

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**21-151**

**CHEMISTRY REVIEW(S)**

Z. McDonald

OCT 26 1999

**DIVISION OF Cardio-Renal DRUG PRODUCTS**  
Review of Chemistry, Manufacturing, and Controls

**NDA #:** 21-151 **DATE REVIEWED:** 13-Oct-99

**REVIEW #:** 1 **REVIEWER:** James H. Short

<u>SUBMISSION TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
ORIGINAL	18-Jun-98		
AMENDMENT	08-Jul-99	09-Jul-99	14-Jul-99
	16-Jul-99	19-Jul-99	22-Jul-99
	22-Jul-99	23-Jul-99	30-Jul-99
	7-Sep-99	8-Sep-99	10-Sep-99
	16-Sep-99	17-Sep-99	22-Sep-99
	28-Sep-99	29-Sep-99	4-Oct-99
	1-Oct-99	4-Oct-99	7-Oct-99

**NAME & ADDRESS OF APPLICANT:**

Berlex Laboratories, Inc.  
340 Changebridge Road  
Montville, NJ 07045-1000

**DRUG PRODUCT NAME**

Proprietary:  
Established:  
Code Name/#:  
Chem.Type/Ther.Class:

Betapace AF (proposed)  
Sotalol Hydrochloride  
MJ 1999-1, MJ5763-1  
1 S

**PHARMACOL. CATEGORY/INDICATION:**

Atrial fibrillation/atrial flutter

**DOSAGE FORM:**

TCM

**STRENGTHS:**

80, 120, 160 mg

**ROUTE OF ADMINISTRATION:**

Oral

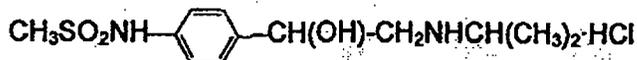
**Rx/OTC:**

Rx  OTC

**SPECIAL PRODUCTS:**

Yes  No

**CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:**



(±)-N-[4-[1-Hydroxy-2-[(1-methylethyl)amino]-ethyl]phenyl]methanesulfonamide Hydrochloride

$\text{C}_{12}\text{H}_{20}\text{N}_2\text{O}_3\cdot\text{HCl}$

308.82

**SUPPORTING DOCUMENTS:**

Type/Number	Subject	Holder	Status	Review Date	Letter Date
NDA 19-865	Betapace	Berlex			
DMF	[Handwritten box]	[Handwritten box]	S-001		
DMF			S-003		
DMF			S-003		
DMF			S-006		
DMF			S-001		
DMF			S-001		
DMF			S-001		
DMF			S-003		
DMF			S-003		
DMF			S-003		
DMF			S-003		
DMF			S-003		
DMF			S-003		
DMF			S-003		

At time of approval of NDA 19-865, the drug product was manufactured and packaged by Bristol-Myers Squibb. S-001 provided for Berlex as packager of the drug product, and S-003 provided for manufacture of the drug product by Berlex. All of the above DMFs, relating to packaging components/operations, have been approved for Betapace tablets. The supplement under which the DMF was approved is indicated under the "Status" column.

**RELATED DOCUMENTS (if applicable):** None

**CONSULTS:** None

**REMARKS:**

NDA 19-865 was originally approved for treatment of acute ventricular arrhythmias. \_\_\_\_\_ was submitted requesting approval for treatment of atrial fibrillation/atrial flutter. No new CMC information

was provided in that supplement. On 18 Jun 99 the Agency requested that the supplement be converted to NDA 21-151.

The tablets to be manufactured under this NDA will be white instead of blue, and will be embossed with "Berlex" on one side, with the strength on the other side. Betapace tablets are embossed with "Betapace" on one side and the strength on the other side. Betapace tablets are distributed in bottles of 100 tablets, and unit dose cartons of 100 tablets. The tablets to be marketed under this NDA will be available in the same unit dose cartons of 100 tablets, but also in a unit dose bottle of 60 tablets. The \_\_\_\_\_ tablet will not be manufactured under this NDA.

The amendment of 8 Jul 99 provides a draft of the proposed Package Insert (PI).

The amendment of 16 Jul 99 requests that the Agency approve "Betapace AF" as the tradename for this product.

A request, dated 20 Jul 99, was sent to the Labeling and Nomenclature Committee requesting approval of the tradename "Betapace AF" for this product. A response was received from OPDRA, dated 11 Oct 99, recommending that the name, "Betapace AF" not be approved.

The amendment of 22 Jul 99 provides the CMC section for this NDA. The applicant certifies that a copy of this amendment has been sent to NWJ-DO. Changes made in this drug product have been summarized above, but for the sake of completeness, this amendment will be briefly reviewed.

The amendment of 7 Sep 99 provides a draft of the proposed Patient Package Insert.

In the amendment of 16 Sep 99, the applicant request that \_\_\_\_\_ be considered as the tradename for this product if Betapace AF is not approved.

Certificates of Analysis (CofAs) are provided in the amendment of 28 Sep 99 for the first six batches of the drug product

A revised draft of the proposed PI is provided in the amendment of 1 Oct 99.

#### CONCLUSIONS & RECOMMENDATIONS:

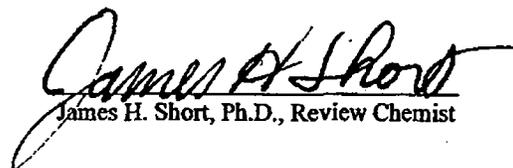
APPROVAL is recommended. The deficiencies noted below should be conveyed to the applicant.

cc:

Org. NDA  
HFD-110/Division File  
HFD-110/JShort/7/21/99  
HFD-110/PM

R/D Init by: KSrinivasachar

filename: N21-151.CR1

  
James H. Short, Ph.D., Review Chemist

*K. Srinivasachar*  
10-26-99

7 Page(s) Withheld

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

§ 552(b)(5) Deliberative Process

§ 552(b)(5) Draft Labeling

Withheld Track Number: Chemistry-1