This part reflects the scientific knowledge and the information about this product available at the time of prequalification. Thereafter, updates may have become necessary which are included in parts 1 to 5 and, if related to pharmaceutical issues, also documented in part 8 of this WHOPAR.

SCIENTIFIC DISCUSSION

Name of the Finished Pharmaceutical Product:	Streptomycin (as sulfate) 1g powder for injection*
Manufacturer of Prequalified Product:	NCPC New Preparation Branch Factory No.115 Hainan Road, Shijiazhuang Economic & Technological Development Zone, Hebei, China.
Active Pharmaceutical Ingredient (API):	Streptomycin
Pharmaco-therapeutic group (ATC Code):	Aminoglycoside antibacterials, Streptomycins (J01GA01)
Therapeutic indication:	Streptomycin (as sulfate) 1 g powder for injection is indicated in combination with other antituberculosis agents for the treatment of tuberculosis caused by streptomycin -sensitive strains of *Mycobacterium tuberculosis*. Streptomycin injection is indicated as a second-line antimycobacterial drug when first-line drugs cannot be used because of resistance or intolerance. Streptomycin should only be used when other second-line injectable agents, aminoglycosides or capreomycin, cannot be used.

* Trade names are not prequalified by WHO. This is the national medicines regulatory authority's (NMRA) responsibility. Throughout this WHOPAR the proprietary name is given as an example only.

1. Introduction

Streptomycin (as sulfate) 1 g powder for injection is indicated in combination with other antituberculosis agents for the treatment of tuberculosis caused by streptomycin -sensitive strains of *Mycobacterium tuberculosis*, when first-line drugs cannot be used because of resistance or intolerance. Streptomycin should only be used when other second-line injectable agents, aminoglycosides or capreomycin, cannot be used.

Streptomycin (as sulfate) 1g powder for injection should be prescribed by a physician experienced in the management of tuberculosis infection.

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)

Streptomycin sulfate (sterile) used in the manufacture of Streptomycin (as sulfate) 1g powder for injection has been prequalified by WHO according to WHO's Procedure for assessing the acceptability, in principle, of active pharmaceutical ingredients for use in pharmaceutical products (WHO Technical Report Series No. 953, 2009, Annex 4). This procedure provides an assurance that streptomycin sulfate (sterile), used in the manufacture of Streptomycin (as sulfate) 1g powder for injection, is of good quality and manufactured in accordance with WHO good manufacturing practices (GMP). API prequalification consists of a comprehensive evaluation procedure that has two components: Assessment of the API master file (APIMF) to verify compliance with WHO norms and standards, and assessment of the sites of API manufacture to verify compliance with WHO GMP requirements.

Other ingredients

The powder for injection contains no excipient.

Finished pharmaceutical product (FPP)

Pharmaceutical development and manufacture

The powder for injection is available as a white or almost white powder presented in a 7 ml Type III colourless glass vial closed with a chlorobutyl rubber stopper and sealed with a flip-off aluminium cap. Each vial contains the equivalent of 1 g streptomycin.
The powder for injection contains no excipient. Sterile streptomycin sulfate powder, as obtained from the API manufacturer, is filled into sterile vials, which are stoppered and sealed under aseptic conditions. The API is very soluble and is fully dissolved before administration hence particle size and polymorphism is not considered to be a critical issue. It is however hygroscopic and should be protected from moisture.

Product specifications

The specifications for the powder for injection are pharmacopoeial based and include tests for characters, identification of the API and sulfate, acidity or alkalinity, streptomycin B (TLC), loss on drying, uniformity of dosage units, average filling weight, visible and sub-visible particles, bacterial endotoxins, sterility, assay (microbiologically), clarity and colour of solution, reconstitution time and related substances (HPLC).

Stability testing

Stability studies have been performed at 30°C/75%RH (zone IVb) as long-term storage condition and for six months at 40°C/75%RH as accelerated condition. All results were within specification limits. A slight increase in LOD and a slight increase in degradation products with slight decrease in assay value were noted. Based on the available stability data, the proposed shelf life and storage conditions of the unopened vials as stated in the SmPC are acceptable. Compatibility studies between the reconstituted powder and the rubber closure were conducted. It was demonstrated that the reconstituted solution is chemically and physically stable for 24 hours when stored at 2 – 8°C in the upright and inverted position.

Conclusion

The quality part of the dossier is accepted.

3. Assessment of Bio-Equivalence

The applicant requested a biowaiver 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.
The appropriate comparator product is Streptomycin sulfate (1 g base/vial injection, X Gen Pharms, US). The proposed product, i.e. Streptomycin 1 g powder for injection, is also a solution for injection. Both formulations do not contain excipients.
As the proposed product meets the biowaiver requirements described above, a biowaiver can be granted.

4. Summary of Product Safety and Efficacy

Streptomycin (as sulfate) 1g powder for injection has been shown to conform to the same relevant standards of quality, efficacy and safety as those required of the innovator product. According to the submitted data on quality Streptomycin (as sulfate) 1g powder for injection is pharmaceutically and therapeutically equivalent and thus interchangeable with the innovator product Streptomycin sulfate X Gen Pharms, 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 Streptomycin (as sulfate) 1g powder is used in accordance with the SmPC.

Bioequivalence

N/A

Efficacy and Safety

Regarding clinical efficacy and safety, Streptomycin (as sulfate) 1g powder for injection is considered effective and safe to use when the guidance and restrictions in the Summary of Product Characteristics are taken into consideration.

Benefit Risk Assessment

Based on WHO's assessment of data on quality, safety and efficacy the team of assessors considered that the benefit–risk profile of Streptomycin (as sulfate) 1g powder for injection was acceptable for the following indication: **"in combination with other antituberculosis agents for the treatment of tuberculosis caused by streptomycin -sensitive strains of *Mycobacterium tuberculosis*, when first-line drugs cannot be used because of resistance or intolerance"** and has advised that the quality, efficacy and safety of Streptomycin (as sulfate) 1g powder for injection allow inclusion of Streptomycin (as sulfate) 1g powder for injection, manufactured at NCPC New Preparation Branch Factory, No.115 Hainan Road, Shijiazhuang Economic & Technological Development Zone, Hebei, China in the list of prequalified medicinal products.