Oral COX-2 inhibitors

for treating pain

Technology Guidance from the MOH Drug Advisory Committee

Guidance recommendations

The Ministry of Health's Drug Advisory Committee has recommended:

- ✓ celecoxib 200 mg capsule; and
- ✓ etoricoxib 60 mg, 90 mg and 120 mg tablets

for treating pain in line with their registered indications in Singapore.

For patients with renal impairment or who have an increased risk of cardiovascular events, clinicians should prescribe COX-2 inhibitors at the lowest effective daily dose for the shortest duration possible.

Subsidy status

Celecoxib 200 mg capsule and etoricoxib 60 mg, 90 mg and 120 mg tablets are recommended for inclusion on the MOH Standard Drug List (SDL) for the abovementioned indication.

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ACE agency for care effectiveness

Factors considered to inform the recommendations for subsidy

Technology evaluation

1.1 The MOH Drug Advisory Committee ("the Committee") considered the evidence presented for the technology evaluation of oral COX-2 inhibitors for treating pain. The Agency for Care Effectiveness conducted the evaluation in consultation with clinical experts from public healthcare institutions. Published clinical and economic evidence for oral celecoxib and etoricoxib was considered in line with their registered indications.

1.2 The evidence was used to inform the Committee's deliberations around four core decision-making criteria:

- Clinical need of patients and nature of the condition;
- Clinical effectiveness and safety of the technology;
- Cost-effectiveness (value for money) – the incremental benefit and cost of the technology compared to existing alternatives; and
- Estimated annual technology cost and the number of patients likely to benefit from the technology.

1.3 Additional factors, including social and value judgments, may also inform the Committee's subsidy considerations.

Clinical need

2.1 COX-2 inhibitors are selective nonsteroidal anti-inflammatory drugs (NSAIDs) which are commonly used in local clinical practice to treat pain due to conditions such as osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, primary dysmenorrhea, chronic lower back pain and acute pain.

2.2 The Committee acknowledged that while there are oral forms of non-selective NSAIDs (such as diclofenac and ibuprofen) for pain management currently listed on SDL, oral COX-2 inhibitors are not subsidised, representing a chemical gap in the MOH Standard Drug List.

Clinical effectiveness and safety

3.1 Randomised controlled trials that directly compare celecoxib with etoricoxib have reported comparable efficacy and safety outcomes for most pain measures.

3.2 Studies have also demonstrated that celecoxib and etoricoxib have comparable efficacy and a similar or improved safety profile compared to non-selective NSAIDs for pain management.

3.3 The Committee acknowledged that in 2005, the US FDA enforced a black box warning for COX-2 inhibitors, highlighting the potential for increased risk of cardiovascular and gastrointestinal events. While some COX-2 inhibitors were withdrawn from the market at that time, studies have demonstrated that these risks are lower for celecoxib and etoricoxib.

Cost effectiveness

4.1 The Committee noted that generic formulations of oral COX-2 inhibitors are available and that the daily cost of generic celecoxib and etoricoxib is comparable.

4.2 While no local cost-effectiveness studies were available, the Committee acknowledged that etoricoxib has been shown to be cost-effective compared to non-selective NSAIDs in the UK context when used to manage pain associated with ankylosing spondylitis and osteoarthritis in patients at low risk of cardiovascular adverse events. The Committee noted that with the availability of generic formulations in Singapore, the COX-2 inhibitors were likely to be at least as cost-effective in local practice.

Estimated annual technology cost

5.1 Value-based pricing discussions were not conducted with the manufacturer due to the availability of generic formulations. The annual cost impact of treating all eligible patients was estimated to be SG$500,000 to less than SG$1 million in the first year of listing on the SDL.

Additional considerations

6.1 The Committee was mindful of the safety risks that may be associated with the use of COX-2 inhibitors, particularly for patients at increased risk of cardiovascular events or with renal impairment. The Committee recommended that clinicians should consider all patient risk factors when prescribing COX-2 inhibitors and that patients should be treated with the lowest effective daily dose for the shortest duration possible, or where appropriate, be prescribed safer alternative analgesic drugs.

Recommendation

7.1 Based on available evidence, the Committee recommended that celecoxib 200 mg capsule and etoricoxib 60 mg, 90 mg and 120 mg tablets be listed on the SDL for treating pain in view of their acceptable clinical and cost effectiveness and comparable daily cost.