

### General Anesthetic and Sedation Drugs – Safety Update

- On December 14, 2016, the [FDA announced](#) that warnings will be added to the labels of general anesthetic and sedation drugs stating that repeated or lengthy use of these products during surgeries or procedures in children < 3 years or in pregnant women during their third trimester may affect the development of children's brains.
- Anesthetic and sedation drugs are necessary for infants, children, and pregnant women who require surgery or other painful and stressful procedures, especially when they face life-threatening conditions requiring surgery that should not be delayed. In addition, untreated pain can be harmful to children and their developing nervous systems.
  - Examples of general anesthetic and sedation drugs that will be affected by the label update include [Suprane™ \(desflurane\)](#), [Amidate™ \(etomidate\)](#), [Forane™ \(isoflurane\)](#), [lorazepam](#) and [midazolam](#). Refer to the FDA announcement for a complete list.
  - No specific anesthetic or sedation drug has been shown to be safer than any other.
- Healthcare providers should balance the benefits and risks of appropriate anesthesia in young children and pregnant women, especially for procedures that may last longer than 3 hours or if multiple procedures are required in children < 3 years, and discuss this information with parents, caregivers and their patients.
- Parents and caregivers should ask for information about the planned surgery or procedure, including the likely duration of surgery and the need, if any, for repeated procedures.
  - Parents should also discuss with their child's healthcare provider the potential adverse effects of anesthesia on brain development and appropriate timing of procedures that can be delayed without jeopardizing their child's health.
  - Pregnant women should have similar conversations with their healthcare providers.
- Examples of life-threatening conditions in newborns and other children < 3 years that require surgery that should not be delayed include serious congenital heart defects, esophageal atresia, and intestinal blockage. Additional conditions may be found in the FDA announcement.
- Examples of other common procedures for non-life-threatening conditions in children < 3 years that are necessary and should not be delayed are cleft lip or palate repair and surgery to repair undescended testicles in boys.
- Examples of surgeries for life-threatening conditions in pregnant women that should not be delayed include, but are not limited to removal of the appendix, removal of the gallbladder, and repair of traumatic injury.
- The safety update is based on the FDA's review of many published animal and human research studies.
- Data from animal studies:
  - In animal studies, use of anesthetic and sedation drugs that block N-methyl-D-aspartate (NMDA) receptors and/or potentiate gamma-aminobutyric acid (GABA) activity for longer than 3 hours has

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been demonstrated to increase neuronal apoptosis in the brain resulting in long-term cognitive deficits.

- Based on comparisons across animal species, the window of vulnerability to these changes in the brain is believed to correlate with exposures in the third trimester of pregnancy through the first year of life, but may extend out to approximately 3 years in humans. The clinical significance of these nonclinical findings is not clear.
- Data from human clinical studies:
  - Recent human data suggest that a single, relatively short exposure to general anesthetic and sedation drugs in infants or toddlers is unlikely to have negative effects on behavior or learning. However, further research is needed to fully characterize how early life anesthetic exposure might affect children’s brain development, particularly for more lengthy or repeated exposures and in more vulnerable children.
  - Some published studies suggest that similar deficits in cognition and behavior may occur in children, particularly after repeated or prolonged exposures to anesthetic drugs early in life. These studies have limitations, and it is not clear if the effects reported are due to the anesthetic/sedation drugs, or to other factors such as the surgery or underlying illness.
- The FDA will continue to monitor the use of these drugs in children and pregnant women and will update the public if additional information becomes available.



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