Over the last 10+ years, the evidence supporting the dose-related risks of certain serious adverse events associated with nonsteroidal anti-inflammatory drugs (NSAIDs) has piled up—the higher the dose, the higher the risk. Using NSAIDs in today's complex therapeutic landscape requires more attention and thought than ever before.

The Climate of Pain Management Is Shifting
Recent concerns about opioid use have led to a decline in opioid prescriptions for the first time since 1996, and may be the reason why NSAID prescriptions are on the rise.

White House asks for more than $1 billion in new funding for opioid addiction treatment.

11% Decrease in opioid prescriptions nationally since 2011
10% Increase in NSAID prescriptions from 2011 to 2015

NSAIDs may now be more on the radar than ever, especially since recent CDC guidelines specifically recommend the use of nonopioid therapies as preferred treatment options for chronic pain.

―Vijay Sikand, MD
Fellow, American Academy of Family Physicians
Adjunct Assistant Professor of Medicine, Tufts University School of Medicine
Risks: The Root of the Dilemma

Pain is very real and can often be managed effectively with NSAIDs—but we must first consider the dose-related risks.

**HIGHER DOSE / HIGHER RISK**

- **28%** Percentage by which CV risk is increased with high NSAID doses compared to low-medium doses.
- **104%** Percentage by which upper GI risk is increased with high NSAID doses compared to low-medium doses.
- **35%** Percentage by which risk of acute renal failure is increased with high NSAID doses compared to low-medium doses.

**16,500 DEATHS**

From NSAID-related GI complications are estimated to occur annually in people with rheumatic diseases.

- **11%** Of preventable drug-related hospital admissions are attributed to NSAID use.

**100,000+**

Patients with rheumatic diseases are estimated to be hospitalized for NSAID-related GI complications each year.

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1-6, 10, 11

Please see references on page 7.
NSAID Doses in Excess

In an effort to ease their patients’ pain, doctors have a tendency to prescribe NSAIDs at high doses.

80% Of prescriptions for the most commonly prescribed NSAIDs are written at the highest approved dosage\(^\text{14}\)

According to national surveys...

8% Of patients taking a prescription NSAID reported frequently consuming more than the exact prescribed dosage\(^\text{15}\)

38% Of patients taking prescription NSAIDs are also taking OTC NSAIDs\(^\text{15}\)

33% Of patients said they believe that their pain requires high NSAID doses\(^\text{14}\)

“Research has shown that after a certain dose threshold, the analgesic response of NSAIDs reaches a ceiling effect, so patients won’t necessarily experience any greater pain relief, but they may have greater potential risk for dose-related adverse events.”

—James Scheiman, MD
Professor, Division of Gastroenterology
Dept of Internal Medicine, University of Michigan Medical School
Perception vs Reality

Your peers have taken notice of the NSAIDilemma and are starting to change how they speak with their patients and how they prescribe NSAIDs.

- **94%**
  - Of physicians believe NSAIDs should be prescribed at the lowest effective dose for the shortest duration.
  - but...
  - Of physicians say they always follow FDA recommendations for NSAID dosing.

- **15%**
  - Of physicians have prescribed NSAIDs at high doses to patients who were also taking an OTC NSAID.
  - but...
  - Of patients report taking more than the recommended dose of OTC NSAIDs.

- **92%**
  - Of physicians believe it is always necessary to talk to their patients about the risks of taking prescription NSAIDs and OTC NSAIDs.
  - but...
  - Of physicians always discuss the increased risks related to taking NSAIDs at high doses before prescribing.

Please see references on page 7.
The FDA Role

Responsible NSAID dosing has been in the spotlight since FDA first released a Public Health Advisory in 2005.

PUBLIC HEALTH ADVISORY, 2005

Required manufacturers of all marketed prescription NSAIDs to revise product labeling to include a Boxed Warning and Medication Guide as well as recommendations to use the lowest effective dose.\(^\text{17}\)

DRUG SAFETY COMMUNICATION, 2015

FDA strengthened the Boxed Warning to include statements that nonaspirin NSAIDs increase the chance of a heart attack or stroke\(^\text{18}\)

PRESCRIPTION LABEL UPDATE, 2016

FDA required manufacturers of all marketed prescription NSAIDs to include revised safety language within their product labels to strengthen warning of potential serious CV adverse events

\(^{180+}\) Number of studies FDA reviewed that led to strengthening cardiovascular label warnings for all nonaspirin NSAIDs\(^\text{18,19}\)

Please see references on page 7
Professional Medical Organizations Are in Agreement

Recommendations from professional medical organizations consistently advise using the lowest effective dose for the shortest duration.¹⁰⁻²⁵

“In all cases, the lowest effective dose should be used for the shortest possible time.”¹⁰

– American Heart Association (AHA)

“If a patient and provider agree to utilize an NSAID...then the lowest effective dose of the least expensive agent should be considered first line.”²³

– American College of Rheumatology (ACR)

“Even with normal kidney function, you should use analgesics:
• At the lowest dose possible
• For the shortest period of time.”²¹

– National Kidney Foundation

“...[NSAIDs] should be used at the lowest effective dose but their long-term use should be avoided if possible.”²⁴

– Osteoarthritis Research Society International

“GI risks may be decreased through similar attention to risk factors and use of cotherapy. Risk can be reduced through the use of the lowest effective dose for the shortest duration of time.”²²

– American Gastroenterological Association

“...dosing for most patients requires initiation with low doses followed by careful upward titration, including frequent reassessment for dosage adjustments and optimum pain relief and for adverse effects.”²⁵

– American Geriatrics Society

We need your help to truly make a difference.
Alert your colleagues and spread the word by sharing NSAIDilemma.com with your peers.
The health care professionals that appear on this Web site are paid consultants of Iroko Pharmaceuticals, LLC.

Geriatr Soc recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. an American College of Rheumatology white paper.


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