

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

75-429

ADMINISTRATIVE DOCUMENTS

ANDA APPROVAL SUMMARY

ANDA: 75-429 DRUG PRODUCT: Sotalol Hydrochloride

RM: Teva Pharmaceuticals Industries, Ltd. DOSAGE FORM: Tablet

STRENGTH: 80 mg, 120 mg, 160 mg and 240 mg

CGMP STATEMENT/EIR UPDATE STATUS:

CGMP certification is satisfactory (See Page 2838).

EIR update : Acceptable on September 22, 1998.

BIO STUDY: Satisfactory.

Fasting and food effect bio studies were performed on the 160 mg lot#K-22947) tablet. A waiver of in-vivo bio study requirements was requested for the 80 mg, 120 mg, 160 mg and 240 mg tablets. The bio.study was reviewed by J.S.Kharida on 11-5-98 and found acceptable. Dissolution spec. NLT 80% (Q) in 30 min.

VALIDATION -(DESCRIPTION OF DOSAGE FORM SAME AS FIRM'S):

MV is acceptable on 7-14-99 and 10-25-99.

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.

Packaging configuration and sizes:

Sotalol Tablets, 80 mg

QTY/Bottle	Bottle	Cap	Filler
100	40 cc HDPE	33 CRC	Cotton coil, 9 g
1000	300 cc HDPE	53 mm Metal Screw	Cotton coil 20 g

Sotalol Tablets, 120 mg

QTY/Bottle	Bottle	Cap	Filler
100	60 cc HDPE	33 CRC	Cotton coil, 9 g
1000	500 cc HDPE	53 mm Metal Screw	Cotton coil 20 g

Sotalol Tablets, 160 mg

QTY/Bottle	Bottle	Cap	Filler
100	100 cc HDPE	38 CRC	Cotton coil, 9 g
1000	750 cc HDPE	53 mm Metal Screw	Cotton coil 20 g

Sotalol Tablets, 240 mg

QTY/Bottle	Bottle	Cap	Filler
100	150 cc HDPE	38 CRC	Cotton coil, 9 g

RELING:

satisfactory per A.Vezza on September 29, 1999.

STERILIZATION VALIDATION (IF APPLICABLE):

NA

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

160 mg tablet: Lot # K-22947; kg)

Sotalol Hydrochloride tablets is compared to the listed drug Betapace. A waiver of in vivo bioavailability testing for the 80 mg, 120 mg, 160 mg and 240 mg tablets was requested and granted.

Firm's source of NDS OK : Yes . DMF#

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

Executed batch sizes:

80 mg tablet: Lot # K-22945;	tablets
120 mg tablet: Lot # K-22946;	tablets
160 mg tablet: Lot # K-22947;	tablets
240 mg tablet: Lot # K-22870;	tablets

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

Production batch size for 80 mg tablets: ets

Production batch size for 120 mg tablets.

Production batch size for 160 mg tablets:

Production batch size for 240 mg tablets:

Manufacturing process is the same as bio.stability.

CHEMIST: S. Basaran

S. Basaran

DATE: 10-25-1999

Team Leader: U. Venkataram

U.V. Venkataram

DATE: 10-²⁷-1999

Telephone Conversation Memorandum

ANDA: 75-429

DRUG: Sotalol Hydrochloride Tablets, 80 mg, 120 mg, 160 mg,
and 240 mg

FIRM: TEVA Pharmaceuticals USA, Inc.

PERSONS INVOLVED: D. Jaskot, TEVA
Tim Ames, FDA

PHONE NUMBER: 215-256-8400

DATE: June 25, 1999

Called firm to request revision to their Drug Substance Specifications (include known and unknown in the limits for the total) and the stability protocol (to include submission of 3 production batch data in the annual report for the purpose of extension of expiration date). Ms. Jaskot asked whether this will be treated as a telephone amendment and I affirmed that. She said that she will contact the firm in Israel on Monday and that they will respond by next Wednesday. I confirmed with her that they will follow the fax with a hard copy.

Ubrani V. Venkataram, Ph.D.
Tea Leader, Branch 8, DCII.

U.V. Venkataram 6/25/99

cc:

E Expedite
5-21-99
update

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

ANDA Number: 75-429

Date of Submission: July 31, 1998

Applicant's Name: TEVA Pharmaceutical USA, Inc.

Established Name: Sotalol Hydrochloride Tablets, 80 mg, 120 mg,
160 mg and 240 mg

Labeling Deficiencies:

1. CONTAINER

We encourage you to differentiate your product strengths by using contrasting colors and/or boxing.

2. INSERT

Revise as follows:

a. GENERAL COMMENTS

- i. Replace the hyphen with the word "to" throughout the text of the insert where it occurs expressing a range of numbers or dosage, or a time period. It is not necessary to do this in your tables.
- ii. Please refer to the attached mocked-up copy of your draft labeling for further revisions.

b. WARNINGS

- i. Mortality - Fourth paragraph, first sentence
... sotalol hydrochloride did ... (see **CLINICAL PHARMACOLOGY, Clinical Actions**).
- ii. Proarrhythmia - First paragraph, last sentence
... (see **Electrolyte Disturbances** below).

c. PRECAUTIONS

Throughout this section make consistent use of format for subsection and sub-subsection headings for example:

- A) "Drug Interactions" is a subsection of the PRECAUTIONS section. Revise the format to be consistent with your other subsection headings.
- B) All of the sub-subsections listed from "Antiarrhythmics" to "Other" are sub-subsections of the Drug Interactions subsection and should be differentiated accordingly.

ii. Pregnancy Category B

Retitle this paragraph as follows:

Pregnancy: Teratogenic Effects:
Pregnancy Category B:

d. DOSAGE AND ADMINISTRATION

i. Dosage in Renal Impairment

- A). This is a subsection of the DOSAGE AND ADMINISTRATION section and should be portrayed as such.
- B). Delete the last paragraph and replace with the following text:

Pharmacokinetic findings in patients requiring chronic hemodialysis is limited to six patients in two studies. In these patients, terminal elimination half life is prolonged to 40 hours in the interdialysis period and approaches 7 hours during dialysis. It is estimated that 20% to 40% of sotalol is removed during dialysis and that a slight rebound of plasma concentration is noted post dialysis. Extreme caution must be taken in dosing patients in renal failure requiring hemodialysis, usual parameters of safety and efficacy (heart rate, QT interval and control of

arrhythmia) must be closely monitored.

ii. **Transfer to Sotalol**

...(see **PRECAUTIONS, Drug Interactions**).

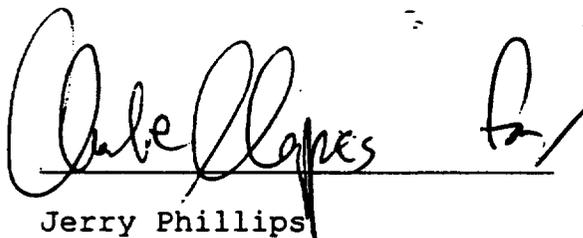
e. **HOW SUPPLIED**

We encourage the use of the symbol "Rx only" or "R only" under the title.

Revise your container labels and package insert labeling as described above, then prepare and submit final printed (or printers proof) package insert labeling and final printed container labels. Please note that final printed insert labeling is not required for tentative approval of an application if it is granted with more than 90 days remaining from the date when full approval can be considered. We will accept final "printers proof" for the insert only.

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.

A handwritten signature in black ink, appearing to read "Jerry Phillips", is written over a horizontal line. To the right of the signature is a checkmark.

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

Attachment: Mocked-up copy of the firm's draft insert labeling