CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 21-038

PHARMACOLOGY REVIEW(S)

N21038 on #21-038 HFD-170 K1.4

N21038 *K1.4*

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 4 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 Date Table of Contents Completed: 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
Tab A-12	Project Management Administrative Information	

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 ANESTHETIC, CRITICAL CARE, AND ADDICTION DRUG PRODUCTS
HFD-170, Room 9B-45, 5600 Fishers Lane, Rockville MD 20857 Tel:(301)443-3741

MEMORANDUM

DATE: November 30, 1999

TO: Dr. Cynthia McCormick

FROM: Dr. Lucy Jean /S/

RE: Team Leader's Summary of NDA 21-038

Introduction: Dexmedetomidine HCl (DEX) is a potent (7x clonidine), and selective alpha$_2$-agonist ———. The drug is to be marketed as a parenteral solution (Trade name) for intravenous infusion. The indication is for supplemental sedation and/or analgesia in ICU for up to 24 hours. The recommended doses are a loading dose of 1µg/kg over 10 minutes, followed by a maintenance infusion of 0.2 to 0.7 µg/kg/hr to the desired level of sedation and/or analgesia.

Efficacy: In the CNS via α_2 -agonist activity, DEX produces sedation, analgesia and reduced anxiety. The sedative/hypnotic (10-30 µg/kg iv), analgesic (3-6 µg/kg iv) and anxiolytic (0.3-2 µg/kg iv) effects were shown in mice and rats; and in dogs the sedative/hypnotic effects as well. No anticonvulsant activity was shown. In rats (3 µg/kg i.v.) DEX reduced ischemic brain damage.

Safety pharmacology: The α_2 - agonist inhibits the release of norepinephrine at neurons. Thus DEX, via its α_2 -agonist activity in the CNS, inhibits sympathetic activity resulting in decreases of blood pressure and heart rate. The CV effects of dec BP & HR were observed in rats, dogs and monkeys. In dogs (1 µg/kg iv), decreases of the heart rate, myocardial contractility, CO, and oxygen demand by the heart (increased AV O_2 saturation) were observed. Similar to some of the imidazole-derivates of intravenous anesthetics, suppression of the HPA was observed only following prolonged infusion. In dogs prolonged sc infusion (10 µg/kg/hr for 7 days) of DEX decreased the ACTH-stimulated cortisol level by 40%, but no effect was observed following single sc dose of

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.