



Bristol-Myers Squibb Company

Bristol-Myers Squibb U.S. Pharmaceutical
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Consumer -1
Encainide HCl
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FOR IMMEDIATE RELEASE

EVANSVILLE, Ind. -- The antiarrhythmic medication Enkaid® (encainide hydrochloride) will be withdrawn from the market effective Dec. 16, it was announced today by Bristol Laboratories, a division of Bristol-Myers Squibb Company.

The company stated that this decision is based upon continuing uncertainty regarding the implications of a government study of several cardiac arrhythmia suppression medications, in addition to the availability of a growing number of alternative therapies.

"It is essential that patients not discontinue medication on their own, but that they consult their physicians," said E. J. Fox, M.D., vice president, medical department, Bristol Laboratories.

"In some cases, physicians may judge that patients with life-threatening ventricular arrhythmias who are already successfully managed on Enkaid should not be changed to another medication," Fox said. "For such patients, Bristol Laboratories will continue to provide Enkaid through their physicians."

The Enkaid Continuing Patient Access Program will provide the medication free of charge to eligible patients who were being treated with Enkaid for life-threatening ventricular arrhythmias as of Sept. 16, 1991.

(more)

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For other patients, a variety of alternative drug therapies and surgical interventions have been developed in recent years. For patients whose doctors discontinue Enkaid® therapy, Bristol Laboratories is establishing a prescription reimbursement program. Patients may obtain a refund by returning the unused portions of their prescriptions to the pharmacies at which they were purchased, the company said.

The future of Enkaid has been uncertain since the drug was removed in April 1989 from the Cardiac Arrhythmia Suppression Trial (CAST), conducted by the National Institutes of Health. The study was designed to determine the effectiveness of three antiarrhythmic drugs in decreasing the risk of sudden cardiac death among patients who had survived heart attacks and had non life-threatening arrhythmias.

Patients taking Enkaid, as well as those taking another drug in the study, had a higher death rate from heart attacks than patients receiving a placebo. More recently, in August 1991, the same negative trend was observed with the final drug remaining in CAST and the trial was stopped altogether. The reasons for the higher death rate continue to confound medical authorities.

Following removal of Enkaid from CAST in April 1989, Bristol Laboratories immediately moved to narrow the indications for the drug. Since that time, Enkaid has been approved for use only in patients with life-threatening ventricular arrhythmias. The drug has not been actively promoted to physicians since it was removed from CAST.

Enkaid was approved for marketing by the U.S. Food and Drug Administration in December 1986 and was first available for prescribing by physicians in April 1987.

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Encainide 1721
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FDA

TALK PAPER

FOOD AND DRUG ADMINISTRATION
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UPDATE: ANTIARRHYTHMIC DRUGS

FDA has been receiving inquiries about two drugs used to treat patients with abnormal heartbeats -- flecainide (Tambocor), approved in 1985, and encainide (Enkaid), approved in 1986. In 1989 both drugs were found to cause increased death rates in patients who had asymptomatic heart rhythm abnormalities after a recent heart attack, a use for which neither drug had been approved by FDA. Encainide is no longer being marketed.

Flecainide is considered safe and effective for two very different groups of patients. One group experiences disabling bursts of rapid heartbeats that do not start in the ventricle, but they have no other heart problems. The other group has life-threatening arrhythmias starting in the ventricle.

The following can be used to answer questions:

FDA originally approved flecainide and encainide for patients with life-threatening arrhythmias and for patients with symptomatic ventricular arrhythmias of lesser severity if their physicians decided the benefits outweighed the risks of the drug.

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The risks included the possibility of worsened heart rhythms and death.

Neither flecainide nor encainide was approved for treatment of people without symptoms, but some physicians did use the drugs in patients without symptoms who had recent heart attacks, if they had abnormal electrocardiograms that showed frequent extra heartbeats (ventricular premature beats or VPBs). The doctors' intent was to improve survival of these patients because it was known that people with frequent VPBs, especially if they had a recent heart attack, were at increased risk of sudden death.

Physicians may use drugs in ways others than those stated in the labeling, but the evidence of safety and effectiveness of such off-label uses is usually well short of such evidence for approved uses. This was the case in the two antiarrhythmic drugs, whose labeling noted the lack of adequate data in patients with a recent heart attack and also pointed out the lack of any evidence that the drugs could improve survival. Due to growing concerns about the ability of all antiarrhythmic drugs to make some heart rhythms worse, FDA began in 1984 and 1985 to require changes in the drugs' labeling to limit the use of such products to symptomatic patients.

In 1987, the National Heart, Lung and Blood Institute began a large study called the CAST (Cardiac Arrhythmia Suppression

Trial) to determine whether heart attack patients with frequent VPBs who had no or minimal symptoms would live longer if their VPBs were reduced with antiarrhythmic drugs. The study was halted in April 1989 when preliminary results showed that the chances of death for the treated patients were two-and-one-half times greater than patients on placebo. In consultations with FDA, manufacturers of both flecainide and encainide notified doctors that the two drugs should be used only in patients with life-threatening arrhythmias, and the labeling was changed to reflect this.

Based on additional evidence, flecainide was later also approved for patients with supraventricular arrhythmias associated with disabling symptoms, but only in patients with no evidence of other heart disease.

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