



Dear Healthcare Provider,

We are excited to inform you about the recent FDA approval regarding the label expansion of **Caldolor®**, an intravenously delivered formulation of ibuprofen. Effective May 15, 2023, Caldolor® is now approved for the treatment of fever and pain in infants between the ages of three to six months. This significant milestone makes Caldolor® the only injectable non-opioid solution for treating pain in this age group.

Three studies have been conducted in the pediatric population, with the most recent supporting the approval in infants ages 3-6 months.<sup>1,2,3</sup> The primary objective of the most recent publication by Glover et al, was to evaluate the pharmacokinetics of Caldolor® in infants younger than 6 months of age.<sup>3</sup> The secondary objective was to evaluate the safety of single and repeated doses of Caldolor® in infants younger than 6 months of age. Hospitalized neonates and infants younger than 6 months of age with fever or expected postoperative pain were enrolled and received 10 mg/kg of Caldolor® every 6 h, with up to four doses per day. A total of 24 children were enrolled in the study, with 15 male patients and 9 female patients. The median age of the cohort was 4.4 months (range 1.1–5.9 months), and the median weight was 5.9 kg (range 2.3–8.8 kg). Time to peak ibuprofen effect and concentration were similar when compared with older pediatric patients. Clearance and volume of distribution were also similar to those reported in older pediatric patients. No drug-related adverse events were reported. Overall, the pharmacokinetic and short-term safety profiles of Caldolor® in pediatric patients 1–6 months of age are comparable to those in children older than 6 months of age.

Thank you for your continuous commitment to patient care. Should you have any questions or require further information, please do not hesitate to reach out to Cumberland Pharmaceuticals Medial Affairs at 615-425-7642 or [Caldolor@cumberlandpharma.com](mailto:Caldolor@cumberlandpharma.com)

Warm regards,

A handwritten signature in black ink that reads "Theresa".

Theresa Human PharmD, PhD, BCPS, FNCS  
MSL, Cumberland Pharmaceuticals

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**INDICATION:**

CALDOLOR is indicated in adults and pediatric patients three months and older for the:

- management of mild to moderate pain and the management of moderate to severe pain as an adjunct to opioid analgesics
- reduction of fever

**DOSAGE AND ADMINISTRATION INSTRUCTIONS**

CALDOLOR must be diluted prior to administration.

Do not exceed 3200 mg total daily dose in adults. Do not exceed 40 mg/kg or 2,400 mg, whichever is less, total daily dose in pediatric patients 6 months to 17 years of age.

**Pediatric Patients**

For Analgesia (pain) and Fever:

*Ages 12 to 17 years*

The dose is 400 mg intravenously every 4 to 6 hours as necessary. Infusion time must be at least 10 minutes. Maximum daily dose is 40 mg/kg or 2,400 mg, whichever is less.<sup>4</sup>

*Ages 6 months to less than 12 years*

The dose is 10 mg/kg intravenously up to a maximum single dose of 400 mg every 4 to 6 hours as necessary. Infusion time must be at least 10 minutes. Maximum daily dose is 40 mg/kg or 2,400 mg, whichever is less.<sup>4</sup>

*Ages 3 months to 6 months*

The dosage is limited to a single dose not to exceed 10 mg/kg or 100 mg, whichever is less.<sup>4</sup>

**IMPORTANT SAFETY INFORMATION****Contraindications**

CALDOLOR is contraindicated in patients with known hypersensitivity (e.g., anaphylactic reactions and serious skin reactions) to ibuprofen or any components of the drug product, and in patients who have a history of asthma, urticaria, or other allergic-type reactions after taking aspirin or other NSAIDs. Severe, sometimes fatal, anaphylactic reactions to NSAIDs have been reported in such patients. CALDOLOR is contraindicated in the setting of coronary artery bypass graft (CABG) surgery.

**Warning and Precautions**

CALDOLOR should be used with caution in patients with known cardiovascular (CV) disease or risk factors for CV disease, a history of peptic ulcer disease and/or GI bleeding, renal or liver disease or symptoms of, hypertension, and heart failure. When used in such patients, attention to using the lowest effective dose for the shortest time period is important to reduce the risk of serious adverse events. Avoid use in pregnant women starting at 30 weeks gestation.

**Adverse Reactions**

The most common adverse reactions are nausea, flatulence, vomiting, headache, hemorrhage and dizziness (>5%). The most common adverse reactions in pediatric patients are infusion site pain, vomiting, nausea, anemia and headache (≥2%).

## **WARNING: RISK OF SERIOUS CARDIOVASCULAR AND GASTROINTESTINAL EVENTS**

### Cardiovascular Thrombotic Events

- Non-steroidal anti-inflammatory drugs (NSAIDs) cause an increased risk of serious cardiovascular thrombotic events, including myocardial infarction and stroke, which can be fatal. This risk may occur early in treatment and may increase with duration of use.
- CALDOLOR is contraindicated in the setting of coronary artery bypass graft (CABG) surgery.

### Gastrointestinal Bleeding, Ulceration and Perforation

- NSAIDs cause an increased risk of serious gastrointestinal (GI) adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients and patients with a prior history of peptic ulcer disease and/or GI bleeding are at greater risk for serious GI events.

1. Moss JR, Watcham MF, Bendel LP, et al. A multicenter, randomized, double-blind, placebo-controlled single dose trial of the safety and efficacy of intravenous ibuprofen for the treatment of pain in pediatric patients undergoing tonsillectomy. *Paediatr Anaesth.* 2014; 24: 483-489.
2. Poster Presentation: Chumpitazi et al., American Academy of Pediatrics National Conference & Exhibition, San Diego, October 10 & 12, 2014.
3. Glover C, Berkenbosch JW, Taylor MB, et al. A Multi Center Evaluation of the Pharmacokinetics and Safety of Intravenous Ibuprofen in Infants 1–6 Months of Age. *Pediatric Drugs*, accepted May 14, 2023. doi.org/10.1007/s40272-023-00576-9
4. Caldolor® (Ibuprofen) Injection [package insert]. Nashville, TN: Cumberland Pharmaceuticals Inc; May 2023