World Health Organization

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In reply please refer to: CPH 35/MS/MC

Your reference:

Digitally signed by Moraru Grigore
Date: 2023.10.17 16:28:35 EEST
Reason: MoldSign Signature
Location: Moldova

Mr Rakesh Chaurasia
Deputy General Manager - Drug Regulatory Affairs
Macleods Pharmaceuticals Limited
Atlanta Arcade, 3rd Floor, Church Road, near Leela Hotel,
Andheri-Kurla Road
Andheri (East)
400 059 Mumbai
Inde

13 March 2007

Dear Mr Chaurasia,

Prequalification Programme: Priority Essential Medicines

Product Reference Number: **TB154** *cycloserine 250 mg - capsule*

This letter is for the **quality** part of the above-mentioned dossier only.

Thank you for submitting the data and information requested for the assessment of the product dossier within the above-mentioned programme of United Nations agencies. A team of evaluators recently assessed the dossier you submitted.

As a result of this assessment, you are kindly requested to submit the following data and information as this was not covered in the product dossier.

Review is near completion of the Quality Part of the dossier for TB154, Cycloserine Capsules USP 250 mg. Please confirm the details in the numbered statements listed in this letter. If you disagree with any points, please amend the text, highlighting the changes you have made, and include in your reply appropriate justifications of your points of disagreement (including references to dated correspondence etc). You should also confirm your agreement to the 'Manufacturer's Commitments' that have been described below and you should respond appropriately to the 'Condition(s)' that has been stipulated below.

It is important that you note that other Parts of the dossier are still under assessment. In particular, the WHO Public Assessment Report (WHOPAR) still has to be reviewed, which may result in changes being made to documents such as the Summary of Product Characteristics (SPC), the Patient Information Leaflet (PIL), any other Package Leaflet(s) (PL) (for technical or professional information) and the Label Texts (LT). Accordingly, you are strongly advised not to initiate bulk production (printing) of these documents until the remainder of the Prequalification Assessment stages has been completed.

1. Labelling for storage:

"Store in the original package below 25 °C. Once removed from the polyethylene bag, the capsules should be used within 7 days".

2. Nature and contents of container:

(100 Capsules pack size) Aluminium foil/Aluminium foil Strip of 10 capsules packed in low density polythene bag along with desiccant (silica gel bag). 10 Strips per carton.

3. Shelf life of Final Pharmaceutical Product (FPP):

24 months.

4. Manufacturing site of FPP:

Macleods Pharmaceuticals Ltd,
Plot No. 25 - 27,
Sr. No. 366, Premier Ind. Estate,
Kachigam,
396 210 Daman
India

5. Batch size of FPP:

100,000 capsules.

6. Manufacturing site of Active Pharmaceutical Ingredient (API):

BAN-WHOL PLANT
Dong-A-Pharmaceutical Co. Ltd.
434-3, Moknae-Dong, Ansan-Si,
Kyungki-Do, Korea

7. Retest period of API:

6 months.

8. API specification Reference Number and/or Version:

SPC/RC-0007-03 (supplied as Annexure-3 to correspondence dated 7 July 2006, company reference CPH30/MS/AL).

9. FPP specification Reference Number and/or Version:

SPC/FG/033/05 (Release).
SPC/FG-0144R-06 (Regulatory = shelf life).
(Both specifications supplied as Annexure-3 to correspondence dated 6 January 2007).

NOTE: Please consult the "Guidance on variations to a prequalified dossier" before implementation of any changes to the above and other approved parts of the dossier.

WHOPAR: It is noted that with its correspondence dated 6 January 2007, Macleods Pharmaceuticals Limited has submitted a draft WHOPAR for TB154 Cycloserine Capsules USP 250 mg.

CONDITION: The 'pharmaceutical changes' to the Summary of Product Characteristics and Product Information Leaflet as outlined in elsewhere in this letter must be confirmed as accepted by Macleods Pharmaceuticals Limited (or renegotiated with WHO), also bearing in mind the important point already mentioned that further changes to these documents may be requested during the preparation of the WHOPAR.

WRITTEN COMMITMENTS OF THE MANUFACTURER:

1. Stability and validation studies (intermediate and long term conditions) will be continued on batches CD 401, CD 402, CD 403, CD 404, CD 501, CD 601 and CD 606 in accordance with Stability Protocol STA/FG/0144-04, submitted on dated 6 January 2006.

2. One commercial batch will be studied in accordance with Stability protocol STA/FG/0144-04, as stated in the letter dated 18 November 2006.

Finished Pharmaceutical Product (cycloserine 250 mg capsules)

Regarding the disposal instructions for the desiccant in various parts of the product documentation (SPC, section 6.6 and PIL), the words "Safe disposal instructions about the desiccant - Please do not tear the desiccant (silica gel) bag; it should be disposed off as such. Check for local requirements with your doctor/pharmacist." should be amended to read "Safe disposal instructions about the desiccant - Please do not chew, swallow or tear the desiccant (silica gel) bag; it should be disposed off intact. Check for local requirements with your doctor/pharmacist."

The storage conditions should be changed to read: "Store in the original package below 25 °C. Once removed from the polyethylene bag, the capsules should be used within 7 days. Keep out of the reach of children". The SPC should be amended accordingly in section 6.3 and similar changes should be made to the PIL.

You are reminded that only products and manufacturers that meet the recommended norms and standards, as referred to below, will be included on the list.

- Product dossiers, as specified in the relevant guidelines for the submission of product data and information (as found on the prequalification web page);
- Manufacturing Sites: Good Manufacturing Practices.

It is recommended that you submit the requested additional data and information, as listed above, to the UNICEF Supply Division, at your earliest convenience. Please ensure that your submission contains all the outstanding information and data requested in the addendum. (All outstanding issues should be addressed in one submission and not be presented as separate submissions.) Kindly ensure that all the outstanding points communicated in previous letters and addenda are covered.

Containers should be clearly marked as indicated below.

CONFIDENTIAL

UNICEF Supply Division

UNICEF Plads - Freeport
DK-2100 Copenhagen
Denmark

Reference: Prequalification Programme (HIV/AIDS, TB, Malaria)
Attention: Dr Matthias Stahl
Additional data/information for Product Reference Number:

Tel: (45) 35 27 35 27
Fax: (45) 35 26 50 48

Please ensure that all correspondence reflects the appropriate product reference number.

For further information, please contact Dr M. Stahl (stahlm@who.int), Dr O. Gross (grosso@who.int) or Miss L. Oakes (oakesl@who.int).

Your cooperation is appreciated.

Yours sincerely,

Dr Matthias Stahl
Quality Assurance and Safety: Medicines
Department of Medicines Policy and Standards