Formulary Drug Listing Decisions

DICLOFENAC SODIUM SOLUTION 1.5%

Indication (s)

Treatment of symptoms associated with osteoarthritis of the knee (duration of treatment not to exceed 3 months).

DAC Recommendation

The Drug Advisory Committee (DAC) recommended that Pennsaid® not be listed on any WSIB formularies as there are no trials providing evidence that it demonstrates an advantage to comparators currently listed on the WSIB formularies.

The WSIB Decision

Based on the DAC's recommendations, the WSIB has decided NOT to list Pennsaid® on any of the formularies at this time.

Formulary Status

Pennsaid® IS NOT listed on WSIB formularies at this time.

Recommendation Highlights

- Diclofenac sodium solution 1.5% is a topical nonsteroidal anti-inflammatory agent (NSAID) marketed under the brand name Pennsaid® in Canada. It is currently approved by Health Canada for the treatment of symptoms associated with osteoarthritis (OA) of the knee.
- Placebo-controlled studies have shown that Pennsaid® is effective in reducing pain scores and improving physical functioning in patients with primary OA of the knee.
- Oral diclofenac and Pennsaid® have been compared in one randomized-controlled trial (RCT). Both drugs were similarly effective in improving pain and physical functioning in primary OA of the knee. Pennsaid® was associated with fewer gastrointestinal side effects.
- There is no evidence demonstrating any clear therapeutic or long-term safety advantage for Pennsaid® compared to other effective agents in OA of superficial joints (e.g., knee). Furthermore, there is no evidence demonstrating that Pennsaid® is effective in treating pain or inflammation for large, deep joints covered by layers of muscle or other soft tissues (e.g., hip and spine).
- The daily cost of Pennsaid® in the treatment of OA of the knee is estimated at $3.85 to $5.18. The cost is significantly more expensive than most other medications proven effective and safe. The cost-effectiveness of Pennsaid® in an environment similar to the WSIB has not been established.
- **The DAC concluded that an independent review of Pennsaid® studies did not indicate any therapeutic or non-therapeutic advantage over appropriate comparators in osteoarthritis of superficial joints.** Consequently, the DAC recommended Pennsaid® NOT be listed on any WSIB formulary.

Drug Profile

Products available in Canada:

Pennsaid® (diclofenac sodium solution 1.5%)

MANUFACTURER: Squire Pharmaceuticals Inc

wsib ONTARIO

DETAILED DISCUSSION

Background

Diclofenac sodium solution 1.5% is a prescription topical NSAID marketed under the name Pennsaid®. Similar to oral NSAIDs (e.g. naproxen, diclofenac, etc.), Pennsaid® exerts its effects through the inhibition of prostaglandin.

Requests for Pennsaid® use in the treatment of superficial joint (e.g., knee) and soft tissue injury have increased over previous years. This has occurred in the absence of strong evidence supporting a benefit in efficacy or long-term safety.

Summary of Committee Considerations

The DAC considered an external, independent review of the clinical efficacy, safety, and cost-effectiveness of Pennsaid® in the treatment of chronic non-cancer pain. The review included published and unpublished, randomized controlled trials (RCTs) that were at least single-blind.

Four RCTs were included in the review. Three studies compared Pennsaid® to placebo and one study compared Pennsaid® to active treatment (oral diclofenac). All studies enrolled subjects with primary OA of the knee. Notably, there are *no studies* assessing the efficacy of Pennsaid® in the treatment of pain or inflammation for large, deep joints covered by layers of muscle or other soft tissues (e.g., hip and spine).

The results of these trials demonstrate that Pennsaid® is better than placebo and similar (but not superior) to oral diclofenac in terms of improving pain and physical function in primary OA of the knee.

The most commonly reported side effects with Pennsaid® were minor skin reactions at the application site. Pennsaid® was associated with fewer reports of gastrointestinal (GI) adverse effects (e.g., dyspepsia) compared to oral diclofenac. The long-term GI safety of Pennsaid® is difficult to determine given the short duration of the trials (the longest trial was 12 weeks). Pennsaid® treatment may actually be more difficult to use than oral diclofenac, as Pennsaid® was associated with higher discontinuation rates than oral diclofenac in the one comparative study.

One study has assessed the cost-utility of Pennsaid® compared to oral diclofenac in treating OA of the knee. The study focused on individuals at high risk of GI complications (e.g., a history of peptic ulcer, older than 60 years, concurrent use of steroids, etc). Pennsaid® was found to be worth the higher cost mainly in the *high-risk, elderly* individuals. The majority of WSIB workers are NOT elderly, high-risk individuals, so the applicability of these results to the WSB is questionable. An additional study limitation is that the source of the data was not identified. Data (including costs) may have come from a society/health care system with marked differences from ours, which makes the relevance of the results further questionable.

Key guidelines were consulted to establish standards of care in osteoarthritis. Acetaminophen is generally recommended as a first-line treatment option, followed by oral NSAIDs (at the lowest effective dose) or COX-2 inhibitors. Topical NSAIDs are generally recommended as alternatives to oral agents in osteoarthritis of the *knee or hand (both supeficial joints)*; they are not recommended for osteoarthritis of the hip (a deep joint).

The Ontario Drug Benefit Program does not fund Pennsaid®.

Based on the evidence considered, the DAC concluded that there was no compelling evidence demonstrating a therapeutic or non-therapeutic advantage for Pennsaid® over comparators in the treatment of osteoarthritis. Furthermore, several alternative drug classes are available on the WSIB formularies that can meet the treatment needs of the majority of workers. Hence, the DAC recommended Pennsaid® not be listed on any WSIB formularies.

Revised: January 29, 2013