A GROWING BODY OF EVIDENCE DEMONSTRATES THAT CALDOLOR® CAN SIGNIFICANTLY DECREASE BOTH SURGICAL PAIN AND OPIOID USE

- *Supported by 10 Phase II-IV clinical studies*[6]

Published data for CALDOLOR supports administering CALDOLOR prior to surgery and throughout the postoperative period, resulting in patients experiencing significantly less pain shortly after waking, remaining in significantly less pain, and also reducing opioid consumption.[1,2] CALDOLOR can be a key component to cost-effective Enhanced Recovery After Surgery (ERAS) multimodal treatment protocols.

Study Summaries Support the Following:

- CALDOLOR patients* reported up to a 58% reduction in opioid use compared to the placebo group that had open access to morphine and scheduled oral acetaminophen[3]
- Up to a 43% reduction in VAS scores at rest compared to opioids alone[2]
- Patients report significantly less pain shortly after waking[1]
- Patients remain in significantly less pain during recovery when CALDOLOR is administered immediately prior to surgery and q6h[1]
- May improve quality of recovery and reduce postsurgical fatigue[4]
- Pediatric indication in patients 6 months and older[5]
- In clinical studies adverse events were similar to placebo[6]

Caldolor is indicated in adults and pediatric patients for the management of mild to moderate pain and management of moderate to severe pain as an adjunct to opioid analgesics, as well as the reduction of fever. It was the first FDA-approved intravenous therapy for fever. Caldolor is contraindicated in patients with known hypersensitivity to ibuprofen or other NSAIDs, patients with a history of asthma or other allergic-type reactions after taking aspirin or other NSAIDs. Caldolor is contraindicated for use during the peri-operative period in the setting of coronary artery bypass graft (CABG) surgery. For full prescribing and safety information, including boxed warning, visit www.caldolor.com.

References:

1.) Singla N, Rock A, and Pavliv L. A multi-center, randomized, double-blind placebo-controlled trial of intravenous-ibuprofen (IV-ibuprofen) for treatment of pain in post-operative orthopaedic adult patients. *Pain Med* 2010; 11(8): 1284-1293.
2.) Moss. JR, Watcha MF, Bendel LP, et al. A multicentre, randomized, double-blind placebo-controlled, single dose trial of the safety and efficacy of intravenous ibuprofen for treatment of pain in pediatric patients undergoing tonsillectomy. *Pediatric Anesthesia* 2014; 24(5): 483-498.
3.) Shephard DM, Jahnke H, White WL, et al. Randomized, double-blinded, placebo-controlled trial comparing two multimodal opioid-minimizing pain management regimens following transsphenoidal surgery. *J Neurosurg* 2018; 128(2): 444-451.
4.) Le V, Kurnutala L, Schianodicola J, et al. Premedication with intravenous ibuprofen improves recovery characteristics and stress response in adults undergoing laparoscopic cholecystectomy: a randomized controlled trial. *Pain Med* 2016; 17(6): 1163-1173.
5.) CALDOLOR [Package Insert] Nashville, TN: Cumberland Pharmaceuticals Inc. 2019.
6.) Southworth SR, Woodward EJ, Peng A, et al. An integrated safety analysis of intravenous ibuprofen (Caldolor) in adults. *J Pain Res* 2015: 8; 753-765.

* (Caldolor treatment group patients also had open access to morphine and scheduled oral acetaminophen)

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.

About CALDOLOR® (ibuprofen) Injection

CALDOLOR is indicated in adult and pediatric patients 6 months an older for:

- Management of mild/moderate pain (single agent)
- Management of moderate/severe pain as an adjunct to opioid analgesics
- Reduction of fever

IMPORTANT DOSAGE AND ADMINISTRATION INSTRUCTIONS

CALDOLOR injection 800 mg /8mL (100mg/mL) **vials must be diluted** prior to administration.
Do not exceed 3,200 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 less that 17 years of age.

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.

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%).

For full prescribing information, including boxed warning, visit www.caldolor.com.