American Society of Anesthesiologists

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CAPT Valerie Jensen, R.Ph.
Associate Director
CDER Drug Shortage Program, FDA
Building #22/Room 6202
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Captain Jensen:

In the United States, patients undergo general anesthesia for surgery or diagnostic procedures over 50 million times annually. Until a few years ago, a majority of these patients received thiopental intravenously for the induction of general anesthesia. In recent years, other agents, the most popular being propofol, became more widely used for induction. Within the last two years, however, the United States experienced significant shortages of propofol as a result of simultaneous manufacturing problems and one of the three propofol manufacturers exiting the market. This led to a sharp increase in the demand for other induction agents, including thiopental. During this time, however, the U.S. saw its thiopental supplies reduced, and domestic production discontinued. These coinciding events have led to a dangerous reduction in the availability of anesthesia induction medications to the point that the safety of American patients is now in jeopardy.

During this crisis period, anesthesiologists are often forced to resort to induction techniques that are known to either be less safe or involve the potential for undesirable side effects. In some cases, surgery must be canceled for lack of an available safe medication. Thiopental remains a mainstay of anesthesia induction medications. Its availability must be ensured.

While the use of thiopental, until the recent shortage of all anesthesia induction medications, may not have been as frequent as it was before the introduction of medications such as propofol and etomidate into clinical practice, and while in many clinical situations thiopental may be interchangeable with propofol or etomidate, there are many clinical circumstances where its use would be the preferred anesthetic choice. These situations include providing anesthesia for geriatric patients or patients with significant cardiovascular disease in whom administration of propofol may be associated with severe and prolonged hypotension. A specific example is patients undergoing neurologic surgery, many of whom are elderly and/or have significant cardiovascular disease.

In neurosurgical patients of any age, hypotension associated with the use of propofol may compromise perfusion of the brain and lead to cerebral ischemia. Although propofol is used by many clinicians for induction of anesthesia in neurosurgical patients, there are multiple warnings in its package insert regarding its use in this patient population. The most specific of these states:

> *DIPRIVAN Injectable Emulsion is used in patients with increased intracranial pressure or impaired cerebral circulation, significant decreases in mean arterial pressure should be avoided because of the resultant decreases in cerebral perfusion pressure. To avoid significant hypotension and decreases in cerebral perfusion pressure, an infusion or slow bolus of approximately 20 mg every 10 seconds should be utilized instead of rapid, more frequent and/or larger doses of DIPRIVAN Injectable Emulsion....when increased ICP is suspected, hyperventilation and hypocarbia should accompany administration of DIPRIVAN injectable Emulsion.*

In obstetric anesthesia, thiopental is still the drug of choice for induction of general anesthesia administered during cesarean delivery. It can be argued that propofol might be just as good overall, but the package insert for DIPRIVAN (propofol) states:

> ***Labor and Delivery:*** *DIPRIVAN Injectable Emulsion is not recommended for obstetrics, including cesarean section deliveries. DIPRIVAN Injectable Emulsion crosses the placenta, and as with other general anesthetic agents, the administration of DIPRIVAN Injectable Emulsion may be associated with neonatal depression.*
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> ***Nursing Mothers:*** *DIPRIVAN Injectable Emulsion is not recommended for use in nursing mothers because DIPRIVAN Injectable Emulsion has been reported to be excreted in human milk and the effects of oral absorption of small amounts of propofol are not known.*

It has come to the attention of the ASA that thiopental is no longer being produced in the United States. We understand, however, that it is possible to import thiopental from FDA-approved foreign production sites. The ASA urges FDA to exercise its authority and work collaboratively with foreign governments to import thiopental from foreign manufacturing sites to alleviate the critical shortage within the United States, and to ensure that patients have access to this important medication when it is clinically indicated. If intervention or authority beyond the FDA is necessary to secure supplies of thiopental within the U.S., we urge the Agency to request such assistance from the Administration.

Thank you in advance for your assistance in this important matter. Please know that you have the full support of the ASA and its members in this endeavor.

Sincerely,

Mark A Warner

Mark A. Warner, M.D.
President
American Society of Anesthesiologists

cc. Bob A. Rappaport, M.D.