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:	[TB318 trade name][*]
Manufacturer of Prequalified Product:	Shanghai Harvest Pharmaceutical Co., Ltd No. 805, Jinhu Road, Pudong, Shanghai, 201 206, P.R. China
Active Pharmaceutical Ingredients (APIs):	Kanamycin (as monosulfate)
Pharmaco-therapeutic group (ATC Code):	Antimycobacterial antibiotics for treatment of tuberculosis. ATC Code J01GB04
Therapeutic indication:	[TB318 trade name] is indicated in combination with other antituberculosis agents for the treatment of tuberculosis caused by kanamycin-sensitive strains of *Mycobacterium tuberculosis*. Kanamycin is only indicated as a second-line antimycobacterial drug when first-line drugs cannot be used because of resistance or intolerance.

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

1. Introduction

[TB318 trade name] is indicated in combination with other antituberculosis agents for the treatment of tuberculosis caused by kanamycin-sensitive strains of *Mycobacterium tuberculosis*. Kanamycin is only indicated as a second-line antimycobacterial drug when first-line drugs cannot be used because of resistance or intolerance.

[TB318 trade name] should be initiated by a health care provider 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)

Kanamycin monosulfate has been prequalified by WHO according to WHO's Procedure for assessing the acceptability, in principle, of active pharmaceutical ingredients for use in in pharmaceutical products (WHO Technical Report Series No. 953, 2009, Annex 4). This procedure provides an assurance that the API, used in the manufacture of [TB318 trade name] 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 inspection of the sites of API manufacture to verify compliance with WHO GMP requirements.

Other ingredients

Other ingredients used in the solution for injection include sodium bisulfite, sodium citrate, sulfuric acid and water for injection. The excipient specifications are pharmacopoeial based.

Finished pharmaceutical product (FPP)

Pharmaceutical development and manufacture

The multisource product is available as a colourless to slightly yellow or yellowish-green clear liquid, filled in 4 mL clear colourless type I mid-content borosilicate glass ampoule.
Each vial contains the equivalent of 500 mg kanamycin activity. Two strengths were developed: 500 mg and 1000 mg. The two strengths are distinguished by means of the volume of the glass vial.
The solution for injection contains sodium bisulfite, sodium citrate, sulfuric acid and water for injection as excipients. The choice and concentration of excipients used for the finished pharmaceutical product are the same as the WHO recommended comparator product Kantrex Injection 1g/3mL (Bristol-Myers Squibb). The product was developed by evaluating the impact of the sequence of addition of the excipients to the API, control of pH, temperature, selection of the pressure of nitrogen and sterilization process (by heat) on the critical quality attributes of the finished pharmaceutical product. Based on the satisfactory data of optimization trials, the formulation was finalized resulting in a product matching the quality target product profile. Appropriate in-process controls were set to ensure batch-to-batch reproducibility.

Specifications

The specifications for the solution for injection include tests for characteristics, colour of solution, identification of the API (HPLC and TLC) and sulfate, pH, related substances (HPLC) bacterial endotoxin, extractable volume, particulate contamination, visible particles, sterility and assay (HPLC).

Stability testing

Stability studies have been performed on samples at 30°C/75%RH (zone IVb) as long-term storage condition and for six months at 40°C/75%RH as accelerated condition. Based on the available stability data, the proposed shelf life and storage conditions as stated in the SmPC are acceptable. Photostability results revealed that a special precautionary statement for protection from light is not necessary.

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 [TB318 trade name].

4. Summary of Product Safety and Efficacy

[TB318 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, [TB318 trade name] is pharmaceutically and therapeutically equivalent and thus interchangeable with the comparator product Kantrex® (kanamycin mono-sulfate, 250mg/ml, Bristol-Myers Squibb) solution for injection for which benefits have been proven in terms of clinical efficacy.

The clinical safety of this product is considered 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 [TB318 trade name] is used in accordance with the SmPC.

Bioequivalence

N/A

Efficacy and Safety

Regarding clinical efficacy and safety, [TB318 trade name] is considered effective and safe when the guidance and restrictions presented in the Summary of Product Characteristics are taken into consideration.

Benefit–risk Assessment

Based on the WHO assessment of data on quality, bioequivalence, safety and efficacy the team of assessors considered that the benefit–risk profile of [TB318 trade name] was acceptable for the following indication: '**in combination with other antituberculosis agents for the treatment of tuberculosis caused by kanamycin-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 [TB318 trade name] allow inclusion of [TB318 trade name], manufactured at Shanghai Harvest Pharmaceutical Co., Ltd, No. 805, Jinhu Road, Pudong, Shanghai, 201 206, P.R. China, in the list of prequalified medicinal products.