FDA NOTE TO CORRESPONDENTS

For Immediate Release: Sept. 16, 2009
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FDA Requires Boxed Warning for Promethazine Hydrochloride Injection

The U.S. Food and Drug Administration is telling manufacturers of the drug promethazine to include a boxed warning regarding the injectable form of the drug. The warning, under FDA's authority to require safety labeling changes, will highlight the risk of serious tissue injury when this drug is administered incorrectly. The agency is also alerting health care professionals to the new boxed warning for this product, which is used as a sedative and to treat nausea and vomiting.

Promethazine should neither be administered into an artery nor administered under the skin because of the risk of severe tissue injury, including gangrene, the boxed warning says. There is also a risk that the drug can leach out from the vein during intravenous administration and cause serious damage to the surrounding tissue. As a result of these risks, the preferred route of administration is injecting the drug deep into the muscle.

A requested revision in the Dosage and Administration section of the label states that if health care professionals choose to administer promethazine intravenously, they should limit the drug's concentration and rate of administration and ensure a properly functioning intravenous line.

The companies that make promethazine are required to submit the requested safety label changes to the FDA within 30 days or provide a reason why they do not believe such changes are necessary. If they do not submit new language, or the FDA disagrees with the language proposed by the companies, the agency can order the label change as deemed appropriate to address the new safety information.

Promethazine was previously sold under the brand name Phenergan, but that formulation was discontinued by Wyeth Pharmaceuticals Inc. A number of companies currently market generic formulations of promethazine hydrochloride injection.

The FDA previously informed consumers and health care professionals about the risks of incorrect administration of promethazine in the December 2006 and February 2008 editions of FDA Patient Safety News. Current prescribing information for the drug contains information about the risk of tissue injury, possibly including gangrene, if the drug is inadvertently administered in the artery, but that information was not highlighted in a boxed warning.

Promethazine first went on the market in 1956. FDA has reviewed the published literature and post-marketing adverse event reports submitted to the agency's Adverse

Event Reporting System from 1969 to 2009 and identified cases of gangrene requiring amputation associated with administration of the drug.

More information is available in this Information for Healthcare Professionals: http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHeathcareProfessionals/ucm182169.htm

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