

# Clinical Pharmacology and Biopharmaceutics Review

## I. Project Identification

NDA number/serial number	20,038/SE8-028-PM
Submission date	February 7, 2003
Drug name	Fludara
Generic name	Fludarabine
Dosage form	lyophilized powder for IV injection
Sponsor	Berlex Laboratories 15049 San Pablo Avenue Richmond, CA 94804-0099
Reviewer	Anne Zajicek, M.D., Pharm.D.
Submission Type	NDA-Supplement

## II. Executive Summary

The applicant submitted the results of two clinical studies of fludarabine in children with relapsed malignancies. Study CCG-097 was a Phase 1 pharmacokinetic study of 23 children with relapsed acute leukemias (n=18) and solid tumors (n=5) who were randomized to receive one of six increasing bolus + 5 day infusion regimens. The pharmacokinetics of fludarabine in these children was markedly different from that reported in adult studies. Mean clearance in the children was 0.61 L/hr/m<sup>2</sup>, compared with 8.7 and 4.1 L/hr/m<sup>2</sup> in two adult studies. Half-life and volume of distribution were similar to adult values (12.4 vs 10.4 hours, and 10.8 vs 7.5 L/m<sup>2</sup> respectively). The explanation of this difference is unclear. Study CCG-0895 was a Phase 1/2 study combining bolus + 2 day infusion fludarabine, followed by a 3 day infusion of increasing dose cytarabine in children with relapsed acute leukemias. There were three children with evaluable data; their clearance values were similar to those seen in CCG-097, ranging from 0.44-2.15 L/h/m<sup>2</sup>.

No labeling changes for pediatric indications or dosing will be made at this time due to inadequate efficacy data generated in the study report.

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CC: NDA 20,038/SE8-028  
HFD-150 Division File  
HFD-150 DPease  
HFD-150 MCohen, JJohnson  
HFD-860 MMehta, CSahajwalla, ARahman, AZajicek  
CDR Biopharmaceutics

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Atiqur Rahman  
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