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To Whom It May Concern:

The American College of Gastroenterology has observed with significant concern recent communications relating to NSAIDs, COX-2s and other pain relief/analgesia items. Our concern is based on our awareness that the likely shift away from COX-2s and the reversion of many more patients and their physicians to traditional NSAIDs is certain to result in an increase in the incidence of serious, potentially life-threatening, gastrointestinal bleeding. We are writing: (1) to establish officially ACG's support for a Citizen Petition recently filed by McNeil Products requesting a labeling change with respect to the maximum recommended dose for aspirin used for cardiovascular and cerebrovascular prevention; and (2) to encourage you and your colleagues to maintain the fair, balanced process of weighing potential benefits and risks of new medications/therapies that has consistently characterized FDA disposition of new treatment approaches in gastroenterology and other fields of medicine.

Gastrointestinal bleeding is a serious health matter which often strikes patients by surprise, including those with or without past symptoms or underlying digestive condition. Gastroenterologists are frequently called upon to see such patients in the emergency room setting, to identify and if possible to treat the source of the bleeding, which if untreated, potentially can be fatal. Historically, use of NSAIDs, including common products such as aspirin, ibuprofen and naproxen sodium, particularly when taken regularly by patients with arthritis or other conditions causing chronic pain, have been associated with GI bleeding. The risk was related to the anti-inflammatory dose and when the relative new class of drugs, called COX-2s came onto the market in the past decade, many patients who were regular users of NSAIDs for analgesia or pain relief, were advised by their physicians to switch to the COX-2 products based on the premise that they could achieve the benefits of good anti-inflammatory activity with no more risk than analgesic doses of traditional NSAIDs. Clinical studies subsequently confirmed that these newer compounds had a lower incidence of gastrointestinal bleeding. Recent scientific findings have challenged some of these COX-2 compounds, not with respect to claims

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of reduced risks of GI bleeding, but because of data relating to potentially increased cardiovascular complications.

The merit of the pending petition rests, in essence, on gaining an accurate assessment of risk/benefit ratio. With respect to aspirin used for cardiovascular and cerebrovascular prevention, we believe that the risk/benefit ratio indeed must be considered favorable to the position stated in the petition if low-dose aspirin is associated with a lower incidence of bleeding complications, and is found to provide comparable efficacy to high-dose aspirin (dosages above 150 mg/day). We believe that the data submitted with the petition demonstrates that the risk/benefit ratio is markedly better with low dose than when higher doses of aspirin are used both for primary and for secondary cardiovascular prevention. It seems that the facts match virtually perfectly with the agency's conclusion a decade ago on this issue; namely, "The positive findings at lower dosages," along with the higher incidence of side effects expected at the higher dosage (in this case 325 mg daily) are sufficient reasons to lower the dosage of aspirin for subjects with TIA and stroke."

In the current environment, it would be easy to lose sight of the solid foundation and priorities which we think are of paramount importance in having the agency serve the long term interests of advancing public health, and patient safety and options.

We recognize that the agency has an extremely difficult job that involves a profound public trust. Striking a credible balance of all factors including significance of the clinical disease, the effectiveness of presently available treatment alternatives, scientific insights on the anticipated therapeutic benefits of new agents, as well as prospective frequency and severity of adverse effects is an incredibly challenging task. We simply want to encourage you to continue to perform that task in a scientifically sound, careful manner that has been FDA's legacy. If we demand universal effectiveness and absolute absence of adverse effects, we would make little progress in medicine; conversely, the public expects and is entitled to an unprejudiced view by the agency to minimize risk of patient harm.

We urge the FDA to approve the Citizen Petition, and to amend the labeling for aspirin to change/reduce the maximum daily dose to 150 mg/daily for both secondary cardiovascular prevention, and to 150 mg/daily also for secondary cerebrovascular prevention, as well as recommending an open approach to the ultimate consideration of new agents which may result in improved pain relief without increased prevalence of gastrointestinal bleeding.

Very truly yours,


Jay Popp, Jr., M.D., FACP
President

cc: Ms. Jane Axelrad
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