PREAMBLE

While several Cox-2 inhibitors have come to market over time, only celecoxib currently remains available. Efficacy of all of the Cox-2 inhibitors is comparable to traditional NSAIDs. The advantage has been indicated to rest with their relative GI sparing in terms of serious complications as compared to traditional NSAIDs. For celecoxib, post-marketing trials have now further clarified this position (CLASS¹). Celecoxib, ibuprofen and diclofenac had comparable rates of ulcer complications. Celecoxib had a lower rate of combined ulcer complications and symptomatic ulcers as compared to ibuprofen, and a comparable rate as compared to diclofenac. Combination of celecoxib with any dose of ASA increased the risk of ulcer complications 4-fold.

Although no longer available, the VIGOR² trial demonstrated an increased rate of cardiovascular events with rofecoxib as compared to the traditional NSAID comparator. The same finding was not demonstrated in the CLASS trial, though the issue of increased cardiovascular risk with celecoxib has subsequently been raised³⁴⁵ and the current recommendation is to limit the maximum total daily dose of celecoxib to 400 mg.

There are no differences from traditional NSAID’s in terms of renal effects, or in hemodynamic and fluid balance effects. For those with renal insufficiency or renal failure, caution should be exercised in prescribing. For those with a creatinine clearance of <30 mL/min, prescription is contraindicated.

Additional contraindications to prescription include active peptic ulcer, GI bleeding or active inflammatory bowel disease; and significant hepatic impairment or active liver disease.

Monitoring of INR is recommended after initiation of a Cox 2 inhibitor for those on warfarin. There is a potentially clinically significant effect on INR, typically leading to increased effect of an administered dose of Warfarin. There is currently no data to indicate whether or not a Cox 2 inhibitor is safer in combination with warfarin in terms of GI complications than the combination of warfarin with a traditional NSAID, such as diclofenac.

Cox 2 inhibitors are restricted to situations where:

- There is documentation of failed trials of acetaminophen with or without codeine or other analgesic agents, in clinical situations where non-NSAID drugs would be a rational choice and
  1. There is documented intolerance to more traditional agents, including diclofenac, in combination with cytoprotection, following a trial of therapy³, or
  2. There is documented intolerance to cytoprotection, where the risks of using unopposed NSAIDs are unacceptably high.
Note: Celecoxib (Celebrex®) is a sulfonamide similar to hydrochlorothiazide, furosemide and glyburide. These drugs may cause rashes. However, there is no evidence that the reason they cause rashes is due to them being sulfonamides. Caution and clinical discretion is advised when prescribing celecoxib to sulfonamide allergic patients.

References:


