IMPORTANT PRESCRIBING INFORMATION

Shire US Inc.
725 Chesterbrook Blvd
Wayne, PA 19087

September, 2007

J. Q. Jones, MD
123 Any Street
NY, NY 11222

Dear Dr. Jones:

Shire notified you in July 2007 that we would no longer be selling Ethmozine® (moricizine hydrochloride) 200 mg, 250 mg and 300 mg tablets. Since then, we have decided that the product will remain available for at least six months to ensure that adequate time is given to find alternative therapy for patients who are treated with Ethmozine. The discontinuation of Ethmozine is not the result of any safety or efficacy concerns with the product.

Physicians are advised to plan accordingly; specifically to cease prescribing Ethmozine to new patients and to transfer existing patients treated with Ethmozine to alternative forms of therapy in anticipation of the lack of available supply of Ethmozine after December 31, 2007.

Until December 31, 2007, patients can still have their prescription filled at their pharmacy. Ethmozine will be available through drop shipment from the wholesaler to the pharmacy each time a new prescription or a refill is requested. Once the refill is requested through this process, it may take several days for the prescription to be filled. Please advise your patients to plan ahead when requesting a refill of Ethmozine. We hope that this process will allow physicians time to identify patients taking Ethmozine and time to transition their patients to an alternative therapy.

Transferring Patients to Another Antiarrhythmic

Please evaluate and advise your patients who are taking Ethmozine that they will require an alternative therapeutic regimen to treat their arrhythmia. Although no generic version of moricizine hydrochloride tablets is available, there are multiple therapeutic alternatives available to the prescribing physician. Caution is indicated if Ethmozine is tapered at the same time that another antiarrhythmic drug is initiated because of possible additive pharmacologic effects. Please see important safety information and enclosed prescribing information. Patients who will be tapered off Ethmozine are at high risk for life-threatening arrhythmias during the tapering process. Because of this high risk, a Cardiologist should initiate Ethmozine taper and withdrawal with close monitoring of the patient.

Should you or your patients have any questions regarding this correspondence, please contact Shire's Medical Information telephone line at 1-800-828-2088 and choose the option "Medical Information". Thank you for your understanding.

Sincerely,

Jonathan Rubin, MD, MBA
Medical Director
Global Medical Affairs
Shire Pharmaceuticals

Important Prescribing and Safety Information

Ethmozine® is indicated for the treatment of documented ventricular arrhythmias, such as sustained ventricular tachycardia, that, in the judgement of the physician are life-threatening. Treatment of patients with asymptomatic ventricular premature contractions should be avoided. Ethmozine is contraindicated in patients with pre-existing second- or third-degree atrial-ventricular block and in patients with right bundle branch block when associated with left hemiblock unless a pacemaker is present. Ethmozine is also contraindicated in the presence of cardiogenic shock or known hypersensitivity to the drug.

In patients with pre-existing conduction abnormalities, Ethmozine therapy should be initiated cautiously. If second- or third-degree atrial-ventricular block occurs, Ethmozine therapy should be discontinued unless a ventricular pacemaker is in place. When changing the dose of Ethmozine or adding concomitant medications which may also affect cardiac conduction, patients should be monitored electrocardiographically. Patients with liver disease, renal disease and congestive heart failure should be carefully monitored while taking Ethmozine.

Mortality

Ethmozine was one of the three antiarrhythmic drugs included in the National Heart Lung and Blood Institute's (NHLBI) Cardiac Arrhythmia Suppression Trial (CAST I), a long-term, multi-center, randomized, double-blind study in patients with asymptomatic non-life-threatening ventricular arrhythmias who had had a myocardial infarction more than six days, but less than two years previously. An excessive mortality or non-fatal cardiac arrest rate was seen in patients treated with both of the Class IC agents included in the trial, which led to discontinuation of those two arms of the trial. The average duration of treatment with these agents was 10 months, The Ethmozine and placebo arms of the trial were continued in the NHLBI-sponsored CAST II. In this randomized, double-blind trial, patients with asymptomatic, non-life-threatening ventricular arrhythmias who had had a myocardial infarction within 4 to 90 days and left ventricular ejection fraction <0.40 prior to enrollment were evaluated. The average duration of treatment with Ethmozine in this study was 18 months. The study was discontinued because of the unlikely possibility of demonstrating a benefit toward improved survival with Ethmozine and because of an evolving adverse trend after long-term treatment, although there was no statistical significance versus placebo.

The applicability of the CAST results to other populations (e.g., those without recent myocardial infarction) is uncertain. Considering the known proarrhythmic properties of Ethmozine and the lack of evidence of improved survival for any antiarrhythmic drug in patients without life-threatening arrhythmias, the use of Ethmozine, as well as other antiarrhythmic agents, should be reserved for patients with life-threatening ventricular arrhythmias.

The most serious adverse reaction reported for Ethmozine is proarrhythmia. Other reactions which have led to discontinuation include ECG abnormalities (conduction defects, sinus pause, junctional rhythm or atrial-ventricular block), congestive heart failure, cardiac death, dizziness, anxiety, drug fever, urinary retention, blurred vision, gastrointestinal upset, and rash. Common adverse events include dizziness, nausea, headache, fatigue, palpitations, dyspnea, sustained ventricular tachycardia, hypesthesias, abdominal pain, dyspepsia, vomiting sweating, cardiac chest pain, asthenia, nervousness, paresthesias, congestive heart failure, musculoskeletal pain, diarrhea, dry mouth, cardiac death, sleep disorders and blurred vision.