Conitec

Recomendation report

DRUGS

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Expansion of the use of naproxen for the treatment of reactive arthritis

Brasília – DF
2022

Technology: Naproxen.

Indication: Reactive arthritis.

Applicant: Secretariat of Science, Technology and Strategic Inputs (Ministry of Health of Brazil).

Background: Reactive Arthritis (ReA) belongs to the group of spondyloarthritis and it is conventionally defined as an arthritis that arises following an extra-articular infection, usually genitourinary or gastrointestinal infection. It is a relatively rare disease that typically occurs in young adults. Treatment usually includes clearing the original infection that triggered ReA and focusing on musculoskeletal manifestations. The use of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) is the initial approach to the treatment of symptomatic joint disease. According to the Clinical Protocol and Therapeutic Guidelines for Reactive Arthritis (2015), ibuprofen is the only NSAID available for ReA in the Brazilian Public Health System - SUS. Naproxen is a non-selective NSAID that has been used and incorporated in the scope of SUS for musculoskeletal conditions (ankylosing spondylitis, psoriatic arthritis, rheumatoid arthritis, knee and hip osteoarthritis), which is considered a safer alternative with respect to cardiovascular events when compared with other NSAIDs.

Question: Is naproxen safe and effective for the treatment of reactive arthritis?

Scientific evidence: Searches were performed in Medline (via Pubmed) and Embase databases. A systematic review on NSAID for spondyloarthritis was eligible, which included five Randomized Controlled Trials (RCTs): three compared naproxen with aceclofenac, butacote, piroxicam; and two compared naproxen with celecoxib and etoricoxib and placebo. The studies that included placebo evaluated efficacy and safety outcomes in patients with ankylosing spondylitis. These RCTs demonstrated a benefit in favour of naproxen in pain relief, patient global assessment, BASDAI score and BASFI score, with no significant increase in adverse events, except for one study that showed a higher rate of gastrointestinal adverse events.

Budget impact analysis: The global annual cost in the baseline scenario was estimated to be approximately BRL 27,000.00, with an impact over five years of about BRL 138,000.00. In the sensitivity analysis, it was observed an amount of BRL 42,000.00 in the most optimistic scenario, and above BRL 516,000.00 in the most pessimistic scenario, over five years. The variable with the greatest impact on the results was the unit cost of naproxen. Comparative analysis with ibuprofen showed an incremental cost between BRL 16.38 to BRL 28.35 per patient treated with naproxen.

International recommendations: Clinical guidelines or health technology assessment agencies recommend the use of NSAIDs in patients with spondyloarthritis, although most do not define the medicine of choice within the class. The American College of Rheumatology considers naproxen as a therapeutic alternative for ReA.

Considerations: No studies evaluating naproxen for ReA were identified, and the RCTs did not compare naproxen with ibuprofen, which is the NSAID available in SUS. It was presented evidence evaluating the efficacy and safety of naproxen compared with placebo in patients with ankylosing spondylitis, a spondyloarthritis that primarily affects the spine. The studies demonstrated the benefit of naproxen, without significantly compromising safety. Despite a lack of evidence on the use of naproxen for ReA, its use is based on clinical experience and evidence of benefit in other musculoskeletal conditions, particularly in other forms of spondyloarthritis. Naproxen has been used and incorporated in the scope of SUS for similar conditions.

Initial Recommendation: Conitec, at its 88th Ordinary Meeting, on July 8, 2020, decided that the subject matter should be made available in a public consultation with a preliminary recommendation in favour of the incorporation of naproxen as a therapeutic option for reactive arthritis, in the scope of SUS.

Public consultation: The Public Consultation No. 43/2020 was held from August 20 to September 8, 2020. A total of 89 contributions were received, of which five (5.6%) were technical-scientific contributions, and 84 (94.4%) were experience or opinion contributions of patients, relatives, friends or caregivers of patients, health professionals or people interested in the subject. Regarding the five technical-scientific contributions, one was

addressing an issue of another public consultation, therefore, only four contributions were taken into consideration. With respect to Conitec's preliminary recommendation, which was in favour of the expansion of the use of naproxen, two contributions agreed with it, and two disagreed. Regarding the 84 experience or opinion contributions, 37 were addressing an issue of another public consultation, so they were not taken into consideration. With respect to Conitec's preliminary recommendation, 18 (38%) contributions agreed with it, one neither agreed nor disagreed, and 28 (59%) disagreed. There were 11 reports on the preliminary recommendation, however, nine of them disagreed with a recommendation against the incorporation of a technology which was not naproxen.

Final Recommendation: The Conitec's members present at the 91st Ordinary Meeting, on October 7, 2020, unanimously decided to recommend the expansion of the use of naproxen for the treatment of patients with reactive arthritis. After analysing the public consultation, considering that the majority of the contributions disagreed with a recommendation against the incorporation of a technology which was not the one evaluated in this report, the members of Conitec's plenary session decided to maintain the preliminary recommendation. The Deliberation Record No. 558/2020 was signed.

Decision: To expand the use of naproxen for the treatment of patients with reactive arthritis, in the scope of the Brazilian Public Health System - SUS, according to Ordinance No. 48, published in the Official Gazette of the Federal Executive No. 217, Section 1, page 144, on November 13, 2020.