CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20545

PHARMACOLOGY REVIEW(S)

DF

NDA 20-545

JAN 27 1995

Pharmacology Review of Original Application

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23 January 1995

Submission Date: 21 December 1994
Center Receipt Date: 22 December 1994
Reviewer Receipt Date: 10 January 1995

Sponsor: Parke-Davis
Ann Arbor, MI

Drug: Procanbid (extended-release procainamide) Tablets, 500 and 1000 mg.

Formulation: Tablets, for oral use, containing 500 or 1000 mg procainamide HCl (PA), compendial excipients, and the following non-compendial ingredients: Polyacrylate (Eudragit NE 30D), Opadry Blue Y-5-4295, Opadry Grey YS-1-7507, and Opacode Black Ink S-1-8109.

Pharmacological Class: Antiarrhythmic

Indication: Ventricular Arrhythmia

Dosage: 1000 to 2500 mg b.i.d.

Prior IND: [ ] (Parke-Davis)

Non-Clinical Studies: None conducted per agreement with FDA at December 19, 1991 pre-NDA meeting. Accordingly, item 5 (Non-Clinical Pharmacology and Toxicology) is not included in this NDA.

Labeling: Conforms to requirements of 21 CFR 201.57. Format and content of carcinogenicity, mutagenicity, fertility, and pregnancy sections are consistent with those of approved labeling for procainamide.

Evaluation: Sponsor proposed marketing procainamide HCl as controlled release tablets in 500 and 1000 mg strengths formulated to allow b.i.d. dosing. As sponsor currently markets their Procan SR at the same total daily dosage and for the same patient population, no animal safety data was submitted - or needed - to support this application. The reformulation creates no inactive ingredient or excipient problem from a pharmacology regulatory standpoint (see below).

Like Procan SR, the BID tablets consist of a wax matrix active ingredient core, but are coated with polyacrylate polymer to control rate of diffusion of PA. There is a slight quantitative

difference in core compendial excipients between reformulated and SR tablets; however, release of PA in vitro from this core is reported to be unaffected.

The only non-compendial component of the controlled-release coating is polyacrylate (Eudragit NE 30D). It is listed in the inactive ingredient guide (Oct. 1993) as part of two currently marketed oral drug products (N62616 and N62538). The three non-compendial components of the BID tablet color coat (Opadry Grey YS-1-7507; Opadry Blue Y-5-4295; and Opacode Black S-1-8109 ink) represent a) synthetic black iron oxide (Opadry Grey; Opacode Black) which is already a component of Procan SR (as Opacode Black ink) and allowable under 21 CFR 73.1200 if the prescribed dosage of Procan BID does not provide more than 5 mg of elemental iron per day, and b) FD and C Blue No. 1 - Aluminum lake (Opadry Blue) listed as an inactive ingredient for 154 approved NDA's, 8 of which are for enteric or sustained action formulations (Inactive Ingredient Guide, Oct. 1993).

Accordingly, this application and labeling is approvable, from animal Pharmacology/ Toxicology perspective, without further animal studies and with proposed formulation. Chemistry is advised to confirm that the reformulation (which now includes synthetic black iron oxide at the 1000 mg strength) will not provide more than 5 mg elemental iron per day (as per 21 CFR 73,1200) at max. recommended human dosage.

/S/

Albert F. DeFelice, Ph.D.
1/25/95

cc:
Orig. NDA
HFD-110
HFD-110/CSO
HFD-110/ADeFelice
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