Information for Healthcare Professionals

Propofol
(marketed as Diprivan and as generic products)

FDA ALERT [6/2007]: FDA is issuing this alert to inform healthcare professionals about several clusters of patients who have experienced chills, fever, and body aches shortly after receiving propofol for sedation or general anesthesia. FDA has tested multiple units of propofol vials and lots used in patients who have experienced these symptoms and to date, these tests have not identified any vials contaminated with bacteria or endotoxins.

FDA recommends that healthcare professionals who administer propofol for sedation or general anesthesia carefully follow the recommendations for handling and use found in the current product labeling.

In addition, please report to the MedWatch program patients who have received propofol for sedation or general anesthesia and subsequently experienced fever, chills, and body aches or other symptoms of an acute febrile reaction (see MedWatch reporting information at the bottom of this page). Patients who develop these symptoms shortly after receiving propofol should be evaluated for bacterial sepsis.

The FDA is working closely with the Centers for Disease Control and Prevention (CDCP) to investigate possible reasons for the patients' illnesses following propofol administration. The FDA will provide more information as it becomes available.

This information reflects FDA's current analysis of available data concerning this drug. Posting this information does not mean that FDA has concluded there is a causal relationship between the drug product and the emerging drug safety issue. Nor does it mean that FDA is advising practitioners to discontinue prescribing the product. FDA is considering, but has not reached a conclusion about, whether this information warrants any regulatory action. FDA intends to provide updated information when it becomes available.

To report any serious adverse events associated with the use of this drug, please contact the FDA MedWatch program using the contact information at the bottom of this page.

Recommendations and Considerations

- Propofol is an intravenous sedative-hypnotic agent for use in the induction and maintenance of anesthesia or sedation. Although propofol vials and prefilled syringes contain an ingredient that retards the growth of microorganisms, propofol products can still support the growth of microorganisms. To minimize the potential for bacterial contamination when using propofol for general anesthesia or procedural sedation:
  - both the vial and prefilled syringe formulations must be used on only one patient;
  - administration must commence immediately after the vial or syringe has been opened; and
  - administration from a single vial or syringe must be completed within six hours of opening.

- ICU sedation with propofol administered directly from a vial must be limited to only one patient, must commence immediately on opening the vial, and must be completed within 12 hours of opening the vial to minimize the risk of product contamination. Carefully follow the

handling procedures including the guidelines for aseptic technique that are included in the current prescribing information for propofol.

- Patients who develop fever, chills, body aches or other symptoms of acute febrile reactions shortly after receiving propofol should be evaluated for bacterial sepsis. Consider evaluating and treating patients for bacterial sepsis by obtaining blood cultures followed by beginning appropriate antimicrobial therapy.

- The FDA urges both healthcare providers and patients to report adverse events from the use of propofol to the FDA's MedWatch Adverse Event Reporting program either
  - on-line at [www.fda.gov/medwatch/report.htm];
  - by returning the postage-paid FDA form 3500 [available in PDF format at [www.fda.gov/medwatch/getforms.htm] to 5600 Fishers Lane, Rockville, MD 20852-9787;
  - faxing the form to 1-800-FDA-0178; or
  - by phone at 1-800-332-1088

Background Information and Data

In the past several months the FDA has received reports of several clusters of patients who have developed fever, chills, and body aches shortly after receiving propofol. To date, the reports have come from Pennsylvania (2 facilities), New Jersey (1 facility), New York (2 facilities), and Tennessee (2 facilities). The symptoms began six to 18 hours following the anesthetic and persisted for up to three days. Several patients have been hospitalized and one patient had seizures. All have recovered without apparent sequelae.

To date, all affected patients received propofol for sedation in gastrointestinal suites. Some facilities where the propofol was administered used propofol vials, intended only for single-patient use, for more than one patient.

To date, there is no evidence that these patients had bacterial sepsis or that the propofol vials and prefilled syringes used were contaminated with bacteria or endotoxins.

The illnesses experienced by patients in the current clusters are similar to illness reports FDA received when propofol was first introduced to the United States market and was manufactured without preservatives or antimicrobial additives. At that time, there were numerous reports of patients who developed reactions that were consistent with possible product contamination including fever, infection and sepsis. The frequency of these reports declined substantially after an agent to retard microbial growth was added to propofol vials and pre-filled syringes and warnings

were added to the product label. These warnings advised to use strict aseptic technique, adhere to the single-use requirement, and discard unused product within the specified time limits.

What the FDA is Doing

The FDA is working with the CDCP on an evaluation of these reports. The CDC is conducting an outbreak investigation by visiting sites of these patient clusters and evaluating affected patients for factors that may explain their illnesses.

The FDA has conducted bacterial contamination testing of multiple units of propofol vials and lots that have been associated with the adverse events experienced by patients; however, to date, these tests have not identified any vials contaminated with bacterial or endotoxins. Similarly, testing of other potential sources, e.g., lidocaine coadministered with propofol and instrumentation sterilization systems, has not identified any potentially causative agents at this time.