CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-428

MICROBIOLOGY REVIEW

Product Quality Microbiology Review

Review for HFD 180
17 March, 2002

NDA: 21-428

Name of Drug: Prevacid® (lansoprazole) Tablets

Review Number: 1

Submission Date: October 30, 2001

Applicant: TAP Pharmaceutical Products, Inc.

Name of Reviewer: James McVey

Product Quality Microbiology Data Sheet

A. 1. NDA 21-428

2. REVIEW NUMBER: 1

3. REVIEW DATE: March 1, 2002

4. TYPE OF SUPPLEMENT: Original application and amendment dated 2/25/02

5. SUPPLEMENT PROVIDES FOR: n.a.

6. APPLICANT/SPONSOR:

Name: TAP Pharmaceutical Products, Inc.
675 Northfield Drive
Lake Forest, IL 60045

Representative: Leslie B. Abelson
Assistant Director, Regulatory Affairs

Telephone: 847-236-2631

7. MANUFACTURING SITE: Takeda Ireland, Ltd.
Wicklow, Ireland

8. DRUG PRODUCT NAME:
Proprietary: Prevacid®, complete trade name not yet established.
Non-proprietary: Lansoprazole Tablets
Drug Priority Classification: Standard

9. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY: 15 and 30 mg, fast disintegrating tablets

10. METHOD(S) OF STERILIZATION: Not sterile.

11. PHARMACOLOGICAL CATEGORY: Proton Pump Inhibitor

B. 1. DOCUMENT/LETTER DATE: October 30, 2001, February 22, 2002.
2. RECEIPT DATE: November 1, 2001, February 25, 2002.
3. CONSULT DATE: December 17, 2001, February 25, 2002.
4. DATE OF AMENDMENTS: n.a.
5. ASSIGNED FOR REVIEW: January 7, 2002, February 25, 2002.
6. SUPPORTING/RELATED DOCUMENTS:

C. REMARKS:

TAP requests skip lot microbial limits testing based on good control of the process and the belief that an adequately dry dosage form (tablets) will not support microbial growth. Currently available data along with the commitments made regarding microbial limits testing support this request. Note: TAP dropped the Loss on Drying Test from the release specifications because no change was seen in the stability testing.

One component, lactose monohydrate microcrystalline spheres, has an accompanying certification regarding BSE.

APPEARS THIS WAY
ON ORIGINAL

Executive Summary

I. Recommendations

A. Recommendation on Approvability – The proposed skip lot testing regime for the microbial limits test is acceptable from a product quality microbiology perspective.

B. Recommendation on Phase 4 Commitments and/or Agreements, if Approvable - None

II. Summary of Microbiology Assessments

Lactose monohydrate microcrystalline cellulose spheres are coated with Lansoprazole, the active ingredient, a base coat, then several protectant and dissolution enhancement layers and finally with a flavor/protectant layer.

Microbial limits testing is performed on ingredients as specified in USP/NF. The bulk formulated components (enteric-coated lansoprazole microgranules, inactive granules and mixed granules) are stored under dry condition in the presence of ——— . prior to tableting. The tablets are packaged in—— based bags for storage prior to final packaging in —— based blister packs. The preliminary stability data provided demonstrate adequate control of these processes to prevent gross contamination or contamination with known potential pathogens. USP <61> microbial limits testing methods are employed for the finished dosage form. Acceptance criteria are —— cfu/g for Total Aerobic Count, —— cfu/g for Total Combined Molds and Yeasts, and freedom from *E. coli*. These are the European Pharmacopoeia specifications. The fact that this is a dry dosage form and is prepared and packaged in a manner that controls moisture ingress provides assurance that the tablets are not likely to support growth after packaging and storage under normal label conditions was implied but not stated in the original application. TAP was asked, in a phone call on January 15, 2002, to clarify their intention with respect to microbial control; which they did in the February 22, 2002, amendment. Microbial control is further verified by the stability testing data provided. Microbial limits testing was added to the post approval stability protocol so that ongoing confirmation of the microbiological quality of the tablets over the 24 month dating period would be provided (pp. 242, 252).

TAP Pharmaceuticals requests that the Microbial Limits testing be phased into a skip lot testing regime. Every lot manufactured in the first year would be tested, every 5th lot would be tested in the second year and every tenth lot would be tested thereafter. If any problems or special circumstances occur, TAP will revert to the first year testing regime.

B. Brief Description of Microbiology Deficiencies – n.a.

C. Assessment of Risk Due to Microbiology Deficiencies- n.a.

III. Administrative

A. Reviewer's Signature _____

B. Endorsement Block
Reviewer: James L. McVey
Microbiology Supervisor: Peter H. Cooney, Ph.D.

C. CC Block
cc:
Original NDA 21-428
HFD-805/Division File/NDA 21-428

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2 Page(s) Withheld

✓ § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(5) Deliberative Process

_____ § 552(b)(5) Draft Labeling

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/s/

James McVey
3/20/02 06:55:24 AM
MICROBIOLOGIST

Peter Cooney
3/20/02 09:38:30 AM
MICROBIOLOGIST