinal products.

Table O-9. Manufacturers of Oxytocin API with CEP Certificate

<table>
<thead>
<tr>
<th>SUBSTANCE</th>
<th>CERTIFICATE HOLDER</th>
<th>CERTIFICATE NUMBER</th>
<th>ISSUE DATE</th>
<th>TYPE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxytocin (monograph number 780)</td>
<td>Aspen Oss B.V. NL 5349 AB Oss, The Netherlands</td>
<td>R1-CEP 2000-150-Rev 03</td>
<td>04/07/2016</td>
<td>Chemistry</td>
</tr>
<tr>
<td>Oxytocin (monograph number 780)</td>
<td>Hemmo Pharmaceuticals Pvt. Ltd In 400 613 Mumbai, India</td>
<td>R1-CEP 2008-029-Rev 01</td>
<td>9/13/2021</td>
<td>Chemistry</td>
</tr>
<tr>
<td>Oxytocin (monograph number 780)</td>
<td>Shanghai Soho-Yiming Pharmaceuticals Co., Ltd. CN 201 707 Chonggu Town, China</td>
<td>R1-CEP 2011-003-Rev 00</td>
<td>8/25/2017</td>
<td>Chemistry</td>
</tr>
</tbody>
</table>
Other manufacturers of oxytocin API should provide evidence for GMP compliance and API quality documentation as per WHO guidelines.  

The specifications of oxytocin API should be in line with a pharmacopeial monograph (Ph.Int., Ph.Eur./BP, or USP), with additional tests/limits for residual solvents and bacterial endotoxins. If intended for use in the aseptic manufacture of oxytocin injection without a further appropriate sterilization procedure, it must comply with the test for sterility.

Oxytocin is hygroscopic. It should be kept in an airtight container, protected from light, at a temperature of 2–8°C or if sterile, in a sterile, airtight, tamper-evident container.

**Excipients**

The excipients of oxytocin injection are as follows. There are no special concerns on the excipients.

<table>
<thead>
<tr>
<th>INGREDIENT</th>
<th>FUNCTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetic acid</td>
<td>pH adjustment</td>
</tr>
<tr>
<td>Chlorobutanol</td>
<td>Preservative</td>
</tr>
<tr>
<td>Ethanol</td>
<td>Co-solvent</td>
</tr>
<tr>
<td>Sodium acetate trihydrate</td>
<td>Buffering agent</td>
</tr>
<tr>
<td>Water for injection</td>
<td>Vehicle</td>
</tr>
</tbody>
</table>

Acetic acid is mainly used for pH adjustment. Some formulations may also include sodium hydroxide for such purpose. The pH adjustment is crucial for oxytocin stability because it was shown by Nachtmann et al.\(^1\) that oxytocin is most stable between pH 3 and 5. Hawe et al.\(^4\) also reported that the degradation of oxytocin was pH- and temperature-dependent and followed (pseudo) first order kinetics. Degradation was fastest at pH 9.0, followed by pH 7.0, pH 2.0, and pH 4.5. Oxytocin degradation in formulations between pH 2.0 and 9.0 follows Arrhenius kinetics, with the pH 4.5 formulation being the most stable. This information is important for formulation development of oxytocin injection.

Chlorobutanol may not be present in some formulations because oxytocin injection 10 IU in 1-mL is intended for a single-dose use, which generally does not require an antimicrobial preservative.

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\(^2\) Based on the formulation of an innovator product, Syntocinon™.


However, some manufacturers may add a preservative as an adjunct in aseptic processing of product where there may be product exposure during transfer, filling, packing operations. However, inclusion of the preservative does not compensate for a lower manufacturing standard.

Where chlorobutanol is included in the formulation as an antimicrobial preservative, the amount used should not exceed that used in the comparator products. The amount of preservative should be at the minimum quantity needed to act effectively, and this should be supported by studies. The assay of chlorobutanol (preservative content) should be included in the FPP specifications. If the lower limit for the proposed acceptance criterion for the assay of chlorobutanol is less than 90.0%, its effectiveness should be established by appropriate studies (e.g., USP or Ph.Eur. general chapters on antimicrobial preservatives) using a batch of the FPP containing a concentration of chlorobutanol corresponding to the lower proposed acceptance criteria.

A single primary-stability batch of the FPP should be tested for effectiveness of the antimicrobial preservative (in addition to preservative content) at the proposed shelf life for verification purposes, regardless of whether there is a difference between the release and shelf life acceptance criteria for preservative content.

Some manufacturers may claim that chlorobutanol acts as a chemical stabilizer, reducing degradation and allowing the product to be stored at 25°C. This claim is unfounded.5

The oxytocin injection formulation that contains chlorobutanol should also include a buffering agent (e.g. sodium acetate) to maintain the pH since chlorobutanol can hydrolyze when exposed to high temperature and form acidic degradation products.6 The product should therefore be kept refrigerated to mitigate against oxytocin degradation.

Manufacturing process

Oxytocin injection is a straightforward medicine to manufacture, but the main quality concern is the sterilization process and sterility of the facility where it is made.

The manufacturing process of oxytocin injection is a standard process—conducted under appropriate aseptic conditions—including the steps of preparation of the solution with adjustment of pH, pre- and sterile filtration, filling and sealing of the ampoules/vials. Satisfactory operating parameters and in-process controls should be defined at each stage of manufacture.

Since oxytocin is susceptible to degradation by heat, terminal steam sterilization cannot be used. Oxytocin injection should be manufactured by aseptic technique for the whole process or sterile filtration of the bulk solution followed by aseptic filling.

When the aseptic processing is used, all the ingredients must be in sterile grade and comply with the test for sterility before use.

The filters used in the sterile filtration should be validated with respect to pore size, compatibility with the product, absence of extractables, and lack of adsorption of the API or any of the components.

Oxytocin injection is prepared by dissolving oxytocin API in the diluent (solution of excipients). Since oxytocin API is hygroscopic (i.e. tend to absorb moisture from the air), it should be kept under the control of relative humidity before introducing into the diluent to avoid degradation. Maintain

the temperature of dispensed oxytocin between 2°C and 8°C with the help of frozen-gel ice packs and thermometer in a thermo cool box. The API, after being dispensed, should be used as soon as possible to avoid exposure to light and oxygen.

The selection of the environment temperature conditions may depend on the length of each of the stages of production, the time between stages and how the bulk solution is packed and stored. Suggested conditions for production are at temperatures not more than 25°C.

Nitrogen purging should be carried out throughout the manufacturing and filling process to minimize the contact with atmospheric and dissolved oxygen. If bulk solution storage is required, store the solution under a nitrogen blanket. The lid of the manufacturing tank should be opened and closed immediately after each addition. The temperature of the bulk solution should be maintained below 10°C ± 5°C until filtration.

For the validation of aseptic processing, simulation process trials should be conducted. This involves filling containers with culture media under normal conditions, followed by incubation. Refer to current WHO GMP guidelines for details.

A manufacturing process validation protocol for the validation of the first three production scale batches should be submitted. In addition, completed process validation reports for the sterile processes for three cycles/runs should be submitted. In cases where the manufacturer is already manufacturing production scale batches, full validation data for the production of at least three (3) consecutive production scale batches should be submitted.

Note: The risk for potential presence of elemental impurities in the finished drug product needs to be assessed according to the ICH Q3D “Guideline for Elemental Impurities”. Elemental impurity sources include the API, excipients, utilities in direct contact with the product or manufacturing equipment (compressed air, water, etc.), the manufacturing equipment and the container closure system. Depending on the risk assessment and results from batches tested for the relevant elemental impurities, routine testing of the final product may not be necessary.

Packaging

Neutral type I glass ampoule or vial should be used.

Suitability of the container should be demonstrated, including the following properties:

Safety

- Glass ampoule/vial must meet compendial requirements such as USP<660> and USP<1660>.
- Rubber stopper (for vial) must meet compendial requirements such as USP<381> and USP<87>/<88>. Composition of the rubber stopper along with a declaration from the supplier that the material is free of 2-mercapto benzothiazoles (2-MCBT) and nitrosamines should be provided.
- Washing and sterilization/depyrogenation, if applicable, should be supported by process validation data.

Protection

Container integrity regarding microbial contamination should be demonstrated by microbial or dye ingress or other methods, such as:
Compatibility
- Extractables/leachables data of the rubber stoppers should be provided.
- Accelerated and long-term stability data on vials stored in inverted orientation should be submitted to further support absence of leachables as well as sorption.
- Compatibility of the FPP with diluents (such as 5% dextrose injection or 0.9% sodium chloride as per the label instruction), if relevant, over the proposed dilution range (label) in specified containers, such as PVC, may also need to be demonstrated.

Bioequivalence requirements
A biowaiver can be requested as per WHO Technical Report Series, No. 992, which indicates that no bioequivalence study is necessary when the pharmaceutical product is to be administered parenterally (e.g., intravenously, subcutaneously or intramuscularly) as an aqueous solution containing the same API in the same molar concentration as the comparator product and the same or similar excipients in comparable concentrations as in the comparator product.

Appropriate comparator products are Syntocinon® (oxytocin 10 IU/mL injection, Novartis or Sigma Tau, Spain), Pitocin® (oxytocin 10 IU/mL injection, PAR Sterile Products LLC, USA), Oxytocin 10 IU/mL injection (West-Ward Pharmaceuticals Int Ltd, USA), and Oxytocin 10 IU/mL injection (Fresenius Kabi LLC, USA). The composition of the proposed product should be the same as the comparator product.