CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75-147

ADMINISTRATIVE DOCUMENTS

ANDA APPROVAL SUMMARY

DA: 75-147 [redacted] DRUG PRODUCT: Isosorbide Mononitrate

FIRM: Teva Pharmaceuticals DOSAGE FORM: Tablet

STRENGTH: 20 mg [redacted]

CGMP STATEMENT/EIR UPDATE STATUS:
CGMP certification is satisfactory (See Page 2024).
EIR update : Acceptable on April 10, 1998.

BIO STUDY: Satisfactory.
Bioequivalence study of Isosorbide Mononitrate Tablet, 20 mg lot# K-20844 is found acceptable on 1-15-98. (see Bio. Review by M. Park on 8-15- 1997).

Bio. dissolution specification same as manufacturing:
Medium : 900 ml water, Apparatus II(paddle) at 50 rpm:

Specification:

LIDATION -(DESCRIPTION OF DOSAGE FORM SAME AS FIRM'S):
is pending.

STABILITY - ARE CONTAINERS USED IN STUDY IDENTICAL TO THOSE IN CONTAINER SECTION?:
Containers used in the stability testing are the same as described in the container section.

Proposed market container/closures:

Fill size	30 tablets	30 tablets	100 tablets	1000 tablets
Bottle manufacturer	[redacted]			
Bottle Size	30cc white,	30cc, white	30cc white,	300cc white,
Closure Manufacturer	[redacted]			
Closure Type	CRC	Metal Screw	CRC	Metal Screw
Closure Size	33 mm	33 mm	33 mm	53 mm

Pharmaceutical Coil Manufacturer				
Cotton Type				

LABELING:
Satisfactory per A. Vezza on 8-11-98.

STERILIZATION VALIDATION (IF APPLICABLE):
NA

SIZE OF BIO BATCH (FIRM'S SOURCE OF NDS OK?):

20 mg tablet Lot # K-20844; tablets

Firm's source of NDS OK : Yes DMF

SIZE OF STABILITY BATCHES - (IF DIFFERENT FROM BIO BATCH, WERE THEY MANUFACTURED VIA THE SAME PROCESS?):

20 mg tablet Lot # K-20844, tablets

PROPOSED PRODUCTION BATCH - MANUFACTURING PROCESS THE SAME AS BIO/STABILITY?:

20 mg tablet: ablets

Manufacturing process is the same as bio. and stability batch.

Revievwer: S.Basaran DATE:10-9-1998 S. Basaran 10/26/98

Team Leader: U.Venkataram DATE:10-9-1998
U.V. Venkataram 10/26/98

F/T by pah/10/26

DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, 314 & 601)

Form Approved: OMB No. 0910-0338
Expiration Date: April 30, 2000
See OMB Statement on last page.

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICATION INFORMATION

NAME OF APPLICANT: **TEVA Pharmaceuticals USA**

DATE OF SUBMISSION: **November 23, 1998**

TELEPHONE NO. (Include Area Code): **(215) 256-8400**

FACSIMILE (FAX) Number (include Area Code): **(215) 256-8105**

APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License Number if previously issued):
1510 Delp Drive
Kulpsville, PA 19443

AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, and ZIP Code telephone & FAX number) IF APPLICABLE

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE NUMBER (If previously issued): **75-147**

ESTABLISHED NAME (e.g., Proper name, USP/USAN name): **ISOSORBIDE MONONITRATE TABLETS**

PROPRIETARY NAME (trade name) IF ANY:

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (If any): **1,4:3,6-Dianhydro-D-glucitol-5-nitrate**

CODE NAME (If any):

DOSAGE FORM: **TABLETS**

STRENGTHS: **20 mg**

ROUTE OF ADMINISTRATION: **ORAL**

PROPOSED INDICATION(S) FOR USE: **Indicated for the prevention and treatment of angina pectoris due to coronary artery disease.**

APPLICATION INFORMATION

APPLICATION TYPE
(check one) ☐ NEW DRUG APPLICATION (21 CFR 314.50) ■ ABBREVIATED APPLICATION (ANDA, AADA, 21 CFR 314.94)
☐ BIOLOGIC APPLICATION (21 CFR part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE ☐ 505 (b) (1) ☐ 505 (b) (2) ☐ 507

IF AN ANDA, OR AADA, IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION

Name of Drug: **MONOKET®** Holder of Approved Application: **SCHWARZ PHARMA**

TYPE OF SUBMISSION
(check one) ☐ ORIGINAL APPLICATION ■ AMENDMENT TO A PENDING APPLICATION ☐ RESUBMISSION
☐ PRESUBMISSION ☐ ANNUAL REPORT ☐ ESTABLISHMENT DESCRIPTION SUPPLEMENT ☐ SUPAC SUPPLEMENT
☐ EFFICACY SUPPLEMENT ☐ LABELING SUPPLEMENT ☐ CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT ☐ OTHER

REASON FOR SUBMISSION: **Telephone Amendment**

PROPOSED MARKETING STATUS (check one) ■ PRESCRIPTION PRODUCT (Rx) ☐ OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED: 1

THIS APPLICATION IS ■ PAPER ☐ PAPER AND ELECTRONIC ☐ ELECTRONIC

ESTABLISHMENT INFORMATION

Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.

Cross References (list related License Application, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)

This application contains the following items: (Check all that apply)	
	1. Index
	2. Labeling (check one) ☐ Draft Labeling ☐ Final Printed Labeling
	3. Summary (21 CFR 314.50 (c))
X	4. Chemistry section
X	A. Chemistry, manufacturing, and controls information (e.g. 21 CFR 314.50 (d) (1), 21 CFR 601.2)
	B. Samples (21 CFR 314.50 (e) (1), 21 CFR 601.2 (a)) (Submit only upon FDA's request)
	C. Methods validation package (e.g. 21 CFR 314.50 (e) (2) (i), 21 CFR 601.2)
	5. Nonclinical pharmacology and toxicology section (e.g. 21 CFR 314.50 (d) (2), 21 CFR 601.2)
	6. Human pharmacokinetics and bioavailability section (e.g. 21 CFR 314.50 (d) (3), 21 CFR 601.2)
	7. Clinical Microbiology (eg. 21 CFR 314.50 (d) (4))
	8. Clinical data section (e.g. 21 CFR 314.50 (d) (5))
	9. Safety update report (e.g. 21 CFR 314.50 (d) (5) (vi) (b), 21 CFR 601.2)
	10. Statistical section (e.g. 21 CFR 314.50 (d) (6), 21 CFR 601.2)
	11. Case report tabulations (e.g. 21 CFR 314.50 (f) (1), 21 CFR 601.2)
	12. Case reports forms (e.g. 21 CFR 314.50 (f) (2), 21 CFR 601.2)
	13. Patent information on any patent which claims the drug (21 U.S.C. 355 (b) or (c))
	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b) (2) or (j) (2) (A))
	15. Establishment description (21 CFR Part 600, if applicable)
	16. Debarment certification
	17. Field copy certification
	18. User Fee Cover Sheet (Form FDA 3397)
	19. OTHER (Specify)

CERTIFICATION

I agree to update this application with new safety information about the product that may reasonably affect the statement of Contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:

1. Good manufacturing practice regulations in 21 CFR 210 and 211, 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR 201, 606, 610 and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR 202.
5. Regulations on making changes in application in 21 CFR 314.70, 314.71 , 314.72, 314.97, 314.99 and 601.12.
6. Regulations on reports in 21 CFR 314.80, 314.81, 600.80 and 600.81.
7. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been reviewed and are certified to be true and accurate.

Warning: a willfully false statement is a criminal offense, U. S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	TYPED NAME AND TITLE	DATE
Deborah Jaskot	**Deborah A. Jaskot** **Senior Director, Regulatory Affairs**	11/23/98

ADDRESS (Street, City, State and ZIP Code)	Telephone Number
TEVA Pharmaceuticals USA **1510 Delp Drive, Kulpsville, PA 19443**	**(215) 256-8400**

Public reporting burden for this collection of information is estimated to average 40 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

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Hubert H. Humphrey Building, Room 531-H
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Washington, DC 20201

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FORM FDA 356h (4/97)

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 75-147 Date of Submission: June 13, 1997

Applicant's Name: **Teva Pharmaceuticals USA**

Established Name: **Isosorbide Mononitrate Tablets 20 mg**

Labeling Deficiencies:

1. CONTAINER 30s, 100s, 1000s

   Satisfactory in draft. However, the Poison Prevention Packaging Act notes that special packaging (child-resistant closures) should be the responsibility of the manufacturers when the container is clearly intended to be utilized in dispensing (unit-of-use packaging). Your proposed container of 30 tablets appears to be in this category, therefore, we believe that this package must comply with the Act. Please comment.

2. INSERT

   a. GENERAL COMMENT

      There is no need to capitalize isosorbide mononitrate tablets unless required by sentence structure.

   b. DESCRIPTION

      Revise the second paragraph to read as follows:

      Isosorbide mononitrate tablets, for oral administration, contain 20 mg of isosorbide mononitrate. In addition, each tablet contains the following inactive ingredients: ...

   c. INDICATIONS AND USAGE

      Revise the first sentence to read as follows:

      Isosorbide mononitrate tablets are indicated ...

   d. PRECAUTIONS (Table)

i. Delete the vertical line segment between "of" and "MRHD*".

ii. Bold the horizontal line which starts between "Rabbit" and "Rat".

iii. Revise the last column of numbers to read: 363, 200, 120, 118, 80, 60.

e. ADVERSE REACTIONS

Relocate the adverse reaction "susurrus aurium from under the "Miscellaneous" category to in between "palpitations" and "tachycardia" under the "Cardiovascular" category.

f. OVERDOSAGE

i. Hemodynamic Effects, first paragraph, last sentence.

... upright posture); air hunger ...
[close the parentheses].

ii. Methemoglobinemia

A). First paragraph, last sentence.

... to 7.8 to 11.1 mg of ...
[replace hyphen with "to"]

B). Last paragraph

... blue, 1 to 2 mg/kg ...
[replace hyphen with "to"]

g. HOW SUPPLIED

i. We encourage the use of the NDC number in this section.

ii. You describe your tablet as ... "scored and debossed "93" on one side and "76" on the other". The picture of the tablet found on page 2041 has the numbers "93" and "76" on the same side of the tablet and is described as ... "scored on one side and debossed on the other side with the numbers "93" and "76". Please comment and/or revise.

Please revise your insert labeling, as instructed above, and submit in final print labels and labeling.

Please note that we reserve the right to request further changes in your labels and/or labeling based upon changes in the approved labeling of the listed drug or upon further review of the application prior to approval.

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

Jerry Phillips
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research