Conitec

Recomendation report

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Ixekizumab for the treatment of active psoriatic arthritis in adult patients with an inadequate response or intolerance to one or more disease-modifying antirheumatic drugs (DMARDs)

Brasília – DF
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Technology: Ixekizumab (Taltz®).

Indication: Active psoriatic arthritis (PsA) in adult patients with an inadequate response or intolerance to one or more disease-modifying antirheumatic drugs (DMARDs).

Applicant: Eli Lilly do Brasil LTDA.

Background: Psoriatic arthritis (PsA) is an inflammatory joint disease associated with psoriasis, and also a polygenic autoimmune disorder of unknown etiology, in which cytokines related to T lymphocytes play a key role as in psoriasis. The overall prevalence of PsA ranges from 0.02% to 0.25%, and 1 in 4 patients with psoriasis have psoriatic arthritis: 23.8% (95% confidence interval [CI]: 20.1%-27.6%). In the Brazilian Public Health System (SUS), patients should be provided with access to drug treatment options, including nonsteroidal anti-inflammatory drugs (NSAIDs) ibuprofen and naproxen; glucocorticoids prednisone and methylprednisolone; synthetic disease-modifying antirheumatic drugs (DMARDs) sulfasalazine, methotrexate, leflunomide and ciclosporin; biological DMARDs (DMARDs-b) adalimumab, etanercept, infliximab and golimumab; and the cytokine inhibitor anti-IL17 secukinumab.

Question: Is ixekizumab effective, safe and cost-effective for the treatment of active psoriatic arthritis (PsA) in adult patients with an inadequate response or intolerance to biological DMARDs?

Scientific evidence: A systematic review with a network meta-analysis aimed to investigate the comparative efficacy and safety of interleukin inhibitor class of biologics (IL-6, IL-12/23 and IL-17 inhibitors) for patients with active psoriatic arthritis. Treatment effects were evaluated based on ACR responses (ACR20, ACR50) at week 24; any adverse event (AE); serious adverse events (SAE); and tolerability (discontinuation due to AE), at week 16 or 24. A total of 329 studies were retrieved; the review included six studies investigating interleukin inhibitors secukinumab, ustekinumab, clazakizumab and ixekizumab, with a total of 2,411 patients. In the risk of bias assessment, no critical flaws were identified, except that all six studies reported the use of the last observation carried forward (LOCF) for imputation of missing data, and all of them received funding from a commercial for-profit organization. The ranking of all treatments available in SUS (not just the drugs addressed in this report), based on the SUCRA (surface under the cumulative ranking curve) values as estimated in the review, indicated that secukinumab 300 mg monthly had the highest efficacy in achieving ACR20 (SUCRA = 96.42) and ACR50 (SUCRA = 91.64) responses. Clazakizumab 200 mg monthly, ustekinumab 45 mg every 12 weeks, and secukinumab 150 mg monthly had the lowest probability of having AEs, SAEs and discontinuation due to AEs. In the ranking of treatments according to the outcomes of effectiveness and safety, secukinumab at both doses of 300 mg and 150 mg was the best treatment option for psoriatic arthritis, and ixekizumab was the last option. The network meta-analysis was updated to include two new studies of ixekizumab (SPIRIT-P2 and SPIRIT-H2H), and secukinumab continued to have the highest probability of being the best treatment in the ranking. The certainty of the evidence was assessed as moderate for the outcomes of effectiveness (downgraded due to the limited similarity of the populations in the reviewed studies with ixekizumab, secukinumab, the line of treatment addressed in this report [anti-TNF failure]), and safety (downgraded for imprecision in the outcome of SAE).

Economic evaluation: The applicant submitted a ‘cost per response’ or ‘cost per responder’ analysis, which had to be updated to include the comparison with secukinumab. Considering the incremental costs and benefits compared with adalimumab, the cost per additional responder for ACR50 was estimated to be BRL 19,350.54 for secukinumab. Ixekizumab did not demonstrate superiority in achieving ACR50 compared with adalimumab, but it was superior in achieving a combined endpoint of ACR50/PASI100, and the cost per additional responder for ACR50/PASI100 was estimated to be BRL 71,284.24. However, such an analysis suffers from a lack of methodological rigour of the full economic evaluations, and its results have serious limitations of interpretation.

Budget impact analysis: The applicant submitted a budget impact model to estimate the impact of incorporating ixekizumab over five years for the treatment of patients with psoriatic arthritis, from the perspective of SUS. After a critical analysis, CONITEC considered the model adequate and consistent with the perspective of SUS, but some important data had to be revised. The applicant's original proposal indicated savings of BRL 5.6 million in five years; but based on the revised and updated data, especially the costs of induction treatment, these savings no longer applied, and the incremental impact was then estimated to be more than BRL 58 million.

International recommendations: The National Institute for Health and Care Excellence - NICE (England) and the Canadian Agency for Drugs and Technologies in Health – CADTH (Canada) recommend ixekizumab for active psoriatic arthritis.

Technology horizon scanning: Six potential drugs were identified for the treatment of psoriatic arthritis in patients with an inadequate response or intolerance to one or more DMARDs: apremilast, bimekizumab, filgotinib, guselkumab, risankizumab, and upadacitinib.

Considerations: Based on the comparative effectiveness estimates from the network meta-analysis, secukinumab, a treatment available in SUS, was shown to be the best treatment option for psoriatic arthritis, compared with other drugs, including ixekizumab, which was the last option in the ranking of treatments according to the outcomes of effectiveness and safety. Apart from that, the incremental impact of incorporating ixekizumab was estimated to be more than BRL 58 million.

Initial Recommendation: CONITEC, at its 85th Ordinary Meeting, on February 4th, 2020, decided not to recommend the incorporation of ixekizumab, in the scope of SUS, for active psoriatic arthritis with an inadequate response or intolerance to disease-modifying antirheumatic drugs (DMARDs).

Public consultation: There were 134 technical-scientific contributions, and 222 experience or opinion contributions, and the majority disagreed with CONITEC's preliminary recommendation. The main points raised were the demand for new therapeutic options, and difficulty in accessing the medication due to its high cost. Moreover, new technical data were included, and limitations of the previous analysis were addressed. However, there were no scientific evidence to support the superiority of ixekizumab over secukinumab, or to provide a higher quality comparison than the indirect one. The manufacturer submitted a new budget impact model indicating a reduction of 2.7% in the price initially proposed and savings up to BRL 49,893,362.00, over five years, considering incorporation of ixekizumab in the same line and same indication of secukinumab. CONITEC decided that there was no sufficient reason to change the preliminary recommendation against the incorporation of ixekizumab, due to the uncertainty of its benefits when compared with the effectiveness and safety profile of the treatment options available in SUS.

Final Recommendation: The CONITEC's members present at the 89th Ordinary Meeting, on August 6th, 2020, unanimously decided not to recommend the incorporation of ixekizumab, in the scope of SUS, for active psoriatic arthritis with an inadequate response or intolerance to disease-modifying antirheumatic drugs (DMARDs). As discussed in the preliminary recommendation, ixekizumab has not been shown to have benefits when compared with the effectiveness and safety profile of the treatment options available in SUS.

Decision: Not to incorporate ixekizumab for the treatment of active psoriatic arthritis in adult patients with an inadequate response or intolerance to one or more disease-modifying antirheumatic drugs (DMARDs), in the scope of SUS, according to Ordinance No. 31, published in the Official Gazette of the Federal Executive No. 160, Section 1, page 118, on August 20th, 2020.