

## Caffeine Citrate



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Caffeine citrate (intravenous and oral) is recommended for the short-term treatment of apnea of prematurity (AOP) in preterm infants between 28 and 33 weeks gestational age. However, it is commonly used off-label in infants younger than 28 weeks gestational age, at higher doses and for a much longer duration than the label indicates. As a result of the following pediatric research, the U.S. Food and Drug Administration (FDA) updated the caffeine citrate label in 2020.

### Studies

**Safety and Efficacy of Caffeine Citrate in Premature Infants (NICHD-2014-CAF01)** evaluated the safety and efficacy of caffeine citrate for treating AOP in preterm infants. The retrospective data analysis study included 87,851 infants, which included more than 30,000 infants younger than 28 weeks gestational age.

### Findings

- Durations and doses of caffeine citrate commonly administered greatly exceeded recommendations at the time of the study:
  - Median durations were up to 60 days versus the 10 to 12 days recommended at the time of the study
  - Median daily dosages were 7 to 8 mg/kg/day versus the 5 mg/kg/day maintenance doses recommended at the time of the study ([PMID: 31101409](https://pubmed.ncbi.nlm.nih.gov/31101409/))
- **Key Outcome:** Caffeine citrate is a safe treatment option for AOP at higher doses and for longer durations than previous dosing recommendations in infants younger than 28 weeks gestation. As a result of this research, the U.S. Food and Drug Administration (FDA) updated the label in 2020.

### Resources

- NICHD's [Data and Specimen Hub](https://dash.nichd.nih.gov/study/19261) provides an overview of the study population and, for registered users, free access to datasets, study reports and documentation.
  - <https://dash.nichd.nih.gov/study/19261>
- FDA Label: <https://bit.ly/2WXhy4Y> (FDA is reviewing BPCA study data for updates.)

**About BPCA:** The NICHD-led BPCA program at NIH helps advance pediatric drug research & development and improves information about and labeling for drugs used in children. The program identifies research gaps in pediatric therapeutics, prioritizes drugs in need of further study, supports research training, and sponsors clinical studies of prioritized drugs through the Pediatric Trials Network. Learn more at <https://www.nichd.nih.gov/BPCA>.



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