Comparing Bute and Firocoxib Safety (AAEP 2010)

by: Stacey Oke, DVM, MSc

March 10 2011 Article # 17907

The non-steroidal anti-inflammatory drug (NSAID) firocoxib had fewer side effects than phenylbutazone in horses after 42 days of treatment, according to scientists from Merial Limited who presented comparative research results at the 2010 Convention of the American Association of Equine Practitioners (AAEP), held Dec. 4-8 in Baltimore, Md.

Phenylbutazone, or "Bute" as it is commonly called, is useful for controlling pain and/or inflammation in many equine veterinary cases, but its use is not without risk. Side effects such as gastric ulcer formation and kidney damage can occur.

Like phenylbutazone, firocoxib is also a non-steroidal anti-inflammatory drug. It is approved to control pain and inflammation associated with equine osteoarthritis at a dose of 0.1 mg/kg once daily for up to 14 days.

Bute, considered a "pioneer" NSAID, inhibits the production of pro-inflammatory molecules (called prostaglandins, produced from fatty acids) by blocking the action of an enzyme called cyclooxygenase (COX, which makes the prostaglandins from the fatty acids). Unfortunately, Bute blocks some "good" prostaglandins, such as those that protect the lining of the stomach. Newer NSAIDs such as firocoxib are more selective and mostly block the production of "bad" prostaglandins; therefore, these are thought to have fewer untoward side effects.

The research team treated 42 horses with various dose levels of firocoxib and phenylbutazone once daily by mouth (orally) for 42 days. They found:

There was an 88% increase in gastric ulceration in the horses treated with therapeutic levels of phenylbutazone (4.4 mg/kg), compared to only an 11% increase in horses in the control group and those treated with elevated levels of firocoxib (0.5 mg/kg);

Microscopic damage to the gastrointestinal tract occurred following phenylbutazone, but investigators did not note any damage even after administering five times the therapeutic level of firocoxib; and

The researchers noted microscopic damage to the kidneys following administration of therapeutic doses of phenylbutazone, but they noted similar damage only in the higher-dose firocoxib-treated horses.
The research team concluded that after 42 days of treatment at therapeutic levels, firocoxib was well-tolerated, whereas phenylbutazone was associated with gastrointestinal ulceration and tubulointerstitial nephropathy (a type of kidney damage that can lead to kidney failure).

**PROSTAGLANDINS AND COX**

COX is the abbreviation for cyclooxygenase—a key enzyme in the production of prostaglandins and thromboxanes from a particular fatty acid called arachadonic acid. Some prostaglandins (such as prostaglandin E) are "bad" prostaglandins because they are potent pro-inflammatory molecules; however, many "good" prostaglandins are also produced. These good prostaglandins play important roles in regular, healthy metabolic pathways such as:

- Blood clotting;
- Kidney function;
- Gastrointestinal health;
- Wound healing;
- Bone metabolism;
- Growth of nerves; and
- Immune function, among others.

Classic NSAIDs, like phenylbutazone, inhibit the production of both the "good" and the "bad" prostaglandins (and related compounds), whereas newer NSAIDs primarily inhibit only the "bad" prostaglandins. This is because there is more than one type of COX. The two main forms of the enzyme existed are COX-1 and COX-2. COX-1 produces many of the "good" prostaglandins whereas COX-2 is primarily responsible for the production of the pro-inflammatory prostaglandins. COX-2 does contribute to some beneficial activities such as wound healing and maintaining blood flow to the kidney. As a result, traditional NSAIDs that block both COX-1 and COX-2 have slowly been replaced with NSAIDs that preferentially block COX-2, thus preserving the function of COX-1. These newer-generation COX-2 NSAIDs selectively block COX-2 rather than COX-1, resulting in potent anti-inflammatory properties with fewer side effects.

---

Stacey Oke, DVM, MSc