



NATIONAL HEMOPHILIA FOUNDATION
for all bleeding disorders

MASAC Document #162

**MASAC RECOMMENDATIONS ON USE OF COX-2 INHIBITORS
IN PERSONS WITH BLEEDING DISORDERS**

The following recommendations were approved by the Medical and Scientific Advisory Council (MASAC) of the National Hemophilia Foundation on April 9, 2005, and adopted by the NHF Board of Directors on June 4, 2005

Individuals with bleeding disorders may require analgesics to supplement their clotting factor treatment plan. This includes individuals with hemophilia and joint pain associated with acute hemorrhages or chronic hemophilic arthropathy, as well as women with a bleeding disorder (e.g. von Willebrand disease) who suffer menorrhagia and menstrual pain. A class of non-steroidal anti-inflammatory drugs (NSAIDs) known as cyclooxygenase-2 (COX-2) inhibitors, with similar efficacy to NSAIDs, is approved for use in arthritis and menorrhagia. Individuals with bleeding disorders and pain have used these agents with good pain relief. Although COX-2 inhibitors are not associated with platelet dysfunction in vitro, there are anecdotal reports that use of these drugs has caused clinically significant bleeding in some individuals with bleeding disorders. In addition, rofecoxib (Vioxx[®]), when used in a colorectal polyp prevention trial; valdecoxib (Bextra[®]), when used in patients undergoing coronary artery bypass grafting; and celecoxib (Celebrex[®]), when used in individuals to reduce development of colorectal cancer, have been associated with increased frequency of thromboembolic events, including heart attacks and strokes. These observations have led to the withdrawal of rofecoxib (Vioxx[®]) and valdecoxib (Bextra[®]) by their manufacturer. Celecoxib (Celebrex[®]) remains the only COX-2 inhibitor available for patient use. Whether similar risks exist with other NSAIDs, such as ibuprofen or naproxen, and whether these risks apply to individuals with bleeding disorders is not yet established.

For these reasons, caution is advised with the use of COX-2 agents (e.g. celecoxib) in individuals with bleeding disorders. For example, thromboembolic risks seem to be greater in those individuals with active or prior coronary artery disease (myocardial infarction, unstable angina, etc.), hypertension, or stroke. The frequency of these adverse events was associated with higher than standard dosing of these medications and with their prolonged use. Therefore, providers should maintain close vigilance for symptoms and signs of heart attack, stroke, or gastrointestinal bleeding and should discuss these potential risks in the context of their potential benefits with their patients. A switch to alternative analgesics may be considered. If a COX-2 inhibitor is prescribed, it should be used at the lowest effective dose for the least necessary duration.



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Recommendations:

1. Caution is advised with use of COX-2 inhibitors in individuals with bleeding disorders. The potential risks of gastrointestinal bleeding, heart attack, and strokes should be weighed against the potential benefits.
2. Individuals sensitive to sulfa should be aware that the COX-2 inhibitor, celecoxib (Celebrex®), contains sulfa groups which may precipitate allergic reactions.
3. Research should be conducted to determine whether alternative COX-2 inhibitors not currently available, such as rofecoxib (Vioxx) which does not contain sulfa, can be safely used in lower doses in individuals with bleeding disorders.
4. Special attention should be paid to the use of COX-2 inhibitors in children, in whom thromboembolic risks remain to be assessed.

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