This part outlines the scientific assessment and knowledge about this product at the time of prequalification. Updates to this information are included in parts 1 to 5 and 8 of this WHOPAR.

SCIENTIFIC DISCUSSION

Name of the Finished Pharmaceutical Product:	[RH079 trade name][1]
Manufacturers of Prequalified Product:	HBM Pharma s.r.o., Sklabinska 30, Martin, 036 80, Slovakia UAB Santonika, Veiveriu str 134B, Kaunas, LT-46353, Lithuania
Active Pharmaceutical Ingredient (API):	Oxytocin
International Nonproprietary Name:	Oxytocin
Pharmaco-therapeutic group (ATC Code):	Posterior pituitary lobe hormones (H01BB02)
Therapeutic indication:	Indicated in women for the active management of the third stage of labour, prevention and treatment of postpartum haemorrhage and for managing pregnancy complications where uterine contraction is clinically desirable

[1]Trade names are not prequalified by WHO. This is the national medicines regulatory authority's responsibility.

1. Introduction

[RH079 trade name] is indicated for women for the active management of the third stage of labour, prevention and treatment of postpartum haemorrhage and for managing pregnancy complications where uterine contraction is clinically desirable.

2. Assessment of Quality

The assessment was done in accordance with the requirements of WHO's *Guidelines on submission of documentation for a multisource (generic) finished pharmaceutical product for the WHO Prequalification of Medicines Programme: quality part.*

Active pharmaceutical Ingredient (API)

A CEP (Certificate of Suitability) issued by the EDQM was submitted, ensuring good manufacturing control and applicability of the Ph.Eur monograph to control quality of the API.

Other ingredients

Other ingredients include chlorobutanol hemihydrate, acetic acid glacial and water for injections. No excipient with the risk of transmitting TSE/BSE is used.

Finished pharmaceutical product (FPP)

Pharmaceutical development and manufacture

The multisource Oxytocin 10 IU/mL Solution for Injection is a colourless, clear, sterile solution contained in a clear type I glass ampoule. The ampoules containing 1mL of the solution for injection have either a break ring or blue open point cut or colour rings (lower turquoise and upper red) with red open point cut. The ampoules should be stored in a refrigerator (2°C – 8°C).

The formulation development is based on the WHO recommended comparator product, Pitocin® 10 IU/ml injection (King Pharmaceuticals, Bristol). The ingredients selected are the same as those used in the comparator. The development strategy was to establish a formulation with good stability. Since an oxytocin solution is more stable in acidic medium, the pH of the solution for injection is adjusted with acetic acid.

The manufacturing process is a standard aseptic process, conducted under appropriate conditions, including the steps of mixing and dissolving all ingredients and water for injection, sterile filtration, followed by filling into empty sterile ampoules and sealing under nitrogen. Satisfactory operating parameters and in-process controls have been defined at each stage of manufacture. Process validation have been conducted on 3 consecutive batches.

Specifications

The finished product specifications include tests for description, identification of the API (HPLC), clarity, colour, pH, extractable volume, particulate contamination (visible and sub-visible), chlorobutanol hemihydrate content, related substances (HPLC), sterility, bacterial endotoxins and assay of oxytocin (HPLC).

Stability testing

Stability studies have been performed at 2°C – 8°C as long-term storage conditions and for six months at 25°C/60% RH as accelerated conditions. A noticeable decrease in oxytocin assay value was observed at the accelerated storage condition, though within agreed limits. Based on the available stability data, the proposed shelf life and storage conditions of the unopened ampoules as stated in the SmPC are acceptable.

Conclusion

The quality part of the dossier is accepted.

3. Assessment of Bioequivalence

According to the WHO guidelines on registration requirements to establish interchangeability for multisource (generic) pharmaceutical products 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.

These conditions are fulfilled for [RH079 trade name].

4. Summary of Product Safety and Efficacy

[RH079 trade name] has been shown to conform to the same relevant standards of quality, efficacy and safety as those required of the comparator product. According to the submitted data on quality [RH079 trade name] is pharmaceutically and therapeutically equivalent and thus interchangeable with the comparator product Syntocinon® (oxytocin 10 units/ml, solution for injection, Novartis) for which benefits have been proven in terms of clinical efficacy.

The clinical safety of this product is considered to be acceptable when guidance and restrictions as stated in the Summary of Product Characteristics are taken into account. Reference is made to the SmPC (WHOPAR part 4) for data on clinical safety.

5. Benefit risk assessment and overall conclusion

Quality

Physicochemical and biological aspects relevant to the uniform pharmaceutical characteristics have been investigated and are controlled in a satisfactory way. The quality of this product is considered to lead to an acceptable clinical performance when [RH079 trade name] is used in accordance with the SmPC.

Bioequivalence

N/A

Efficacy and Safety

Regarding clinical efficacy and safety, [RH079 trade name] is considered effective and safe to use when the guidance and restrictions presented in the Summary of Product Characteristics are taken into consideration.

Benefit–risk Assessment

Based on the WHO's assessment of data on quality, bioequivalence, safety and efficacy the team of assessors considered that the benefit–risk profile of [RH079 trade name] was acceptable for the indications shown in the SmPC and has advised that the quality, efficacy and safety of [RH079 trade name] allow inclusion of [RH079 trade name], manufactured at HBM Pharma s.r.o., Sklabinska 30, Martin, 036 80, Slovakia and at UAB Santonika, Veiveriu str 134B, Kaunas, LT-46353, Lithuania, in the list of prequalified medicinal products.