CENTER FOR DRUG EVALUATION AND RESEARCH

ADVISORY COMMITTEE: DRUG ABUSE ADVISORY COMMITTEE

DATE OF MEETING: 12/12-13/96

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SUMMARY MINUTES

Food and Drug Administration
Center for Drug Evaluation and Research

SUMMARY MINUTES OF THE DRUG ABUSE ADVISORY COMMITTEE

December 12, 1996
Holiday Inn, Bethesda, MD

Members Present
Drug Abuse Committee

Max A. Schneider, M.D., CADC, Chair
Ann Andorn, M.D.
John E. Franklin, Jr., M.D.
Llyn A. Lloyd, R.PH...
Eric C. Strain, M.D.
Delores Yoroma, R.N.

Members Not Present

Elizabeth Khuri, M.D.
Alice M. Young, Ph.D.
Harriet deWit, M.D.
Carol L. Falkowski

FDA Participants

Curtis Wright, M.D.
Celia Winchell, M.D.

FDA Consultants

David J. Brunswick, Ph.D.
Thomas L. Kurt, M.D., M.P.H.
Phillip Woodson, B.S., M.A., Dr.Sc.Nat..

Executive Secretary

Tracy Riley

These summary minutes for the December 12, 1996, meeting of the Drug Abuse Advisory Committee were approved on 4/22/97.

I certify that I attended the December 12, 1996, Committee meeting and that these minutes accurately reflect what transpired.

Tracy Riley
Executive Secretary

Max A. Schneider, M.D., CADC
Chairperson

On Thursday, December 12, 1996, the Drug Abuse Advisory Committee met in open session to discus NDA 20-711, bupropion sustained release tablets, Glaxo Wellcome, Inc., for use as an aid in smoking cessation. The Committee members had been supplied with a background briefing book from the sponsor and staff reviews from the FDA. The meeting was held in the Versailles Ballrooms I & II of the Bethesda Holiday Inn, 8120 Wisconsin Avenue, Bethesda, Maryland. The meeting was attended by approximately 250 persons.

At 9:00 am, the meeting was called to order by Max Schneider, M.D., Chairman, followed by the Conflict of Interest Statement which was read by Tracy Riley, Executive Secretary, and introductions of the meeting participants. Dr. Schneider opened the public hearing and Ms. Riley read a statement into the record from John Slade, M.D., Chair, Committee on Nicotine Dependence of the American Society of Addiction Medicine.

Matthew Bars, a Master's level Clinical Psychologist, Paula Kaiser, a patient who has used the drug, Gregory Connolly, D.M.D., M.P.H., Director, Tobacco Control Program, Massachusetts Department of Public Health, and Dr. James F. Callahan, Executive Vice President and CEO of the American Society of Addiction Medicine, presented statements of their positions on aspects of smoking cessation. All spoke in favor of approving the product for smoking cessation. Additionally, Dr. Connolly stated his opinion that one of the obligations of sponsors is to focus on the benefits of quitting smoking rather than merely to compete for market share in their advertisements.

Sponsor Presentations:

Efficacy of Bupropion - Andy Johnston, Pharm.D., Senior Clinical Program Head, CNS Clinical Research

Safety of Bupropion - John Ascher, M.D., Senior Research Physician, CNS Clinical Research

Conclusions - Andy Johnston, Pharm.D.

FDA Medical Officer Presentation by Celia Jaffe Winchell, M.D., Drug Abuse Team Leader

An interactive discussion of the issues concluded with a vote on Question #1, "Does the Committee feel that there is substantial evidence of the safety and efficacy of bupropion SR in the smoking cessation indication?"

VOTE:	Safety:	Yes: 8	No: 0
	Efficacy:	Yes: 8	No: 0

Sponsor Presentations:

The Place of Bupropion in the Treatment of Smoking Cessation:

Richard D. Hurt, M.D., Director, Nicotine Dependence Research Center, Mayo Clinic, Rochester, Minnesota

Michael Fiore, M.D., M.P.H., Director, Center for Tobacco Research & Intervention, University of Wisconsin Medical School

FDA Presentation:

Celia Winchell, M.D., Special Risks of Bupropion and Risks of Other Smoking Cessation Products

Question #2, "What is the place of bupropion in the treatment of tobacco dependance?" was redefined to mean "Do you have reservations about the use of bupropion as a first-line drug in smoking cessation?" Interactive discussion of the issues concluded with the following vote. Concerns were discussed regarding the incidence (0.1%) of seizures with the recommended dose.

VOTE: No reservations: 8 Reservations: None

Presentations on Dual Name Marketing:

Sponsor: Richard Kent, M.D., World Wide Director for Clinical Research

FDA: Dr. Celia Winchell

Interactive discussion of the issues concluded with a vote on Question #3, Part 1, "Does the Committee agree that this product should be marketed with distinct name, separate dosing recommendations, and unique labeling, distinct from Wellbutrin SR (which is marketed for depression)?"

VOTE: Yes: 4 No: 4

Question #3, Part 2, in light of the split vote, was restated to be "What additional precautions adequate to protect the public should be taken to avoid inadvertent dual prescription?"

Labeling with strong warnings about the potential for seizures with dual dosing

Education programs for providers and patients

Pharmacy software to warn of dual prescribing

Questioning of patients about concomitant medications from other providers

Different name

Same name with different suffix

Question #4, "Does the committee have any other recommendation with regard to the labeling of the product?" Interactive discussion of the issues produced the following recommendations and concerns.

Concerns were raised regarding formulary limitations. Packaging could allow for provision of the accompanying behaviormodification program materials separately to providers.

Strengthening the label warnings against PRN use

Mention of data in labeling that would show level of effectiveness in the event of incomplete patient abstinence

The meeting was adjourned by the Chairman at approximately 4:00 pm.

Food and Drug Administration
Center for Drug Evaluation and Research

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December 13, 1996
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Elizabeth Khuri, M.D.
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Carol L. Falkowski

FDA Participants

Curtis Wright, M.D.
Jack Longmire, M.D.
Tom Permutt, Ph.D.
Suresh Doddapaneni, Ph.D.

These summary minutes for the December 13, 1996, meeting of the Drug Abuse Advisory Committee were approved on 4/2/97.

I certify that I attended the December 13, 1996, Committee meeting and that these minutes accurately reflect what transpired.

Tracy Riley
Executive Secretary

Max A. Schneider
Max A. Schneider, M.D., CADC
Chairperson

On Friday, December 13, 1996, the Drug Abuse Advisory Committee met in open session to discuss NDA 20-714, Nicotrol Inhaler (nicotine inhalation system), Pharmacia & Upjohn, Inc., for use as an aid in smoking cessation. The Committee members had been supplied with a background briefing book from the sponsor and staff reviews from the FDA. The meeting was held in the Versailles Ballrooms I & II of the Bethesda Holiday Inn, 8120 Wisconsin Avenue, Bethesda, Maryland, and was attended by approximately 150 persons.

At 9:00 am, the meeting was called to order by Max Schneider, MD, Chairman, followed by the Conflict of Interest Statement which was read by Tracy Riley, Executive Secretary, and introductions of the meeting participants. Dr. Schneider opened the public hearing.

Louis W. Sullivan, MD, former Secretary of HHS and FDA Advisory Committee member, Dr. James F. Callahan, Executive Vice President and CEO of the American Society of Addiction Medicine, Al Munzer, MD, Chief of Pulmonology, Washington Adventist Hospital, Takoma Park, Maryland, and past president of the American Lung Association, and Scott D. Ballin, J.D., American Heart Association, presented statements of their positions on aspects of smoking cessation. All participants spoke in favor of having an additional product for use in smoking cessation.

Sponsor.Presentations:

Introduction - Raymond E. Dann, PhD, Regulatory Affairs

Background - Karl Orlov Fagerstrom, PhD, Director, Scientific Information, Nicotine Replacement Therapy

Pharmacokinetics - Erik Lunell, MD, PhD, Department of Clinical Pharmacology

Efficacy, Dosing Rationale, and Safety - Mikael Franzon, PhD, Medical Dept.

Abuse Potential - John R. Hughes, MD, Professor of Psychiatry, University of Vermont

Conclusions - Dr. Fagerstrom

FDA Presentations:

Medical Officer Presentation of Pivotal Trials and Abuse Liability - Jack Longmire, MD, Drug Abuse Team Leader

Statistical Reviewer Presentation of Integrated Summary of Efficacy - Tom Permutt, PhD

Pharmacokinetics Reviewer Presentation - Suresh Doddapaneni, PhD

Question and Answer Session with Sponsor

An interactive discussion of the issues concluded with a vote on Question #1, "Based on the information provided, does the Committee consider the Nicotrol Inhaler to be effective?"

VOTE: Yes: 8 No: 0

An interactive discussion of Question #2, "Based on the information provided, does the Committee consider the product to be of acceptable risk, used as directed?" proceeded. Members of the committee recommended conditions to the marketing as follows:

a) the packaging and inhalation system need to be made more safe in terms of labeling about preventing access by children and animals;
b) the device cartridge needs to be redesigned to prevent disassembly (a unitary design was suggested);
c) instructions about cleaning the device should be provided; the device needs to be radiopaque to permit imaging in case of ingestion; and
d) information should be provided to poison control centers about treatment of ingestion.

VOTE: Yes, with conditions as stated: 8 No: 0

Interactive discussion of the issues of Question #3, "Are labeling changes needed for this product?" concluded with the following vote.

VOTE: Yes: 8 No: 0

In the opinion of the Committee, the following labeling issues need to be addressed:

Education programs for providers and patients

Behavior modification programs for patients

Note possible morbidities from use of the device, such as cough, oral inflammation, headache and nausea, which may need treatment, in information received by the patient

Clearly mark all parts of the product with "Keep out of reach of children and animals"

Discourage use past 6 months

Discourage sharing of product

Include instructions on cleaning and proper disposal

Ensure that goal of smoking cessation is emphasized

Interactive discussion of the issues of Question #4, Part 1, "Should the sponsor study this product in a population with cardiac or pulmonary disease as a Phase 4 commitment?" concluded with the following vote.

VOTE: Yes: 1 No: 7

Interactive discussion of the issues of Question #4, Part 2, "If not, could the Agency's concerns about use in this population be addressed sufficiently with language in the labeling?" proceeded.

During the discussion, concerns were raised regarding use of the product in patients with bronchospastic disease, severe cardiovascular and/or respiratory illness and whether there is the necessity for further formal study by the sponsor. The Committee recommended that the product be labeled to indicate that until there is adequate data to support use by these patients, use of another smoking cessation product should be considered for first-line use.

Additional Committee Business:

Dr. Andorn proposed the establishment of a subcommittee to consider clinical trial issues such as adequate endpoints, treatment duration and evaluations of effectiveness. Dr. Schneider volunteered to participate and solicited further member participation. Dr. Andorn agreed to participate as chairman and will work with the Advisors and Consultants staff to plan a meeting.

Dr. Schneider complimented the sponsor for the quality of their presentations and their responsiveness to the queries of the Committee; Dr. Wright also complimented the sponsors on this and the previous day for the completeness, fairness and balance of their presentations which made the review and Committee processes go very smoothly. He offered this as an example to other sponsors in the future.

Dr. Schneider also complimented the FDA Review Division and Advisors and Consultants Staff for their efforts.

The meeting was adjourned by the Chairman at approximately 12:30 pm.