Formulary Drug Listing Decisions

PIROXICAM

Indication (s)

Piroxicam is used to treat pain and a variety of inflammatory conditions.

DAC Recommendation

The Drug Advisory Committee (DAC) has recommended that piroxicam be removed from all WSIB formularies following a Health Canada safety review that cited piroxicam's, *acute*, *short-term* increased risk of serious skin conditions and gastrointestinal intestinal (GI) problems compared to other nonsteroidal anti-inflammatory drugs (NSAIDs).

The WSIB Decision

Based on the DAC's recommendations, the WSIB has decided to **remove** piroxicam from all formularies at this time.

Formulary Status

Piroxicam HAS BEEN REMOVED from WSIB formularies at this time.

Recommendation Highlights

- Piroxicam is a non-selective NSAID that has been used in the treatment of pain and various inflammatory conditions.
- A recent review by Health Canada concluded that piroxicam should no longer be used to treat short-term pain and inflammation, although it can still be prescribed for the symptomatic relief of chronic pain and inflammation in patients suffering from certain types of chronic arthritis (e.g., osteoarthritis, rheumatoid arthritis and ankylosing spondylitis). This labeling change for piroxicam is relevant for the WSIB population, many of whom are prescribed NSAIDs for treatment of acute, short-term pain.
- Piroxicam was cited as having an increased risk of serious skin reactions (e.g., Stevens-Johnson syndrome and toxic epidermal necrolysis) and gastrointestinal problems relative to other NSAIDs.
- There are a number of equally effective NSAIDs (e.g., ibuprofen, diclofenac) that can be used for treatment of inflammatory conditions, both on an acute and chronic basis.
- **The DAC recommended that piroxicam be removed from WSIB formularies based on a Health Canada review of studies suggesting an increase in GI toxicity and an increased risk of development of serious skin reactions (which has resulted in labeling changes by Health Canada) and on the availability of equally effective NSAIDs for treatment of inflammatory conditions.**

Drug Profile

Products available in Canada:

Apo-Piroxicam, Dom-Piroxicam, Gen-Piroxicam, Novo-Pirox, Nu-Pirox, PMS-Piroxicam, Pro-Piroxicam

MANUFACTURER: Variety of generic manufacturers

wsib ONTARIO

DETAILED DISCUSSION

Background

Piroxicam is a non-selective nonsteroidal anti-inflammatory drug (NSAID) that has been used in the treatment of various inflammatory conditions. Non-selective NSAIDs, including piroxicam, exert their effects by inhibiting all forms of cyclooxygensase, an enzyme that mediates pain and inflammation. All NSAIDs are associated with an elevated risk of gastrointestinal toxicity and the rare occurrence of serious skin reactions. However, a recent safety review by Health Canada determined the risks of these serious adverse events may be higher with the use of piroxicam relative to other NSAIDs (e.g., ibuprofen and naproxen) in the acute, short-term treatment pain (i.e., during the initial weeks of therapy).

Summary of Committee Considerations

The DAC considered information from a Health Canada Safety Review of piroxicam. This review concluded that piroxicam was associated with a short-term increased risk of serious skin reactions and gastrointestinal toxicity relative to other NSAIDs during the initial weeks of treatment.

Upper GI symptoms (e.g., dyspepsia) are extremely common, occurring in up to 35% of all NSAID users. Serious upper GI complications (e.g., major bleeding, perforation, obstruction) occur less frequently; the annual incidence of complicated GI events in arthritis patients is approximately 1-1.5%. Upper GI symptoms correlate poorly with NSAID-associated ulcers or complications.

Evidence from observational studies suggests that piroxicam may be associated with a higher risk of serious GI toxicity compared to other NSAIDs. In one such study, ibuprofen ranked lowest amongst the NSAIDs for GI complications, followed closely by diclofenac. Ketoprofen, tolmetin and piroxicam ranked highest and indomethacin, naproxen, sulindac and aspirin had intermediate risks. Although a comparison of adverse effects reported in randomized controlled trials suggest that piroxicam may be better tolerated in terms of GI toxicity than some other NSAIDs such as indomethacin and naproxen, most observational studies indicate that piroxicam has one of the highest risks for the development of GI toxicity.

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are severe cutaneous hypersensitivity reactions that cause rash, skin peeling, and sores on the mucous membranes. These disorders are extremely rare, affecting between 1 and 5 people/million users.

Data from an international case-control study and a population-based registry both concluded that piroxicam was associated with the greatest increase in risk of SJS/TEN compared to other NSAIDs. When the risk for recently initiated use was compared to that for long-term use of these agents (>8 weeks), the relative risk of SJS/TEN associated with initial use of piroxicam was significantly increased.

Based on the review of evidence, Health Canada concluded that the risks associated with the short-term use of piroxicam outweighed the benefits, given the availability of alternative NSAIDs. As such, piroxicam is no longer indicated for the acute, short-term treatment of pain and inflammation. Piroxicam can still be prescribed for the treatment of chronic pain and inflammation in patients suffering from certain types of chronic arthritis (e.g., osteoarthritis, rheumatoid arthritis and ankylosing spondylitis). A similar review in 2007 in the United Kingdom resulted in the same restrictions for the use of piroxicam.

Based on this evidence, the DAC recommended that piroxicam be removed from all WSIB formularies based on (i) the availability of equally effective NSAIDs for treatment of inflammatory conditions; (ii) the increased risk of development of serious skin reactions (i.e., SJS/TEN) compared to other NSAIDs; (iii) suggestion of increased GI toxicity; and (iv) labeling change for piroxicam in Canada that it should not be used for acute, short-term pain (a large portion of injured workers).

Revised: January 29, 2013