

Food and Drug Administration
Center for Drug Evaluation and Research

**SUMMARY MINUTES
ARTHRITIS ADVISORY COMMITTEE**

February 4, 1997
Gaithersburg Hilton
620 Perry Parkway, Gaithersburg, MD

Members Present

Michelle Petri M.D., M.P.H., Chair
Steven B. Abramson, M.D.
Barbara C. Tilley, Ph.D.
Leona Malone, MSW
Frank Pucino, Jr., Pharm.D.
Daniel J. Lovell, M.D., M.P.H.
Matthew Liang, M.D., M.P.H.
David Felson, M.D., M.P.H.
Lee Simon, M.D.
Harvinder Luthra, M.D.
Felix Fernandez-Madrid, M.D., Ph.D.

FDA Participants

Wiley A. Chambers, M.D.
Kent Johnson, M.D.

Consultants

Karyl S. Barron, M.D.
M. Clinton Miller, Ph.D.
Patience H. White, M.D.
Joseph McGuire, M.D.
Andrew Whelton, M.D.

Guest Experts

Members Absent

Executive Secretary

Kathleen R. Reedy

These summary minutes for the February 4, 1997 meeting of the Arthritis Advisory Committee were approved on 2/4/97.

I certify that I attended the February 4, 1997 meeting of the Arthritis Advisory Committee and that these minutes accurately reflect what transpired.


Kathleen R. Reedy,
Executive Secretary


Michelle A. Petri, M.D., M.P.H.
Chairperson

The Arthritis Advisory Committee of the Food and Drug Administration, Center for Drug Evaluation and Research met at the Gaithersburg Hilton, 620 Perry Parkway, Gaithersburg, MD. on February 4, 1997 to discuss NDA 50-735, Neoral®, (cyclosporine) sponsored by Sandoz Pharmaceuticals. The Committee had been provided with a background document in preparation for the meeting by the sponsor and the agency. Approximately 200 people attended the meeting.

The meeting was called to order at 8:30 am by Michelle Petri, M.D., M.P.H. Chairperson of the Arthritis Advisory Committee, and began with the introduction of those present at the discussion table. The meeting statement regarding conflict of interest was read by Kathleen Reedy, Executive Secretary, followed by welcoming comments by Wiley A. Chambers, M.D., Acting Director of the Division of Anti-Inflammatory, Analgesic and Ophthalmic Drug Products. There were no speakers at the Open Public Hearing.

The Sponsor Presentation consisted of an introduction by Michael S. Perry, DVM, PhD, Vice President, Drug Registration and Regulatory Affairs at Sandoz Pharmaceuticals Corporation. The Clinical Efficacy and Safety presentation and Dosing Guidelines were presented by Helen Torley, MB, ChB, MRCP, Head of Medical Affairs at Sandoz Pharmaceuticals. A Clinical Perspective was presented by Peter Tugwell, MD, Chairman of the Department of Medicine, University of Ottawa, Canada.

The FDA Presentation was by Medical Officer Kent R. Johnson, MD, of the Division of Anti-Inflammatory, Analgesic and Ophthalmic Drug Products, FDA.

Discussion followed which considered Questions #1 and #2.

1. Has Neoral demonstrated efficacy in controlled trials and does it have an acceptable risk/benefit ratio?

The committee unanimously agreed that the drug is effective.

The risk/benefit ratio suggestions: Labeling

Limited to patients with normal renal function

Patients with hypertension (>140/90) be treated with

antihypertensive drugs (beta or calcium channel blockers)

Malignancy warning

Some note on lipids

Drug interaction guidance (ace inhibitors)

2. How should its indication section read?

In which "set" of RA patients?

Note RA stage

Use as additive or second line treatment to MTX

Monotherapy after failure of two others or MTX

In combination with background therapy (i.e. methotrexate)?

Yes

a. Should separate recommendations (dosing, monitoring, etc.) be recommended in the presence of background methotrexate?

Clear cautionary note

Monitor hypertension and renal function, creatinine

b. Is there a significant PK interaction with Neoral and methotrexate?

Unknown, need more data

Quantify drug interaction.

Is it clinically significant? Perhaps.

Needs post-marketing study: liver, pulmonary, cardiovascular, lipid effects; drug metabolism; hypertension, renal function, carcinomas

Registry, long term, 5+yr; some with MTX cotreatment

If so, what are its implications regarding labeling?

Labeling for RA should be different from transplant and specific labeling for NSAID interaction included.

The Sponsor Presentation of Pediatric Data was by Vibeke Strand, MD, FACP of the Clinical Faculty at Stanford University, CA.

Discussion of Question #3 followed:

3. What additional data, if any, would be needed in JRA to permit the labeling (via the "pediatric rule") for polyarticular JRA.

Appears safe and effective at the recommended dose extrapolated for poly JRA. Additional studies: small bioavailability study, long term effects, glucocorticoid/steroid sparing?

The meeting was adjourned at 4:40 pm.

Kathleen R. Reedy, Health Scientist Administrator
Executive Secretary, Arthritis Advisory Committee