Drug Benefit Council (DBC) Recommendation and Reasons for Recommendation

FINAL

Non-steroidal anti-inflammatory drugs (NSAIDs)
Various Manufacturers

Description:

The DBC was asked to review and provide direction on the following policy questions:

1. Based on the information provided, what is your recommendation to the British Columbia Ministry of Health (the Ministry) regarding PharmaCare's coverage of non-steroidal anti-inflammatory drugs (NSAIDs), including celecoxib and meloxicam?
2. If the decision is to recommend the changes suggested below, should patients who currently have Special Authority (SA) coverage for a current non-reference NSAID (which now becomes a Limited Coverage drug) be grandfathered indefinitely for this coverage?

In their review, the DBC considered the following: Enthoven WTM, Roelofs PDDM, Deyo RA, van Tulder MW, Koes BW, Non-steroidal anti-inflammatory drugs for chronic low back pain (Cochrane Database of Systematic Reviews 2016, Issue 2. Art. No.: CD012087. DOI: 10.1002/14651858.CD012087); an evidence document from the University of British Columbia reviewing the Efficacy and Safety of NSAIDs (Hong 2019); a National Institute for Health and Care Excellence (NICE) advice document on Non-Steroidal Anti-Inflammatory drugs; the Therapeutics Initiative's Therapeutics Letter, February 1995, "Should we be using NSAIDS for the treatment of Osteoarthritis and 'Rheumatism"; a PowerPoint presentation on the Reference Drug Program, focused on NSAIDs and Nitrates; and a Budget Impact Assessment.

Dosage Forms:

ECT-ASA enteric coated tablets and capsules 325mg, 500mg, 650mg
Ibuprofen tablet 200mg, 400mg, 600mg
Naproxen tablet 250mg, 375mg, 500mg
Diclofenac tablet 25mg, 50mg
Celecoxib capsule 100mg, 200mg
Meloxicam tablet 7.5mg, 15mg
Diclofenac with misoprostol tablet 50mg/200mcg, 75mg/200mcg
Diflunisal tablet 250mg, 500mg
Flurbiprofen tablet 50mg, 100mg
Indomethacin capsule 25mg, 50mg

Ketoprofen capsule and enteric coated forms 50mg, 100mg, 200mg
Naproxen EC enteric coated tablet 250mg, 375mg, 500mg

Recommendations:

1. The Drug Benefit Council (DBC) recommends the following changes to the NSAID RDP category:
    a. **Changes to reference tier:**
        i. Remove Enteric Coated ASA (ECT-ASA) and ibuprofen 200mg from reference tier.
        ii. Ibuprofen 400mg, naproxen to remain as reference NSAIDs.
        iii. Ibuprofen 400mg to continue to set the reference price.
    b. **Changes to non-reference tier**
        i. Move the higher cost/lesser used NSAIDs from the non-reference tier to Limited Coverage (LC): diclofenac/misoprostol; diflunisal; flurbiprofen; indomethacin; ketoprofen; naproxen SR, thereby removing the need to provide partial coverage to those using the medications without SA coverage in place.
        ii. The new non-reference tier would become: diclofenac; diclofenac SR; naproxen E;
        iii. New criteria for non-reference tier:
            1. Diagnosis of rheumatoid arthritis (RA) or psoriatic arthritis (PA) or ankylosing spondylitis (AS) or gout or lupus <u>OR</u> failed both ibuprofen and naproxen.
            2. Patients will receive SA coverage for non-reference NSAIDs, celecoxib and meloxicam when these criteria are met.
    c. **LC drugs and criteria after change**:
        i. Move ketoprofen, diflunisal, flurbiprofen, indomethacin, diclofenac/misoprostol, naproxen SR to current LC NSAIDs nabumetone, piroxicam, sulindac, tenoxicam, tiaprofenic acid.
        ii. New Limited Coverage criteria for coverage will become:
            1. Diagnosis of RA or PA or ankylosing spondylitis or gout or lupus, **<u>OR</u>** osteoarthritis (OA) having tried acetaminophen AND failed ibuprofen **AND** naproxen **AND** diclofenac **AND** a COX-2 (i.e. celecoxib OR meloxicam).
    d. **Change to celecoxib and meloxicam Limited Coverage criteria**
        i. New LC criteria to change to align with that of non-reference tier:
            1. Diagnosis of RA or PA or ankylosing spondylitis or gout or lupus, **<u>OR</u>** failed **both** ibuprofen and naproxen
            2. Patients will receive coverage for both non-reference and cyclooxygenase-2 enzyme (COX-2) inhibitors when these criteria are met.
2. The COX-2 inhibitors should remain as Limited Coverage drugs with their criteria aligned to that of the non-reference tier.

3. The Ministry of Health should decide internally whether patients who currently have SA coverage for a current non-reference NSAID should be grandfathered indefinitely for this coverage.

Reasons for the Recommendation:

1. Summary

- The drugs within the therapeutic category of NSAIDs are generally similar in efficacy.
- Celecoxib, ibuprofen, and naproxen likely have safer CV and GI risks compared to other NSAIDs, although naproxen likely has a higher GI risk. The NICE advice document indicated that naproxen and low-dose ibuprofen have the most favourable thrombotic CV safety profiles of the NSAIDs.
- The forecasted budget impact to PharmaCare in the next three fiscal years would be similar with or without grandfathering, although the budget impact would be higher with grandfathering.

2. Clinical Efficacy

- The DBC considered the 2016 Cochrane review of non-steroidal anti-inflammatory drugs for chronic low back pain, which included 13 trials. The Cochrane review identified no difference in efficacy between different NSAID types, including selective versus non-selective NSAIDs.
- The evidence document reviewing the Efficacy and Safety of NSAIDs found that, in most therapeutic indications, all NSAIDs likely have similarly efficacy. The most commonly referenced comparisons for efficacy were between celecoxib, ibuprofen, naproxen, indomethacin, and diclofenac.

3. Safety

- The Cochrane review was unable to make a firm statement about the occurrence of adverse events or whether NSAIDs are safe for long-term use.
- The evidence document found that diclofenac is identified to have higher CV and hepatotoxicity risk. Celecoxib, ibuprofen, naproxen likely have safer CV and GI risks, with the exception that naproxen has slightly higher GI risk than the two others. Safety information on indomethacin is lacking, thus other NSAIDs are favored.
- The NICE advice document indicated that naproxen (1,000 mg/day or less) and low-dose ibuprofen (1,200 mg/day or less) have the most favourable thrombotic CV safety profiles.

4. Economic Considerations

- The Reference Drug Program (RDP), introduced in October 1995, is a PharmaCare policy to encourage cost-effective first-line prescribing for common medical conditions. The RDP groups drugs into categories with similar therapeutic application but different active ingredients. Within an RDP category, there are designated reference drugs and non-reference drugs. Among the reference drugs, one or more

drugs are selected as the comparators, and its Pharmacare claimed price is used to set the reference price for the non-reference drugs. Full coverage, subject to the usual PharmaCare plan rules, is provided for all the drugs established as reference drugs, including the reference drug comparator. Partial coverage up to the reference price is provided for the non-reference drugs in the category. Non-reference drugs become full benefits for a patient who has received SA coverage for them.

- In 1995, PharmaCare established NSAIDs as a category within the RDP. The reference drugs were chosen by PharmaCare as they were assessed to be the most cost-effective of the available NSAIDs at that time. The COX-2 inhibitor NSAIDs were not yet available on the Canadian market.
- Some NSAIDs were included in the RDP while others were listed with Limited Coverage criteria only. Patients taking NSAIDs that are not listed as a reference or non-reference drug within the RDP receive no coverage until they have met PharmaCare coverage criteria and have been granted coverage through application via PharmaCare's SA process.
- There have been no substantial changes to the NSAID RDP category since 1995. Since then, their cost-effectiveness has changed and COX-2 inhibitor type NSAIDs (celecoxib and meloxicam) have also become available.
- The Budget Impact Analysis considered the impact of PharmaCare changing coverage status for drugs in the NSAID RDP category and modifying the Limited Coverage criteria for celecoxib and meloxicam.
- In the first scenario (no grandfathering) patients who currently receive full coverage for non-reference drugs under the status quo but who do not meet the new Limited Coverage criteria will switch to other non-reference drugs to maintain full coverage.
- In the second scenario (grandfathering) patients who currently receive full coverage for non-reference drugs under the status quo but who do not meet the new Limited Coverage criteria will be grandfathered to receive full coverage. In the second scenario (non-grandfathering).
- The forecasted budget impact to PharmaCare in the next three fiscal years was similar for both the first scenario, no grandfathering (~$400,000) and the second scenario, grandfathering (~$497,000).