Preface

This supplement was developed from a roundtable entitled **"Coxibs: Evolution of a Revolutionary Class,"** held on August 4 and 5, 2001, in New York, New York. Subtitled *"Evolving Concepts and Issues Surrounding COX-2 Inhibitors,"* this event involved 10 experts representing perspectives from various specialty areas concerned with COX-2–selective inhibitors, including gastroenterology, rheumatology, nephrology, cardiology, pharmacology, anesthesiology, and primary care. Participants were asked to present information to their colleagues that would form the basis for the supplement articles. The interactive discussions initiated by the presentations helped shape the articles. Guest editor Marc C. Hochberg, MD, MPH, moderated the roundtable discussions and provided input during the article development process. The overall goal of the supplement is to provide a comprehensive analysis of the current role of coxibs in various chronic and acute treatment settings, and to characterize some of the underutilized and potential use areas of these agents. Furthermore, points of particular interest to the primary care physician are highlighted throughout each article.

The following objectives will be addressed in the supplement:

- The evolution of the NSAID class and the role of COX-2–selective inhibitors
- The clinical profiles of particular COX-2–selective inhibitors and their appropriate applications
- The class side effect profile of the NSAIDs and points of differentiation for the COX-2–selective inhibitors
- The use of particular NSAIDs in various patient types
- The current and potential uses of coxibs in the perioperative setting
- New research into potential use areas for coxibs.

Foreword

MARC C. HOCHBERG, MD, MPH, EDITOR

The discovery of cyclooxygenase-2 (COX-2) has led to the development of an important new subclass of nonsteroidal anti-inflammatory drugs (NSAIDs) with similar efficacy to nonselective NSAIDs, but with an improved toxicity profile. Like many nonselective NSAIDs, coxibs are currently used to treat osteoarthritis (OA), rheumatoid arthritis (RA), menstrual pain, and acute pain. OA and RA are among the most prevalent chronic illnesses and the leading causes of disability in the United States. These ailments result in a significantly reduced quality of life and confer a substantial economic burden. Coxibs have proven to be useful in a variety of therapeutic areas and ongoing research may identify additional applications. The first article in the supplement, by Clifton O. Bingham III, MD, traces the development of the COX-2–selective inhibitors and provides the foundation for the subsequent articles in the supplement.

Elucidation of the structures of COX isoenzymes has been key in the development of coxibs. The second supplement article, by Bruce N. Cronstein, MD, summarizes some of the key aspects of COX

biochemistry, structure, and function and the evolution of understanding the mechanism of action of COX-2–selective inhibitors.

In numerous clinical trials, coxibs have been shown to be at least as effective as nonselective NSAIDs in relieving pain and inflammation associated with OA and RA, and, notably, with a significantly lower risk of NSAID-related adverse gastrointestinal (GI) events. Thomas J. Schnitzer, MD, PhD, and I review existing efficacy data regarding coxibs in OA and RA, and discuss appropriate use of coxibs in these clinical settings.

GI complications associated with NSAID use often emerge without the appearance of prior symptoms. David A. Peura, MD, reviews risk factors associated with GI complications and discusses risk-reduction strategies, including appropriate use of coxibs in particular patient populations. Additionally, James M. Scheiman, MD, reviews four major GI outcomes studies comparing coxibs to nonselective NSAIDs, including an in-depth review of the GI outcomes from Vioxx Gastrointestinal Outcomes Research (VIGOR) trial and Celecoxib Long-term Arthritis Safety Study (CLASS).

While a significant difference in GI complications between nonselective NSAIDs and coxibs has been well established, other safety comparisons are less well characterized. Marvin A. Konstam, MD, and Matthew R. Weir, MD, provide perspective on issues surrounding the comparative cardiovascular safety profiles of the nonselective NSAIDs, aspirin, and coxibs. In a subsequent article, Dr. Weir reviews the renal effects of nonselective NSAIDs and coxibs. In both articles, appropriate use of these agents and proper precautions are described.

Pharmacoeconomic considerations for the use of coxibs among patients with varying degrees of risk for GI injury are discussed by A. Mark Fendrick, MD. This article examines some of the key factors in determining the cost-effectiveness of coxib therapy. Clinical and economic data are presented on issues from basic costs to clinical effects and economic consequences of available treatment options.

The final two supplement articles discuss the use of coxibs in the acute and perioperative pain settings, as well as important future use areas. There is concern about preoperative use of nonselective NSAIDs, mainly because of the potential for excessive bleeding. The use of opioids has long been a concern in the perioperative setting, because of the potential for tolerance and other problematic postoperative complications such as constipation. Warren A. Katz, MD, reviews the use of coxibs in the acute and perioperative settings. In the final article, Mark J. Lema, MD, PhD, reviews some emerging clinical areas for coxibs and discusses research into novel therapeutic applications. The rationale and data on the use of coxibs in treating the progression of both Alzheimer's disease and colorectal cancer are discussed. Dr. Lema also discusses the role of coxibs in the management of cancer pain.

It is clear that the benefits of COX-2–selective inhibitors have continued to expand into a variety of therapeutic categories since their initial development for pain associated with arthritis. Accompanying this expansion has been an increased understanding of the mechanisms underlying inflammation and pain and the more complex roles coxibs may play. It is our hope that this supplement will serve to provide those clinicians who serve a broad spectrum of patients and specialty areas with the most recent data and, indeed, the most current discussion on evolving concepts and issues surrounding these truly revolutionary agents.

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