CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 21-038

MEDICAL REVIEW(S)

DRUG NAME: Precedex (dexmedetomidine hcl injection)

REC 12/28/99

APPLICANT: ABBOTT LABORATORIES

CHEMICAL & THERAPEUTIC CLASS:1S

Review Cycles

Review Cycle: 1 **Submission Date:12-18-98** **Receipt Date:12-18-98** **Goal Date:12-18-99** **Action:AP**	**Review Cycle: 2** **Submission Date:** **Receipt Date:** **Goal Date:** **Action:**
Review Cycle: 3 **Submission Date:** **Receipt Date:** **Goal Date:** **Action:**	**Review Cycle: 4** **Submission Date:** **Receipt Date:** **Goal Date:** **Action:**

CORE REVIEW TEAM MEMBERS

PROJECT MANAGER/ CSO :Susmita Samanta **Phone # & Office Room #:301-827-7410, 9B-45**
MEDICAL:Patricia Hartwell, M.D., M.B.A.
CHEMISTRY:Michael Theodorakis, Ph.D.
PHARM/TOX:Harry Geyer, Ph.D.
BIOPHARMACEUTICS:Suresh Doddapaneni, Ph.D.
BIOMETRICS: Z.Jonathan Ma, Ph.D.
ABUSE LIABILITY: BeLinda A. Hayes, Ph.D.
MICROBIOLOGIST: Patricia Hughes, Ph.D.

Volume 2 of 4

Administrative volume #(s): 1
Clinical volume #(s): 2
CMC volume #(s): 3
Pharmacology/Toxicology volume #(s): 4

ODE II ACTION PACKAGE TABLE OF CONTENTS

Application #21-038

Drug Name: Precedex (dexmedetomidine Hydrochloride injection), 2 mL ampule/2 mL vial, 100 mcg/mL

Applicant: Abbott Laboratories Chem./Ther. Type:1S

CSO/PM: Susmita Samanta Phone: 301-827-7410 HFD-170

Original Application Date: December 18, 1998 Original Receipt Date: December 18, 1998

CURRENT USER FEE GOAL DATE: December 18, 1999 DateTableofContentsCompleted:9/13/99

Section A:	**Administrative Information**	**X** (completed), **N/A** (not applicable), or Comment
Tab A-1	Action Letter(s) Current Action:AP	X
Tab A-2	Phase 4 Commitments:	
	a. Copy of applicants communication committing to Phase 4	NA
	b. Agency Correspondence requesting Phase 4 Commitments	NA
Tab A-3	FDA revised Labels & Labeling and Reviews: (Separate each version/cycle with a colored sheet)	
	a. Package Insert	X
	b. Immediate Container and Carton Labels	NA
Tab A-4	Original Proposed Labeling	X
Tab A-5	Foreign Labeling:	
	a. Foreign Marketing History.....	NA
	b. Foreign Labeling and Review(s)	NA
Tab A-6	Labeling and Nomenclature Committee's Tradename Review	X
Tab A-7	Summary Memoranda (e.g., Division Director, Group Leader, Office)	X
Tab A-8	Copy of Patent Statement	X
	Exclusivity Checklist (and any requests for exclusivity)	X
	Debarment Statements	X
Tab A-9	Correspondences, Faxes, & Telecons	X
Tab A-10	Minutes of Meetings:	
	a. End-of-Phase II meeting	NA
	b. Pre-NDA meeting(s)	NA
	c. Filing meeting	X
	d. Other meetings	X
Tab A-11	Advisory Committee Meeting:	
	a. Questions Considered by the committee	NA
	b. List of Attendees	NA
	c. 24 hour alert memorandum	NA

ODE II ACTION PACKAGE TABLE OF CONTENTS (continued)

Application #21-038 Drug Name: Dexmedetomidine HCL

Section B:	Clinical Information	X (completed), N/A (not applicable), or Comment
Tab B-1	Clinical Reviews and Memoranda	X
Tab B-2	Safety Update Reviews	X
Tab B-3	Pediatric Page	X
Tab B-4	Statistical (Clinical) Review and Memoranda	X
Tab B-5	Biopharmaceutics Review and Memoranda	X
Tab B-6	Abuse Liability Review	X
Tab B-7	DSI Audits	X
Tab B-8	Summary of Efficacy (from the summary volume of the application)	NA
Tab B-9	Summary of Safety (from the summary volume of the application)	NA

Section C:	Chemistry, Manufacturing, and Controls (CMC) Information	X (completed), N/A (not applicable), or Comment
Tab C-1	CMC Reviews and Memoranda	X
Tab C-2	DMF Reviews	X
Tab C-3	EA Reviews/FONSI	X
Tab C-4	Micro Review (validation of sterilization)	X
Tab C-5	Statistical Review of drug stability	NA
Tab C-6	Inspection of facilities => Decision:_____ Date:_____	X
Tab C-7	Methods Validation Information	PENDING

Section D:	Pharmacology/Toxicology Information	X (completed), N/A (not applicable), or Comment
Tab D-1	Pharmacology/Toxicology Reviews and Memoranda	X
Tab D-2	Carcinogenicity Review (statistical)	NA
Tab D-3	CAC/Executive Committee Report	NA

ADDITIONAL NOTES:

FDA CENTER FOR DRUG EVALUATION AND RESEARCH
DIVISION OF ANESTHETICS, CRITICAL CARE, AND ADDICTION DRUG PRODUCTS

HFD-170, Room 9B-45, 5600 Fishers Lane, Rockville MD 20857
Tel:(301) 827-7410

MEMORANDUM

to: John K. Jenkins, MD
Director,
Office of Drug Evaluation II

Division File: NDA # 21-038

from: Cynthia G. McCormick, MD
Director, Division of Anesthetics, Critical Care and Addiction Drug Products

/S/

subject: Dexmedetomidine NDA

date: November 30, 1999

This memorandum summarizes for the file the basis for the approval action recommended by the Division of Anesthetics, Critical Care, and Addiction Drug Products for NDA #21-038, Dexmedetomedine HCl for Injection, a sedative/hypnotic agent intended for use in the intensive care setting.

Background

Dexmedetomidine is the dextro-enantiomer of the racemic mixture, medetomidine[1] and a selective α-2-adrenoreceptor agonist. It has been shown in standard animal models of efficacy to have anxiolytic activity (0.3-2.0 μg/kg IV), analgesic activity (3-6 μg/kg IV), and sedative properties (10-30 μg/kg IV) in a dose-related manner in mice, rats and dogs. Dexmedetomidine was developed in humans primarily for its sedative properties and was studied as a sedative in the intensive care setting, delivered by continuous intravenous infusion.

It was anticipated that dexmedetomidine would provide effects similar to those of clonidine, also an α-2-adrenergic agonist which has been used as an anesthetic adjuvant producing analgesia and sedation, and purported to decrease anesthetic requirements and

[1] Medetomidine is a veterinary sedative widely available in Europe and approved in the US in 1997.

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