Indian Health Service
National Pharmacy and Therapeutics Committee
(Non-steroidal Anti-Inflammatory Drugs)
NPTC Formulary Brief
May 2014

Background: The IHS National Pharmacy and Therapeutics Committee (NPTC) reviewed non-steroidal anti-inflammatory drugs (NSAIDs) as part of a larger review of medications used in chronic pain management. The review utilized data from several large drug class reviews as well as from reviews from the Cochrane database and national guidelines regarding NSAID use specifically in patients with heart disease and/or with gastrointestinal risk factors. The review focused largely on issues of efficacy and safety. The review and discussion led to the removal of sulindac from the National Core Formulary (NCF) due to concerns regarding safety. It also led to the addition of diclofenac (any formulation) for its availability of a topical formulation and the addition of meloxicam for its procurement value and once daily dosing regimen. The nonselective NSAIDs, ibuprofen, naproxen and indomethacin, also remain on the NCF.

Discussion: NSAIDs are some of the most widely used drugs worldwide. They play a key role in the management of both acute and chronic pain. They work primarily from the inhibition of cyclooxygenases (COX1 and COX2). As clinicians, we sometimes group all NSAIDs together. They actually fall into a number of distinct chemical classes (for example, propionic acid derivatives such as ibuprofen and naproxen, and acetic acid derivatives such as indomethacin and diclofenac). NSAIDs do have safety concerns and the commonality of their use can translate into potential drug-induced morbidity and mortality. Approximately 5-7 % of hospital admissions are related to adverse effects of drugs and ~11-12% of these are attributable to NSAID use.

*Efficacy***:** Despite the many claims of their manufacturers there is little data to suggest that any of the NSAIDs are more efficacious than another. However, there is evidence to suggest that there can be significant differences in response from one NSAID to another in a particular individual. Therefore, it is reasonable if an individual does not respond to a particular NSAID that another NSAID be utilized.

*Safety***:** The NSAIDs are associated with a number of common risks such as: gastrointestinal bleeding, increased cardiovascular risk, kidney damage, a worsening of hypertension and heart failure, as well as some less common risks: liver damage, neurologic side effects, pulmonary effects, skin manifestations and hematologic effects. While for many of these risks there appears to be no data suggesting any of the NSAIDs are more or less dangerous, there do appear to be some differences with regards to cardiovascular risk and risk of gastrointestinal events (GI bleeds).

Cardiovascular risk**:** While the use of almost all NSAIDs increase the risk of cardiovascular events, naproxen taken at prescription doses and low dose ibuprofen (<1200mg/day) appear to be risk neutral with regards to increasing cardiovascular events. It should be noted, however, that use of these agents in patients with cardiovascular disease may negate the anti-platelet benefits of aspirin taken for cardiovascular protection.

Gastrointestinal risk**:** The gastrointestinal risks that are associated with NSAID use increases significantly with age, especially in the >65 year age group. There is some short term data that suggests the use of COX2 selective, Celebrex® (celecoxib), and the partially COX2 selective agent, nabumetone, may be associated with lower adverse gastrointestinal events. This is particularly true if these agents are used in combination with a proton pump inhibitor or with misoprostol. The 2009 American College of Gastroenterology Guidelines provides a good reference for approaching prescribing NSAIDs in patients with Cardiovascular and/or Gastrointestinal risk factors.

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov. For more information about the NPTC, please visit the NPTC website.

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