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DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: June 26, 1991

FROM: Solomon Sobel, M.D., Director, Division of Metabolism and Endocrine Drug Products

SUBJECT: Approval of Aredia (pamidronate sodium)

TO THE FILE: NDA 20-036 (Aredia)

The approval of this NDA rests primarily on two studies:

(1) A study comparing the response in patients with hypercalcemia of malignancy to intravenous pamidronate sodium at 3 daily dosage levels - 30 mg, 60 mg, and 90 mg. This treatment followed a period of rehydration with intravenous saline solution.
(2) A comparative study with intravenous etidronate as a positive control. Intravenous etidronate has been approved with a regimen of 7.5 mg/kg daily for 3 days.

Pamidronate at doses of 60 mg appeared to have a more profound and prolonged hypocalcemic effect than etidronate. The one possible advantage of etidronate was perhaps a more rapid onset of action. This was not shown to be statistically significant.

The toxicity of pamidronate is acceptable.

The place of biphosphonates in the treatment of hypercalcemia associated with malignancy is further established by the studies in this NDA.

Dr. Young of the Division of Scientific Investigation informed us that the inspections of the Boston and Oklahoma sites revealed a satisfactory performance of the studies. The N.Y. site remains to be inspected. We discussed the relative importance of the remaining inspection and decided that the crucial inspections were in Oklahoma and Boston and it was highly unlikely that the N.Y. inspection would alter our view of the validity of the studies.

The spectrum of treatment now includes mithramycin, phosphates, gallium, calcitonin, and etidronate. The specific advantages and usage of these agents probably will revolve about pharmacokinetic, pharmacodynamic and toxicity issues in particular clinical situations.

Recommendation: The Division recommends approval of this NDA.