

Dexmedetomidine for Pediatric Patients

By the Health Technology Assessment Group – Health Policy Development and Planning Bureau

KEY MESSAGE

- Dexmedetomidine (Precedex®) is not recommended for use in children due to treatment-emergent adverse events in this population, such as hypotension, hypokalemia, pyrexia, anger, and agitation.
- The labeling update of dexmedetomidine (Precedex®) in June 2013 stated that the safety and efficacy of the drug have not been established for procedural or ICU sedation in pediatric patients. This update was based on studies reporting that primary efficacy endpoints were not met, and safety data was insufficient to fully characterize the safety profile of dexmedetomidine (Precedex®) in this patient population.

CONTEXT

- Dexmedetomidine was disapproved for inclusion in the Philippine National Formulary last December 2017. This decision was based on evidence suggesting that dexmedetomidine does not provide a better level of sedation over propofol or other benzodiazepines for adult patients in an intensive care unit (ICU) setting.
- During the Formulary Executive Council (FEC) meeting held last August 1, 2017, the Philippine Heart Center (PHC) reported that dexmedetomidine is beneficial for pediatric cardiac surgery patients on the basis of clinical studies showing reduction of the risk for post-cardiac surgical tachyarrhythmia and junctional ectopic tachycardia. Given this potential benefit of dexmedetomidine for pediatric cardiac patients, the FEC recognized that the prior disapproval of dexmedetomidine in the Philippine National Formulary left a subset of patients seen in specialty hospitals at a disadvantage.
- The National Kidney and Transplant Institute (NKTI), José R. Reyes Memorial Medical Center (JRRMC), and Philippine Heart Center (PHC) requested for exemption to use dexmedetomidine. However, the published literature that submitted in support of the request for exemption only examined adult patients.

FDA-APPROVED INDICATION OF DEXMEDETOMIDINE

- Precedex® is the only brand of dexmedetomidine that is currently registered and marketed in the Philippines. It is manufactured by Hospira Incorporated, a subsidiary of Pfizer.
- Dexmedetomidine (Precedex®) is an alpha-2 adrenergic agonist indicated for the 1) sedation of intubated and mechanically ventilated patients during treatment in an intensive care setting and 2) sedation and anxiolysis of non-intubated **adult patients** prior to and/or during surgery and other procedures¹.

USE OF DEXMEDETOMIDINE IN PEDIATRIC PATIENTS

- The previous label of Precedex® stated that there have been no clinical studies to establish the safety and efficacy of Precedex® in pediatric patients below 18 years of age. Moreover, it was also stated that the pharmacokinetic profile has not been studied in this patient population³.
- Labeling updates for Precedex® were made in 2013 based on the findings of 3 pediatric studies — one assessor-blinded trial in pediatric patients and two open-label studies in neonates that assessed



efficacy of Precedex® for ICU sedation. The label update is as follows²:

“Safety and efficacy have not been established for procedural or ICU sedation in pediatric patients. One assessor-blinded trial in pediatric patients and two open label studies in neonates were conducted to assess efficacy for ICU sedation. These studies did not meet their primary efficacy endpoints and the safety data submitted were insufficient to fully characterize the safety profile of Precedex for this patient population.”

- As denoted on the latest product information from Pfizer, which was revised in March 2018, dexmedetomidine (Precedex®) is not recommended for use in children¹.
 - The manufacturer conducted 3 preliminary studies: 2 studies in 42 neonates between 28 to 44 weeks of gestational age and a study in 175 children between 1 month to less than 17 years of age, all in an intensive care setting for up to 24 hours.
 - They found that the most frequent treatment-emergent adverse events in neonates between 28 to 44 weeks of gestational age were anger (6/42, 14.3%) and hypokalemia (3/42, 7.1%).
 - For children between 1 month to less than 17 years of age, the most frequent treatment-emergent adverse events were hypokalemia (14/175, 8.0%), pyrexia (12/175, 6.9%), hypotension (11/175, 6.3%), and agitation (9/175, 5.1%).
 - Among the events reported in pediatric patients, the events of anger in neonates and hypokalemia in older children occur with greater frequency in pediatrics than in adults.
- In addition, the use of Precedex® for procedural sedation and conscious sedation in pediatric patients has not been evaluated^{1,2}.

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Information briefs are based on a limited literature search and are not systematic reviews. The intent is to provide a list of sources of the best evidence on the topic that the Health Technology Assessment (HTA) Study Group could identify using all reasonable efforts within the time allowed.

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Research Center for Health System Development (RCHSD)

rlc.rchsd.doh@gmail.com

651-7800 loc 1326

Research Division - Health Policy Development and Planning Bureau
Department of Health Building 3 2/F San Lazaro Compound, Rizal Avenue,
Sta. Cruz, Manila

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