ANTIVIRAL DRUGS ADVISORY COMMITTEE
JULY 25, 2000

AGENDA AND ADVISORY COMMITTEE QUESTIONS

July 25, 2000 Agenda

8:30 Welcome

8:35 Conflict of Interest Statements

8:45 Introduction/Opening Remarks
Heidi Jolson, M.D., M.P.H, Division Director, DAVDP

9:00 Clinical Pharmacology Overview from the Antiviral Perspective–
Kellie Schoolar Reynolds, Pharm.D., Pharmacokinetics Team Leader, OCPB

10:00 Break

10:15 Anti-infective Perspective
Alex Rakowsky, M.D., Medical Officer, DAIDP

10:45 Antiretroviral PK/PD Overview
Richard Hoetelmans, Pharm.D., Ph.D., Slotervaart Hospital Dept. of Pharmacy & Pharmacology Amsterdam, The Netherlands

11:15 Future Considerations for PK/PD Research
Terrence F. Blaschke, M.D., Professor of Medicine and Molecular Pharmacology, Stanford University

11:45 Lunch

1:00 Open Public Hearing

David Pasquarelli, ACTUP San Francisco

Jules Levin, National AIDS Treatment Advocacy Project, New York

2:00 Charge to the Committee –
Kimberly Struble, Pharm.D., Regulatory Review Officer, DAVDP

2:15 Committee Discussion

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Questions

PK/Efficacy Issues:

1. What is the role of pharmacokinetic data in the evaluation of new formulations and alternative dosing regimens for approved antiretroviral drugs? Given the available data, please discuss the strengths and limitations of specific exposure measures, such as AUC and C_{min} or other measures, in predicting virologic response.

   A. What data are needed to rule out the relevance of any exposure measures for efficacy?

   B. What is the role of intracellular concentrations in the evaluation of new formulations and alternative dosing regimens for approved NRTIs?

   C. In what circumstances would clinical efficacy data be necessary?

   D. PK and virologic response relationships have mainly been established in antiretroviral naïve patients. Are these relationships applicable to antiretroviral experienced patients? Are there cases where additional PK and/or efficacy data are necessary for different patient populations?

PK/Safety Issues:

2. Do the scientific data at present correlate any particular exposure measure with toxicity?

3. What amount and duration of safety data are needed to support new formulations/ new dosing regimens of approved antiretroviral drugs with increased exposure measures?

Drug Interaction Issues

4. Which exposure measures should be considered when providing labeling information on concomitant administration of antiretrovirals?

   A. If one or more exposure measures are decreased, should additional clinical data be required? If so, how much? In what circumstances are clinical data necessary?

B. How should several dosing possibilities be addressed? What criteria should be used for placing specific recommendations in labels?

Pediatric Issues:

5. Once an alternate regimen has been identified in adults, should we expect identical PK profiles in children (i.e., all PK parameters equivalent) or only equivalent critical parameters (i.e., AUC or Cmin)? Does this apply to all drugs and all pediatric sub-populations or are there some situations in which more clinical/virologic data will be necessary?

Future Research Issues:

6. What kinds of studies are needed to better define pharmacokinetic/ pharmacodynamic relationships for antiretroviral drugs?