CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

50-755

CHEMISTRY REVIEW(S)

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

NDA #: 50-755 **CHEM.REVIEW #:** 2 **REVIEW DATE:** 28-SEP-2000

SUBMISSION/TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
ORIGINAL	31-OCT-97	31-OCT-97	6-NOV-97
AMENDMENT (EA Exclusion)	18-NOV-97	19-NOV-97	21-NOV-97
AMENDMENT (Facility change)	30-MAR-98	31-MAR-98	31-MAR-98
AMENDMENT (Label Comments)	2-JUL-98	6-JUL-98	13-JUL-98
AMENDMENT (Amendment)	02-OCT-98	05-OCT-98	16-OCT-98
RESUBMISSION (50-755az)	05-APR-00	06-APR-00	13-APR-00
AMENDMENT (50-755BC Formulation change)	08-AUG-00	09-AUG-00	09-AUG-00
AMENDMENT (50-755BC New Stability)	24-AUG-00	25-AUG-00	01-SEP-00
AMENDMENT (50-755BC New Stability)	06- SEP -00	07- SEP -00	07-SEP-00
AMENDMENT (50-755BC Stability Amendment)	13- SEP -00	14- SEP -00	14-SEP-00

NAME & ADDRESS OF APPLICANT: SMITHKLINE BEECHAM PHARMACEUTICALS
One Franklin Plaza P.O. Box 7929
Philadelphia,
PA 19101-7929

DRUG PRODUCT NAME

Proprietary: Augmentin ES™ Oral Suspension
Nonproprietary/USAN: Amoxicillin/Clavulanate Potassium For Oral suspension

Code Names/#'s:
Chemical Type/
Therapeutic Class: 3 S

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

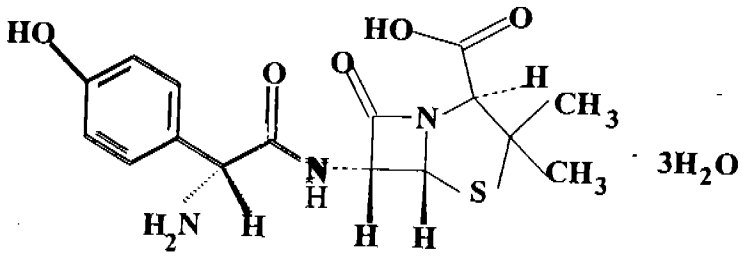
PHARMACOLOGICAL CATEGORY/INDICATION: Anti-infective

DOSAGE FORM: powder for oral suspension
STRENGTHS: 600/42.9 mg per 5 mL

ROUTE OF ADMINISTRATION: oral
DISPENSED:
X Rx ___ OTC

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

Amoxicillin Trihydrate $C_{15}H_{19}N_3O_5S.3H_2O$
(2S,5R,6R)-6-[(R)-(-)-2-amino-2-(p-hydroxyphenyl)acetamido]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0] heptane-2-carboxylic acid trihydrate.
CAS-61-336-70-7
M.W. 419.46



Clavulanate Potassium $C_8H_8KNO_5$

Potassium (Z)-(2R,5R)-3-(2-hydroxyethylidene)-7-oxo-4-oxa-1-azabicyclo[3.2.0]-heptane-2-carboxylate
CAS 61177-45-5
M.W. 237.25

SUPPORTING DOCUMENTS:
Review #1 dated 7/21/98
Amoxicillin trihydrate drug substance

Clavulanate potassium

[redacted]

No DMF authorization needed, the DMF's are held by the sponsor.

RELATED DOCUMENTS (if applicable)
USP 23 Page 100
USP 23 Page 102
Other related Augmentin NDAs
NDA 50-726 - chewable tablet, 200mg and 400 mg
NDA 50-564 - tablet, 250mg and 500 mg
NDA 50-575 - Oral Suspension, 125 mg/5 mL and 250 mg/5 mL
NDA 50-725 - Oral Suspension, 200 mg/5 mL and 400 mg/5 mL

For HDPE bottles, No DMF authorization need, the DMFs are held by the sponsor.

Other DMFs:

[redacted]

The firm has provided DMF authorization letters.

REMARKS/COMMENTS:
In addition to the 4 facilities listed, [redacted] was added through an amendment on 30-MAR-98. All five facilities were approved based on either profile or actual inspection.

CONSULTS:
A consult was sent to OPDRA, and the nomenclature was found to be acceptable.

REMARKS/COMMENTS :
This review addressed the CMC deficiencies sent by facsimile transmission on March 4, 1999 to SB in Chemistry Review #1, dated 3/26/99. Deficiencies in the original in the resubmission are all resolved. A modified formulation without the raspberry flavored was proposed and then withdrawn on 8/24/00.

CONCLUSIONS & RECOMMENDATIONS:

Recommend approval from the manufacturing and controls standpoint. All pending issues have been satisfactory resolved. All manufacturing facilities are currently in acceptable GMP compliance.

/S/

Andrew Yu, Review Chemist

cc: Orig. NDA 50-755
HFD-520
HFD-520/DivDir/GChikami
HFD-520/Chem/AYu
HFD-520/MO/MMakhene
HFD-520/MAlbuerne
HFD-520/Pharm/ROsterberg
HFD-520/Micro/SAltaire
HFD-520/CSO/SSusmita
R/D Init by: HFD-520/TmLdrChem/ DKatague /S/ 9/25/06

18 page(s) have been removed because it contains trade secret and/or confidential information that is not disclosable.

25-SEP-2000

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST SUMMARY REPORT

Application: **NDA 50755/000**
Stamp: **31-OCT-1997** Regulatory Due: **06-OCT-2000**
Priority: **3S**
Action Goal: **31-AUG-1998**
Org Code: **520**
District Goal: **01-JUL-1998**

Applicant: **SKB PHARMS**

1 FRANKLIN PLAZA
PHILADELPHIA, PA 191017929

Brand Name: **AUGMENTIN(AMOXICILLIN/CLAVULANATE POTASS**
Established Name:
Generic Name: **AMOXICILLIN/CLAVULANATE POTASSIUM**
Dosage Form: **FOS (FOR ORAL SUSPENSION)**
Strength: **600 MG/5ML**

FDA Contacts: **A. YU (HFD-520)** **301-827-2143 , Review Chemist**
D. KATAGUE (HFD-520) **301-827-2174 , Team Leader**

Overall Recommendation:
ACCEPTABLEon 15-MAY-2000by M. GARCIA(HFD-322)301-594-0095
ACCEPTABLEon 21-APR-1998by J. D AMBROGIO (HFD-324)301-827-0062

Establishment: **9611207**
BEECHAM PHARMACEUTICALS PTE LTD
DMF No:
AADA No:

[redacted]

Profile: **CSN** OAI Status: **NONE**

Responsibilities: [redacted]

Last Milestone: **OC RECOMMENDATION**

Milestone Date: **09-MAY-2000**

Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Establishment: [redacted]
DMF No:
AADA No:

Profile: **CTL** OAI Status: **NONE**

Responsibilities: **FINISHED DOSAGE RELEASE TESTER**

Last Milestone: **OC RECOMMENDATION**
Milestone Date: **09-MAY-2000**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Establishment: **9610449**
SMITHKLINE BEECHAM
CHEMICALS
AYRSHIRE,
SCOTLAND,
IRVINE, UK

DMF No:
AADA No: **050725**

Profile: **CFN** OAI Status: **NONE**

Last Milestone: **OC RECOMMENDATION**

Responsibilities:

Milestone Date: **12-MAY-2000**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Establishment: **1047293**
SMITHKLINE BEECHAM
PHARMACEUTI
201 INDUSTRIAL DR
BRISTOL, TN 37620

DMF No:
AADA No:

Profile: **LIQ** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **09-MAY-2000**
Decision: **ACCEPTABLE**
Reason: **BASED ON FILE REVIEW**

Responsibilities:

Establishment: **9610412**
SMITHKLINE BEECHAM
PHARMACEUTI

WORTHING, WEST SUSSEX, , UK

DMF No:
AADA No:

Profile: **CSN** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **09-MAY-2000**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Responsibilities: