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	[TB286 trade name][*]
Manufacturer of Prequalified Product	Mylan Laboratories Limited F-4, F-12, Malegaon M.I.D.C. Sinnar, Nashik – 422113 Maharashtra state India
Active Pharmaceutical Ingredient(s) (API)	Moxifloxacin
Pharmaco-therapeutic group (ATC Code)	Quinolone antibacterials, Fluoroquinolones (J01MA14)
Therapeutic indication	[TB286 trade name] is indicated in combination with other antituberculosis agents for the treatment of tuberculosis caused by *Mycobacterium tuberculosis.*

1. Introduction

[TB286 trade name] is indicated in combination with other antituberculosis agents for the treatment of tuberculosis caused by *Mycobacterium tuberculosis.*

[TB286 trade name] 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)

Based on scientific principles the WHO Prequalification Team – Medicines has identified moxifloxacin (as hydrochloride) up to 400 mg oral dose as a BCS class 1 API, eligible for BCS-based biowaiver applications. The API is thus regarded highly soluble in terms of the BCS.

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.

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

Other ingredients used in the core tablet formulation include microcrystalline cellulose, croscarmellose sodium, copovidone and magnesium stearate, all being pharmacopoeial controlled.

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

The commercially sourced proprietary film-coating mixture contains hypromellose, titanium dioxide, macrogol and iron oxide red. BSE/TSE compliance declarations were provided for all excipients.

Finished pharmaceutical product (FPP)

Pharmaceutical development and manufacture

The multisource product is a pink, film-coated, capsule shaped, biconvex, bevelled edge tablet debossed with 'M' on one side of the tablet and 'MO2' on other side. The tablets are presented in clear transparent PVC/PVDC-Al blisters and white opaque HDPE bottles with screw caps.

The multisource product was developed as an immediate release, solid oral tablet dosage form that would be bioequivalent to the comparator product, Avelox® 400 mg tablets. The excipients selected for the core tablets are conventional pharmaceutical ingredients, included in the formulation at suitable levels for recognised purposes. The compatibility of the excipients with the API was demonstrated by API-excipient studies performed on binary mixtures.

Due to poor flow properties of the API and its high content in the formulation, the direct compression process was not explored. In order to prepare a blend with good flow and compressibility, dry and wet granulation processes were evaluated. After initial trials, the wet granulation process was selected. The formulation and process parameters were optimised, targeting the dissolution profiles of the comparator product. Appropriate in-process controls were set to ensure batch-to-batch reproducibility.

Specifications

The finished product specifications include appropriate tests for description, identification of the API (TLC and UV) and colorants, uniformity of dosage units (by mass variation), dissolution (UV detection), assay (UV at release, HPLC during stability), related substances (HPLC), water content (KF) and microbial limits. The test procedures have been adequately validated.

Stability testing

Stability studies have been conducted at 30°C/75%RH (zone IVb) as long-term storage condition and for six months at accelerated conditions in the packaging proposed for marketing of the product. The product proved to be quite stable at both long term and accelerated storage conditions with no apparent negative trend in all packaging configurations, except for a slight increase in water content. Based on the available stability data, the proposed shelf life and storage conditions as stated in the SmPC are acceptable.

Conclusion

The quality part of the dossier is accepted.

3. Assessment of bioequivalence

No bioequivalence study has been performed. As moxifloxacin is selected by the WHO being eligible for a BCS based biowaiver, a request for a biowaiver has been made. In accordance with the WHO guidance and criteria for biowaivers, supporting data have been provided regarding formulation comparability and in vitro dissolution data.

Comparability between the reference Avelox® 400 mg tablet (Bayer Healthcare) and the test [TB286 trade name] (Mylan Laboratories Ltd., India) regarding the qualitative and quantitative composition of the formulations have been sufficiently proven. In addition, comparable in vitro dissolution at a pH 1.2, 4.5 and 6.8 have been shown. Accordingly, the test tablet [TB286 trade name] (Mylan Laboratories Ltd., India) meets the criteria for a BCS based biowaiver and is therefore considered bioequivalent to the reference Avelox® 400 mg tablet (Bayer Healthcare).

4. Summary of product safety and efficacy

[TB286 trade name] has been shown to conform to the same relevant standards of quality, efficacy and safety as those required of the comparator product. [TB286 trade name] fulfilled all criteria for waiving an in-vivo bioequivalence study as per relevant WHO guidance. The clinical safety of [TB286 trade name] is considered acceptable when guidance and restrictions stated in the summary of product characteristics (SmPC) are considered. Refer 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 [TB286 trade name] is used in accordance with the SmPC.

Bioequivalence

[TB286 trade name] fulfilled all criteria for waiving an in-vivo bioequivalence study as per relevant WHO guidance. Hence, [TB286 trade name] and Avelox® 400 mg tablet (Bayer Healthcare) can be considered bioequivalent.

Efficacy and Safety

Regarding clinical efficacy and safety, [TB286 trade name] is considered effective and safe to use when the guidance and restrictions in the SmPC 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 [TB286 trade name] was acceptable for the following indication: **'in combination with other antituberculosis agents for the treatment of tuberculosis caused by Mycobacterium tuberculosis'**, and would allow inclusion of [TB286 trade name], manufactured at Mylan Laboratories Limited, F-4, F-12, Malegaon M.I.D.C., Sinnar, Nashik – 422113, Maharashtra, State, India in the list of prequalified medicinal products.