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	[NT012 trade name]*
Manufacturer of Prequalified Product	Medopharm Private Limited Unit II, No. 50, Kayarambedu Village Guduvanchery - 603 202 Tamil Nadu India Tel.:0091-44-27438251/27438460/27438470 /27438450/27438449 Fax:0091-44-27438410
Active Pharmaceutical Ingredient (API)	Albendazole
Pharmaco-therapeutic group (ATC Code)	Anthelminthics for treatment of trematodes, nematodes and cestodes causing the infections (P02CA03)
Therapeutic indication	[NT012 trade name] is indicated for the treatment of cestode infections, lymphatic filariasis and other nematode infections

1. Introduction

[NT012 trade name] is indicated for the treatment of cestode infections, lymphatic filariasis and other nematode infections

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 for albendazole ensuring good manufacturing control and applicability of the respective Ph.Eur monograph to control the quality of the API. Albendazole is of BCS low solubility, hence particle size distribution (PSD) and polymorphism are considered critical parameters and form part of the FPP manufacturer's API specifications.

Other ingredients

Other ingredients used in the tablet formulation include croscarmellose sodium, lactose monohydrate, maize starch, colour lake of sunset yellow / FD&C yellow #6, povidone, saccharin sodium,

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

polysorbate 80, orange flavourant, sodium lauryl sulfate, microcrystalline cellulose and magnesium stearate, all of which are controlled by acceptable specifications. Lactose monohydrate and magnesium stearate are from bovine and vegetable origin, respectively. TSE/BSE compliance declarations were provided for the excipients.

Finished pharmaceutical product (FPP)

Pharmaceutical development and manufacture

The multisource product is a pale orange, oval, uncoated, mottled tablet. It is biconvex (rounded on top and bottom) with a flat edge. The tablet has a break line on one side and is plain on the other side. The break line is intended for subdivision of tablet when a half dose is to be administered. The tablets are packaged in a sealed transparent plastic (polyethylene) bag inside an HDPE pot.

The aim of the formulation development strategy was to obtain a stable multisource product bioequivalent to the WHO recommended comparator product, Eskazole (Albendazole 400 mg tablets). The selection of the excipients was primarily based on the qualitative composition of the comparator product and API-excipient compatibility studies. The flavouring agent and sweetener were used to improve the taste of the chewable tablets. A wet granulation manufacturing process was selected to achieve an immediate release tablet with release profile similar to that of the comparator product. Various experiments were performed to select and optimize the concentration of excipients and other process parameters to obtain tablets of desired characteristics, including dissolution profile similarity with the comparator product. Satisfactory in-process controls have been established.

According to a risk evaluation by the applicant, the FPP has no potential to contain N-nitrosamine impurities and hence no risk was identified, though the manufacturer undertook to conduct confirmatory testing for potential N-nitrosamines on selected batches post prequalification.

Specifications

The finished product specifications include tests for description, identification of the API (TLC and HPLC), average weight, uniformity of dosage units (by mass variation), disintegration time, water content (KF), tablet dimensions (length, width and thickness), hardness, friability, average and uniformity of mass of subdivided parts (half tablet), dissolution (UV detection), related substances (HPLC), assay (HPLC), albendazole polymorphic form-II (p-XRD) 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 conditions and for six months at accelerated conditions in the packaging proposed for marketing of the product. The product proved to be quite stable at these storage conditions, with little degradation observed. 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

The following bioequivalence study has been performed in 2024 according to internationally accepted guidelines.

Single dose oral bioequivalence study of Albendazole chewable tablets 400 mg and Eskazole (albendazole) chewable tablet 400 mg in healthy adult human subjects under fed conditions (study no. C1B04248).

The objective of the study was to compare the bioavailability of the stated Albendazole 400 mg chewable tablet manufactured by/for Medopharm Private Ltd., India (test drug) with the reference

formulation Eskazole® (Aspen Pharmacare Australia Pty Ltd.) and to assess bioequivalence. The comparison was performed as a single centre, open label, single dose, randomized, fully replicate crossover study in healthy subjects under fed conditions. Each subject was assigned to receive each of the following two treatments twice in a randomized fashion:

Treatment T:	Test – 1 chewable tablet abendazole 400 mg (albendazole 400 mg) Batch no. 222053001.
Treatment R:	Reference – 1 tablet Eskazole® 400 mg (albendazole 400 mg) Batch no. 6S2K.

A 7-day wash-out period was observed between administration of test and reference. Serial blood samples (1 pre-dose sample and 22 samples within 24 h post dose) were taken during each study period to obtain bioavailability characteristics AUC, C_{max} and t_{max} for bioequivalence evaluation. Drug concentrations for albendazole were analyzed using a validated LC-MS/MS method. The limit of quantification was stated to be about 0.25 ng/mL for albendazole.

The study was performed with 56 participants; data generated from a total of 53 subjects were utilized for analysis to establish pharmacokinetic parameters and assess bioequivalence.

Arithmetic mean and geometric mean values of the pharmacokinetic variables for albendazole as well as statistical results are summarised in the following table:

Albendazole

Pharmacokinetic Parameter	**Test formulation (T)** arithmetic mean ± SD (geometric mean)	**Reference (R)** arithmetic mean ± SD (geometric mean)	**log-transformed parameters**	
			Ratio T/R (%)	**Conventional** 90% CI (ANOVAlog)
t_{max} * (h)	3.08 ± 0.96	3.02 ± 1.00	–	–
C_{max} (ng/mL)	50 ± 47 (31)	53 ± 54 (30)	105.2	89.8 – 123.1
AUC_{0-t} (ng·h/mL)	197 ± 205 (118)	194 ± 201 (106)	110.6	94.7 – 129.1
AUC_{0-inf} (ng·h/mL)	207 ± 218 –	204 ± 210 –	–	–

* median (range)

The results of the study show that widened acceptance limits (based upon within-subject variability of Reference C_{max} and AUC) are met by both AUC and C_{max} values regarding albendazole. Accordingly, the test Albendazole 400 mg tablet meets the criteria for bioequivalence with regard to the rate and extent of absorption and is therefore bioequivalent to the reference Eskazole® (Aspen Pharmacare Australia Pty Ltd.).

4. Summary of product safety and efficacy

[NT012 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 and bioavailability, [NT012 trade name] is pharmaceutically and therapeutically equivalent and thus interchangeable with the comparator product Eskazole® (Aspen Pharmacare Australia Pty Ltd.). for which benefits have been proven in terms of clinical efficacy. The clinical safety of

[NT012 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 [NT012 trade name] is used in accordance with the SmPC.

Bioequivalence

[NT012 trade name] has been shown to be bioequivalent with Eskazole® (Aspen Pharmacare Australia Pty Ltd.).

Efficacy and Safety

Regarding clinical efficacy and safety, [NT012 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 [NT012 trade name] was acceptable for the following indication: 'for the treatment of cestode infections, lymphatic filariasis and other nematode infections ', and would allow inclusion of [NT012 trade name], manufactured at Medopharm Private Limited, Unit II, No. 50, Kayarambedu Village, Guduvanchery – 603 202 Tamil Nadu, India in the list of prequalified medicinal products.