Caffeine citrate

Essential medicine status ✓

Section: 22. Medicines for reproductive health and perinatal care > 22.6. Medicines administered to the neonate [c]

EMLc | ATC codes: N06BC01

Indication	Apnoea of newborn ICD11 code: KB2A.Z
Medicine type	Chemical agent
List type	Core (EML) (EMLc)
Formulations	Parenteral > General injections > IV: 20 mg per mL (equivalent to 10 mg caffeine base per mL) (EMLc) Oral > Liquid: 20 mg per mL (equivalent to 10 mg caffeine base per mL) (EMLc)
EML status history	First added in 2007 (TRS 946)
Sex	All
Age	Newborn (< 1 month)
Therapeutic alternatives	The recommendation is for this specific medicine
Patent information	Patents have expired in most jurisdictions Read more about patents.
Wikipedia	Caffeine citrate
DrugBank	Caffeine citrate (Caffeine)

Summary of evidence and Expert Committee recommendations

During its meeting in 2005, the Committee deferred a decision on listing caffeine citrate for apnoea of prematurity on the Model List because of limited evidence of efficacy and the lack of longer-term safety data. The Committee was waiting for the results of a large randomized controlled trial then underway. A second application for the inclusion of caffeine citrate was received from the Royal Children's Hospital, Melbourne, Australia. The Committee noted that the efficacy data were largely unchanged from those in the previous application and that the long-term safety results of the large randomized controlled trial were still not available. As noted by the expert reviewers, data from two Cochrane reviews 1, 2) are available. Although they are based on small numbers of trials and patients, they support the efficacy of methylxanthines in managing apnoea in preterm infants and suggest that while it had similar efficacy, caffeine citrate was associated with fewer adverse events than theophylline. Limited safety data are provided in these reviews. Schmidt et al. 2006 (3) reported short-term, secondary safety outcomes in the large Caffeine for Apnoea of Prematurity trial. No differences were noted between caffeine citrate and placebo in the incidence of retinopathy of prematurity, necrotizing enterocolitis or ultrasonographic signs of brain injury. However data on the primary study outcome (a composite of death, cerebral palsy, cognitive delay, deafness, or blindness at a corrected age of 18–21 months) are not yet available. The inclusion criteria of the study may have excluded the most vulnerable infants from evaluation i.e. the smallest infants on ventilation for long periods of time. The efficacy of caffeine in this population remains uncertain. The WHO Pocket book of hospital care for children (2005, p. 55) states that caffeine citrate and aminophylline prevent and treat apnoea in premature babies. Caffeine is preferred if it is available. Dosing recommendations are consistent with this application. No valid cost-effectiveness data were provided and limited cost comparisons are possible for caffeine citrate, aminophylline and theophylline. Neither aminophylline nor theophylline is currently on the Model list. Based on the evidence for efficacy and safety, the Committee decided to include caffeine citrate on the Model List. References 1. Steer PA, Henderson-Smart DJ. Caffeine versus theophylline for apnea in preterm infants. Cochrane Database of Systematic Reviews, 1998, Issue 2. Art. No.: CD000273. DOI: 10.1002/14651858.CD000273 (most recent amendment February 1998). 2. Henderson-Smart DJ, Steer P. Methylxanthine treatment for apnea in preterm infants. Cochrane Database of Systematic Reviews, 2001, Issue 3. Art. No.: CD000140. DOI: 10.1002/14651858.CD000140 (most recent

amendment April 2001). 3. Schmidt B et al. Caffeine therapy for apnea of prematurity. New England Journal of Medicine, 2006, 354:2112.