CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-105

CHEMISTRY REVIEW(S)

NOV 16 [illegible]

DIVISION OF ANTI-INFECTIVE DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls

NDA #: 21-105 **CHEM.REVIEW #:** 1 **REVIEW DATE:** 17-Sep-99

SUBMISSION/TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
ORIGINAL:original	2/18/99	2/22/99	3/29/99
AMENDMENT/AC			

NAME & ADDRESS OF APPLICANT: Able Laboratories Inc.
6 Holywood Court
South Plainfield,N.J.07080

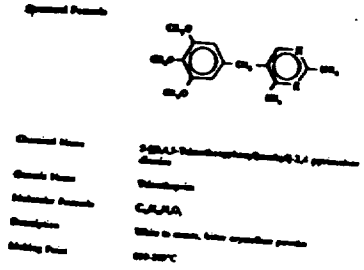
DRUG PRODUCT NAME
Proprietary:ZOTRIM UTI Therapy
Nonproprietary/USAN:sulfamethoxazole 800mg,
Trimethoprim160mg
,phenazopyridine 200mg.
Chemical Type/3s
Therapeutic Class: **Antibacterial**

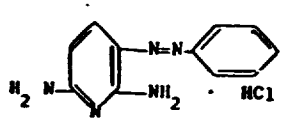
ANDA Suitability Petition/DESI/Patent Status:
N/A [if applicable]

PHARMACOLOGICAL CATEGORY/INDICATION: UTI Therapy

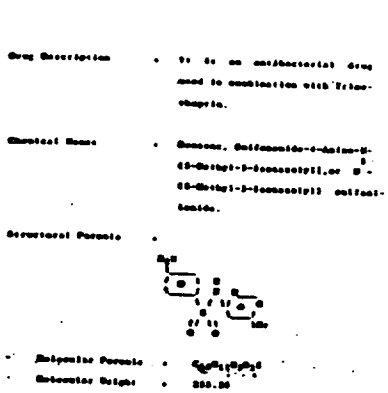
DOSAGE FORM:tablets
STRENGTHS:TMP-SMZ:160-800mg;phenazopyridine Hcl:200mg
ROUTE OF ADMINISTRATION:oral
DISPENSED: XX **Rx** ____ **OTC**

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA. MOL.WT:





Phenazopyridine Hydrochloride
MW 249.7



SUPPORTING DOCUMENTS:

RELATED DOCUMENTS (if applicable):

NA

CONSULTS:

1.EER has been requested on June 29,1999
2.Trade name assessment has been requested on 7/7/1999
3.Method validation has been requested on 7/7/1999.

REMARKS/COMMENTS:Zotrim is a combination product.It consists of sulfamethoxazole/trimethoprim(800mg/160mg respectively) and phenazopyridine 200mg.They are blister packaged for UTI Therapy.The drug product,sulfamethoxazole/trimethoprim has been marketed as generic drug product under the trade name,COTRIM.The drug,phenazopyridine(pyridium),sulfamethoxazole (gantanol)and trimethoprim(trimpex) are in use in the United States.The combination of sulfamethoxazole and phenazopyridine(Azo-Gantrisin) and combination of sulfamethoxazole and trimethoprim (bactrim,cotrim) are also marketed in the United States.The treatment regimen for sulfamethoxazole /trimethoprim will be BID for 10 days and for phenazopyridine ,it will be TID for two days.The product will be used to treat urinary tract infection.This is a paper NDA with respect to clinical and pharmacological data.

CONCLUSIONS & RECOMMENDATIONS:The NDA is not approvable.

The firm should respond to the deficiencies mentioned under list of deficiencies.

/S/ 10/27/99

B.Vithal Shetty,Ph.D.
Review Chemist

cc: Orig. NDA #21-105
HFD-520/Division File
HFD-520/B.V.Shetty
HFD-520/MO/HAMILTON
HFD-520/Pharm/Sathler
HFD-520/Micro/Silver
HFD-520/CSO/DurallMiller
HFD-520/TL:Katague D. /S/ 11/16/99
R/D Init by: TL

APR 25 2000

DIVISION OF ANTI-INFECTIVE DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls

NDA #: 21-105 **CHEM.REVIEW #:** 2 **REVIEW DATE:** 3/15/00

SUBMISSION/TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
AMENDMENT	**1/24/2000**	**1/27/2000**	

AMENDMENT/AC

NAME & ADDRESS OF APPLICANT: Able Laboratories Inc.
6 Holywood Court
South Plainfield,N.J.07080

DRUG PRODUCT NAME
Proprietary:ZOTRIM UTI Therapy
Nonproprietary/USAN:sulfamethoxazole 800mg,
Trimethoprim160mg
,phenazopyridine 200mg.
Chemical Type/3s
Therapeutic Class: **Antibacterial**

ANDA Suitability Petition/DESI/Patent Status:
N/A [if applicable]

PHARMACOLOGICAL CATEGORY/INDICATION: UTI Therapy

DOSAGE FORM:tablets
STRENGTHS:TMP-SMZ:160-800mg;phenazopyridine Hcl:200mg
ROUTE OF ADMINISTRATION:oral
DISPENSED: **Rx** X_____ **OTC**

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOL.WT:

SUPPORTING DOCUMENTS:

RELATED DOCUMENTS (if applicable):

NA

CONSULTS:

1.EER has been requested on June 29,1999
2.Trade name assessment has been requested on 7/7/1999
3.Method validation has been requested on 7/7/1999.

REMARKS/COMMENTS: The present review is the REVIEW #2.In reply to FDA letter of November 17,1999 regarding CMC deficiencies,the firm has submitted the following information:

1.With regard to question #1,which requests flow chart and characterization of sulfamethoxazole,the firm refers to their approved The firm states that all the relevant information for the Trimethoprim and sulfamethoxazole drug substances as well as for the Sulfamethoxazole/Trimethoprim DS tablets,USP drug product are referred to ANDAand DMF.The firm has submitted a letter of authorization dated October 8,1998 to refer to their

Adequate

2.With regard to question #2,which requests method of preparation and specification for sulfamethoxazole reference standard,the firm states that they will use USP or in-house reference standard.For USP reference standard,potency is taken as being 100% unless specified otherwise,USP 24<11>,"Reference Standards".The potency for in-house reference standard shall be within .The potency factor will be used in the respective test calculations.

Adequate

3. With regard to question #3 which requests impurity profile for sulfamethoxazole ,the firm refers to The firm has also submitted a letter of authorization dated October 8,1998 to refer to their

Adequate

4.With regard to question #4,which requests in-process tests for the manufacture of Sulfamethoxazole/Trimethoprim DS tablets.The firm refers to [redacted].The tablets are manufactured by Teva.The firm has submitted a letter of authorization dated October 8,1998 to refer to their [redacted]

Adequate

5.With regard to question #5,which requests specifications and test methods for [redacted],thefirm refers to their approved [redacted].The firm states that detailed manufacturing information including weight composition of active and ingredients per tablet are given in the approved ANDA.

Adequate

6.With regard to question #6 which requests a statement as to whether a reprocessing of Sulfamethoxazole/Trimethoprim tablets are carried out,the firm states that no re-processed batch will be used.

Adequate

CONCLUSIONS & RECOMMENDATIONS:The NDA is APPROVABLE.
In summary,1.Method Validation has been approved as per a letter dated November 29,1999 from the Director,Science Branch,SIN -DO,HFR-SE560 which states that the methods can be used for quality control and regulatory purposes.
2.Inspection of Manufacturing and Control Facilities. A letter dated February 2,2000 from Mr.Bruce W.Hartman of Compliance Branch,HFD-324 recommends approval. only
3.Chemistry,Manufacturing and Control recomends approval.

/S/ 3/15/00

B.Vithal Shetty,Ph.D.
Review Chemist

cc: Orig. NDA #21-105
HFD-520/Division File
HFD-520/B.V.Shetty