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INTRODUCTION

Nonsteroidal anti-inflammatory drugs and their risk: a story still in development

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NSAIDs are anti-inflammatory, analgesic, and antipyretic agents, and they are typically used chronically to reduce pain, decrease stiffness, and improve function in patients with osteoarthritis, rheumatoid arthritis, and other forms of arthritis. Additionally, NSAIDs are also used for the more acute treatment of pain including headache, dysmenorrhea, and postoperative pain [1-4]. However, NSAID use conveys potential significant adverse events that include gastrointestinal ulcers with consequential bleeding, perforation or obstruction, renal dysfunction and consequent renal failure, cardiovascular events, as well as the risk for death [5-11]. Despite the many available forms of NSAIDs, including injectable as well as topical, oral dosing is the most common route, usually the one route consistently associated with chronic use and thus the one that carries the most risk. In the last several years, several topical NSAIDs including either diclofenac ibuprofen or salicylates for chronic pain have been approved in the United States while similar drugs have been available in Europe for years. One study of a diclofenac topical liquid included an oral diclofenac comparator, and demonstrated no difference in efficacy between the two therapies in treatment for the pain of osteoarthritis in the knee [12].

The risk for potential gastrointestinal damage due to systemic exposure of NSAIDs is well defined, including gastrointestinal symptoms such as dyspepsia and abdominal pain, increased incidence of endoscopic ulcers, bleeding, and death. A history of prior gastrointestinal symptoms or bleeding, the presence of other risk factors such as advancing age, higher doses of NSAID, duration of NSAID use, as well as the frailty of the patient all increase the risk for upper gastrointestinal damage and consequent bleeding [13]. Use of NSAIDs with a longer half-life probably places patients at greater risk of adverse events.

Strategies to decrease the risk for damage to the gastrointestinal tract have included the transition to other types of drugs, use of lower dose systemic NSAIDs, and the use of topical NSAIDs, but there are still patients who require more chronic exposure to higher dose therapy. In addition, other strategies include the addition of prostaglandin analogues, H_2 receptor antagonists, or proton pump inhibitors as concomitant therapies [14-18]. More recently, combination products have been developed [19,20]. This supplement will review the continued importance of NSAIDs as part of a strategy to continue to treat pain adequately as well as the attempts to mitigate the risks associated with the use of these drugs.

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Abbreviations
NSAID, nonsteroidal anti-inflammatory drug.

Competing interests
LSS serves as a clinical and regulatory consultant in drug development and has served as such consultant for companies which manufacture and market NSAIDs including Pfizer, Pozen, Horizon Pharma, Logical Therapeutics, Nuvo Research, Iroko, Imprimis, JRX Pharma, Nuvon, Medarx, and Asahi.

Declaration
This article has been published as part of *Arthritis Research & Therapy* Volume 15 Suppl 3, 2013: 'Gastroprotective NSAIDS'. The full contents of the supplement are available online at http://arthritis-research.com/supplements/15/S3. The supplement was proposed by the journal and developed by the journal in collaboration with the Guest Editor. The Guest Editor assisted the journal in preparing the outline of the project but did not have oversight of the peer review process. The Guest Editor serves as a clinical and regulatory consultant in drug development and has served as such consultant for companies which manufacture and market NSAIDs including Pfizer, Pozen, Horizon Pharma, Logical Therapeutics, Nuvo Research, Iroko, Imprimis, JRX Pharma, Nuvon, Medarx, Asahi. The articles have been through the journal's standard peer review process. Publication of this supplement has been supported by Horizon Pharma Inc. Duexis (ibuprofen and famotidine) is a product marketed by the sponsor.

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