



Pre and Post-Operative Use of Caldolor(R) (Ibuprofen) Injection Significantly Reduces Pain and Opioid Use in Newly Published Study

- Study demonstrates IV ibuprofen can be safely administered at induction of anesthesia as well as throughout the post-operative period - IV ibuprofen decreases morphine use by more than 30% while improving pain control

NASHVILLE, Tenn., Aug 30, 2010 /PRNewswire via COMTEX News Network/ -- **Cumberland Pharmaceuticals Inc.** (Nasdaq: CPIX) today announced the publication of new data supporting the safety and efficacy of Caldolor(R) (*ibuprofen*) Injection in pre and post-operative orthopedic surgery patients. The study, which was published in the August edition of the peer-reviewed journal *Pain Medicine*, concludes that IV ibuprofen significantly decreased pain and morphine use when compared with placebo.

In the United States, more than 60% of patients with moderate or severe pain following surgery receive morphine.(1) Both the World Health Organization and the American Society of Anesthesiologists Task Force recommend a multi-modal approach to pain management, with nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen as baseline therapy, which can minimize the risk of opioid-related side effects including sedation, nausea, vomiting, cognitive impairment and respiratory depression.(2,3)

"These findings are significant in that they not only confirm that Caldolor is effective in reducing both post-operative pain and morphine use, but also demonstrate that it can be safely administered prior to the induction of anesthesia," said Neil Singla, M.D., Chief Executive Officer of Lotus Clinical Research, Inc. and principal investigator of the study. "This gives physicians additional options for controlling the onset of post-operative pain, which can help improve patient comfort and thereby facilitate recovery."

This multi-center, randomized, double-blind placebo-controlled trial evaluated 185 adult patients undergoing orthopedic surgery at eight hospitals. Patients were randomized to receive either 800 mg IV ibuprofen or placebo every six hours, and pain was measured through patient self-assessment using a visual analog scale (VAS) and a verbal response scale (VRS) in the immediate post-operative period through hour 28 of the study. All patients had access to intravenous morphine. The study met its primary endpoint as patients who received IV ibuprofen reported a 26% reduction in pain with movement ($p < 0.001$). The study also met its secondary endpoints as pain assessed during rest was reduced by 32% in patients receiving IV ibuprofen ($p < 0.001$), and these patients used nearly 31% less morphine than those who received placebo ($p < 0.001$). There was no significant difference between placebo and IV ibuprofen in the number of patients with bleeding adverse events, the incidence of blood transfusions or other serious adverse events. More patients receiving IV ibuprofen experienced vomiting and more patients receiving placebo experienced dyspepsia.

The study demonstrated that both pre-operative and post-operative administration of Caldolor diminished post-surgical pain. In previous clinical studies of IV ibuprofen, the initial dose was administered intra-operatively. However, patients in this study received the first dose of study drug at the induction of anesthesia through a peripheral or central venous catheter. Pain assessments were performed at regular intervals following surgery, with the average first assessment occurring 2.8 hours post-operatively. The difference in pain scores between patients receiving Caldolor plus morphine compared to morphine alone was significant at this first measurement and remained significant at every point of measurement throughout the study period.

"This clinical study is so important because it provides strong safety and efficacy data supporting use of Caldolor in surgical patients not only during recovery, but also when administered prior to surgery," said A.J. Kazimi, Chief Executive Officer at Cumberland Pharmaceuticals. "Caldolor is the only IV-NSAID available in the United States that does not carry a contraindication for pre-operative use, and we believe this data will provide physicians with a new level of comfort in using IV ibuprofen to more effectively manage post-operative pain for their patients."

The new data supports a previous randomized, placebo controlled trial in surgical patients, which demonstrated that 800 mg of IV ibuprofen dosed every six hours produced a significant reduction in pain and morphine use in surgical patients. The study, entitled "A Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial of Intravenous Ibuprofen 400 and 800 mg Every 6 Hours in the Management of Post-operative Pain," was published in Volume 31, Number 9 of the peer-reviewed journal *Clinical Therapeutics* in October 2009.

Introduced in 2009, Caldolor is the first new injectable product available in the United States in 20 years for IV pain treatment, and provides safe and effective relief from both pain and fever. The newly published study, entitled "A Multicenter, Randomized, Double-Blind Placebo-Controlled Trial of Intravenous-Ibuprofen (IV-Ibuprofen) for Treatment of Pain in Post-

Operative Orthopedic Adult Patients" appears in Volume 11 of *Pain Medicine*. The publication can be found online at <http://onlinelibrary.wiley.com/doi/10.1111/j.1526-4637.2010.00896.x/pdf>.

About Caldolor

Caldolor is indicated for the management of mild to moderate pain and management of moderate to severe pain as an adjunct to opioid analgesics, and for the reduction of fever in adults. It is the first FDA approved intravenous therapy for fever. Caldolor is contraindicated in patients with known hypersensitivity to ibuprofen or other NSAIDs, patients with asthma, urticaria, or 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. Caldolor should be used with caution in patients with prior history of ulcer disease or GI bleeding, in patients with fluid retention or heart failure, in the elderly, those with renal impairment, heart failure, liver impairment, and those taking diuretics or ACE inhibitors. Blood pressure should be monitored during treatment with Caldolor. For full prescribing information, including boxed warning, visit www.caldolor.com.

About Cumberland Pharmaceuticals

Cumberland Pharmaceuticals Inc. is a Tennessee-based specialty pharmaceutical company focused on the acquisition, development and commercialization of branded prescription products. The Company's primary target markets include hospital acute care and gastroenterology. Cumberland markets Acetadote(R) for the treatment of acetaminophen poisoning, Caldolor (R), the first injectable treatment for pain and fever available in the United States, and Kristalose(R), a prescription laxative. Cumberland is dedicated to providing innovative products which improve quality of care for patients. For more information on Cumberland Pharmaceuticals, visit www.cumberlandpharma.com.

About Pain Medicine

Pain Medicine is a multi-disciplinary journal dedicated to the pain clinician, teacher and researcher. It is the Official Journal of the American Academy of Pain Medicine and of the Faculty of Pain Medicine of the Australian and New Zealand College of Anaesthetists. The journal is devoted to the advancement of pain management, education and research.

Important Note Regarding Forward-Looking Statements

This press release contains forward-looking statements that reflect Cumberland's current views with respect to future events, based on what it believes are reasonable assumptions. No assurance can be given that these events will occur. As with any business, all phases of operations are subject to influences outside of the Company's control. Risk factors that could materially affect results of operations include, among others, those factors discussed in Cumberland's Annual Report filed on Form 10-K as filed with the SEC on March 19, 2010. There can be no assurance that results or developments anticipated by Cumberland will be realized or, even if realized, that they will have the expected effects. Readers are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. Cumberland undertakes no obligation to release publicly any revisions to these statements to reflect events or circumstances after the date hereof or to reflect the occurrence of unanticipated events.

(1) Carr DB, Miaskowski C, Dedrick SC, Williams GR, Management of perioperative pain in hospitalized patients: A national survey. *J Clin Anesth* 1998; 10:77-85.

(2) World Health Organization. Pain relief and palliative care. In: *Clinical Management of HIV and AIDS at District Level*. New Delhi, India. WHO Regional Office for South-East Asia Web site. http://www.searo.who.int/linkfiles/publications_ch11.pdf. Updated April 26, 2006. Accessed July 15, 2009.

(3) The American Society of Anesthesiologists Task Force. Practice guidelines for acute pain management in the perioperative setting. *Anesthesiology*. 2004; 100(6): 1573-1581.

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