

IMPORTANT DRUG WARNING

December 4, 2001

Dear Health Care Professional,

Reports of deaths associated with QT prolongation and torsades de pointes in patients treated with doses of INAPSINE (droperidol) above, within, and even below the approved range have prompted Akorn to revise sections of the prescribing information, specifically 1) WARNINGS (including a new Box Warning), which call attention to the potential for serious morbidity and mortality, 2) INDICATIONS, which reinforces the appropriate patient population for whom this product is intended, and 3) DOSAGE AND ADMINISTRATION, which clarifies the available dosing information.

There have been a number of reports of patients who have been treated with droperidol and who developed suspected or established torsades de pointes, at times leading to death. There have been additional cases of symptomatic arrhythmia associated with a pro-longed QT interval after droperidol administration that have been submitted via ongoing safety surveillance activities. In addition, clinical investigators have reported a dose-related increase in QT prolongation with droperidol and replication of cardiac changes in a patient rechallenged with droperidol. Therefore, Akorn, Inc. has made important changes to the INAPSINE label.

The labeling changes will be implemented within the next several weeks. In the meantime, we want you to be aware of this important safety information. Listed below are highlights of important changes to WARNINGS and INDICATIONS. You should consult the full prescribing information accompanying this letter for all of the changes.

The following BOX WARNING has been added:

WARNING

Cases of QT prolongation and/or torsades de pointes have been reported in patients receiving INAPSINE at doses at or below recommended doses. Some cases have occurred in patients with no known risk factors for QT prolongation and some cases have been fatal.

Due to its potential for serious proarrhythmic effects and death, INAPSINE should be reserved for use in the treatment of patients who fail to show an acceptable response to other adequate treatments, either because of insufficient effectiveness or the inability to achieve an effective dose due to intolerable adverse effects from those drugs (see Warnings, Adverse Reactions, Contraindications, and Precautions).

Cases of QT prolongation and serious arrhythmias (e.g., torsades de pointes) have been reported in patients treated with INAPSINE. Based on these reports, all patients should undergo a 12-lead ECG prior to administration of INAPSINE to determine if a prolonged QT interval (i.e., QTc greater than 440 msec for males or 450 msec for females) is present. If there is a prolonged QT interval, INAPSINE should **NOT** be administered. For patients in whom the potential benefit of INAPSINE treatment is felt to outweigh the risks of potentially serious arrhythmias, ECG monitoring should be performed prior to treatment and continued for 2-3 hours after completing treatment to monitor for arrhythmias.

INAPSINE is contraindicated in patients with known or suspected QT prolongation, including patients with congenital long QT syndrome.

INAPSINE should be administered with extreme caution to patients who may be at risk for development of prolonged QT syndrome (e.g., congestive heart failure, bradycardia, use of a diuretic, cardiac hypertrophy, hypokalemia, hypomagnesemia, or administration of other drugs known to increase the QT interval). Other risk factors may include age over 65 years, alcohol abuse, and use of agents such as benzodiazepines, volatile anesthetics, and IV opiates. Droperidol should be initiated at a low dose and adjusted upward, with caution, as needed to achieve the desired effect.

This is also reinforced in WARNINGS, as well as in CONTRADICTIONS.

The INDICATIONS AND USAGE section now reads:

INAPSINE (droperidol) is indicated to reduce the incidence of nausea and vomiting associated with surgical and diagnostic procedures.

The DOSAGE AND ADMINISTRATION section now reads:

Dosage should be individualized. Some of the factors to be considered in determining the dose are age, body weight, physical status, underlying pathological condition, use of other drugs, type of anesthesia to be used and the surgical procedure involved.

Vital signs and ECG should be monitored routinely.

Adult dosage: The maximum recommended initial dose of INAPSINE is 2.5 mg IM or slow IV. Additional 1.25mg doses of INAPSINE may be administered to achieve the desired effect. However, additional doses should be administered with caution, and only if the potential benefit outweighs the potential risk.

Children's dosage: For children two to 12 years of age, the maximum recommended initial dose is 0.1 mg/kg, taking into account the patient's age and other clinical factors. However, additional doses should be administered with caution, and only if the potential benefit outweighs the potential risk.

It is important that you forward any adverse event information associated with the use of droperidol to Akorn at 888-519-8384. You can also report this information directly to the FDA via the MedWatch system at 1-800-FDA-1088, by fax at 1-800-FDA-0178, by mail (using a postage-paid form), or the internet at www.FDA.gov/medwatch.

Sincerely,



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