SCIENTIFIC DISCUSSION

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.

Name of the Finished Pharmaceutical Product:	Ceftriaxone (as sodium) 500mg Powder for Injection [1*]
Manufacturer of Prequalified Product:	Egyptian International Pharmaceutical Industries Co. (EIPICO) Tenth of Ramadan City- Industrial Area B1- Egypt P.O. Box: 149 Tenth of Ramadan Telephone: 02-2-015 361 663 Fax: 02-2-015 364 377
Active Pharmaceutical Ingredient (API):	Ceftriaxone (as sodium)
Pharmaco-therapeutic group (ATC Codes):	Antibacterials , Third-generation cephalosporins, ATC code: J01DD04. Antimycobacterials, thiocarbamide derivatives (J04AD01)
Therapeutic indication:	Ceftriaxone (as sodium) 500mg Powder for Injection is indicated for the treatment of bacterial infections in Human Immunodeficiency Virus (HIV)/AIDS patients.

1 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

Ceftriaxone (as sodium) 500mg Powder for Injection is indicated for the treatment of bacterial infections in Human Immunodeficiency Virus (HIV)/AIDS patients.

Ceftriaxone (as sodium) 500mg Powder for Injection should be co-administered with other antibacterial agents whenever the possible range of causative bacteria would not fall within its spectrum.

Ceftriaxone (as sodium) 500mg Powder for Injection should be initiated by a health care provider experienced in the management of bacterial infections in Human Immunodeficiency Virus (HIV)/AIDS patients.

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, sterile ceftriaxone sodium.

Stability testing was conducted according to the requirements of WHO. The proposed re-test period is justified based on the stability results when the API is stored in the original packing material.

Other ingredients

The powder for injection contains no excipient.

Finished pharmaceutical product (FPP)

Pharmaceutical development and manufacture
The multisource product is a sterile white or yellowish crystalline powder for single use, containing 1.193 g ceftriaxone sodium equivalent to 1 g ceftriaxone. The powder is presented in a colourless Type II glass vial with a grey bromobutyl rubber stopper then capsulated with an aluminium pilfer-proof cap. The sterile powder is dissolved in sterile water for injections for intravenous injection and in 1% sterile lidocaine hydrochloride solution for intramuscular injection. The solvents for intravenous infusion are listed in the SmPC.

Similar to the comparator product, Rocephin® 1 g powder for injection, the multisource product contains no excipient. The manufacture, under aseptic conditions, entails filling of pre-sterilized vials with the sterile ceftriaxone sodium powder and closing of the vials with pre-sterilized bromobutyl rubber stoppers. Satisfactory operating parameters and in-process controls have been established. Sufficient validation data were provided.

Specifications
The finished product specifications include tests for description, identification of API, uniformity of dosage units (by weight variation), pH, clarity and colour of solution, rate of dissolution, visible and sub-visible particulate matter, water content, assay, related substances (HPLC), bacterial endotoxins and sterility.

Stability testing
Stability studies on the unopened vials, in upright and inverted position, have been performed at 25□C/60%RH and 30□C/65%RH as long-term storage conditions and for six months at accelerated conditions. The data showed little change with time and were well within the agreed specifications at both storage conditions. Based on the available stability data, the proposed shelf life and storage conditions of the unopened vials as stated in the SmPC are acceptable.

The in-use storage times and conditions of the solutions for injection and infusion appearing in the SmPC are supported by in-use chemical and physical stability testing.

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 Ceftriaxone (as sodium)500mg Powder for Injection.

4. Summary of Product Safety and Efficacy

Ceftriaxone (as sodium) 1 g 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 Ceftriaxone (as sodium) 1 g Powder for Injection is pharmaceutically and therapeutically equivalent and thus interchangeable with the innovator product Rocephin® 1 g powder for injection Rocephin 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 Ceftriaxone (as sodium) 1 g Powder for Injection is used in accordance with the SmPC.

Efficacy and Safety

Regarding clinical efficacy and safety, Ceftriaxone (as sodium) 500mg 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, bioequivalence, safety and efficacy the team of assessors considered that the benefit–risk profile of Ceftriaxone (as sodium) 500mg Powder for Injection was acceptable for the following indication: **" treatment of bacterial infections in Human Immunodeficiency Virus (HIV)/AIDS patients** and has advised that the quality, efficacy and safety of Ceftriaxone (as sodium) 500mg Powder for Injection allow inclusion of Ceftriaxone (as sodium) 500mg Powder for Injection , manufactured at Egyptian International Pharmaceutical Industries Co. (EIPICO), Tenth of Ramadan City- Industrial Area B1- Egypt, in the list of prequalified medicinal products.