ABBOTT

Pharmaceutical Products Division

Abbott Laboratories
200 Abbott Park Road
Abbott Park, IL 60064-6182

July, 2000

IMPORTANT DRUG WARNING

Dear Health Care Professional:

This communication is to advise you of an update to the WARNINGS section in the labeling for Depakote® Tablets (divalproex sodium delayed-release tablets, Abbott), Depakote® Sprinkle Capsules (divalproex sodium coated particles in capsules, Abbott), and Depacon® (valproate sodium injection, Abbott). Similar changes have been made to the Depakene® (valproic acid capsules and syrup, Abbott) label. Although there has been no increase in the reported rate of pancreatitis associated with valproate use, based on discussions with the Food and Drug Administration (FDA), the labeling has been revised to provide additional information regarding pancreatitis. Pancreatitis has been listed in the package inserts of valproate products since 1981.

The revised black box warning includes the following addition:

PANCREATITIS:
CASES OF LIFE-THREATENING PANCREATITIS HAVE BEEN REPORTED IN BOTH CHILDREN AND ADULTS RECEIVING VALPROATE. SOME OF THE CASES HAVE BEEN DESCRIBED AS HEMORRHAGIC WITH A RAPID PROGRESSION FROM INITIAL SYMPTOMS TO DEATH. CASES HAVE BEEN REPORTED SHORTLY AFTER INITIAL USE AS WELL AS AFTER SEVERAL YEARS OF USE. PATIENTS AND GUARDIANS SHOULD BE WARNED THAT ABDOMINAL PAIN, NAUSEA, VOMITING, AND/OR ANOREXIA CAN BE SYMPTOMS OF PANCREATITIS THAT REQUIRE PROMPT MEDICAL EVALUATION. IF PANCREATITIS IS DIAGNOSED, VALPROATE SHOULD ORDINARILY BE DISCONTINUED. ALTERNATIVE TREATMENT FOR THE UNDERLYING MEDICAL CONDITION SHOULD BE INITIATED AS CLINICALLY INDICATED. (See WARNINGS and PRECAUTIONS.)

The WARNINGS section includes the following additional information:

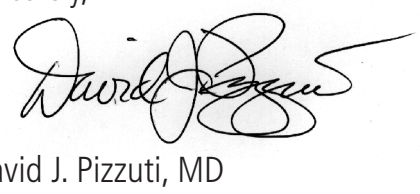
Pancreatitis
Cases of life-threatening pancreatitis have been reported in both children and adults receiving valproate. Some of the cases have been described as hemorrhagic with a rapid progression from initial symptoms to death. Some cases have occurred shortly after initial use as well as after several years of use. The rate based upon the reported cases exceeds that expected in the general population and there have been cases in which pancreatitis recurred after rechallenge with valproate. In clinical trials, there were 2 cases of pancreatitis without alternative etiology in 2416 patients, representing 1044 patient-years experience. Patients and guardians should be warned that abdominal pain, nausea, vomiting, and/or anorexia can be symptoms of pancreatitis that require prompt medical evaluation. If pancreatitis is diagnosed, valproate should ordinarily be discontinued. Alternative treatment for the underlying medical condition should be initiated as clinically indicated (see **BOXED WARNING**).

Changes consistent with the revised black box warning have been made to the Information for Patients subsection of the PRECAUTIONS section of the labeling. Identical revisions are being made to the package inserts for our other valproate products. Additional changes have been added to the safety sections of the valproate products package inserts. For detailed information on approved indications and additional safety information, please refer to the respective package insert. A full copy of the revised Depakote Tablets package insert is enclosed.

As with all medical products, health care professionals are strongly encouraged to report any serious adverse events that occur with the use of Depakote, Depacon, or Depakene products either to Abbott Laboratories (1-800-633-9110), or to the FDA's MedWatch program by phone (1-800-FDA-1088), fax (1-800-FDA-0178), via the MedWatch website at www.FDA.gov/medwatch, or by mail (using postage-paid form) to MedWatch, HF-2, 5600 Fishers Lane, Rockville, MD 20852-9787.

If you have any questions, our Medical Services Department may be reached at 1-800-633-9110.

Sincerely,



David J. Pizzuti, MD
Divisional Vice President
Medical Affairs

Enclosure:
Depakote® Tablets (divalproex sodium, Abbott) Package Insert

00F-731-1361A