NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Ixekizumab for treating active psoriatic arthritis following inadequate response to disease-modifying anti-rheumatic drugs

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of ixekizumab within its marketing authorisation for treating active psoriatic arthritis in people whose disease has not responded adequately to previous disease-modifying anti-rheumatic drug (DMARD) therapy, or for whom DMARDs are not tolerated or contraindicated.

Background

Psoriatic arthritis (also called psoriatic arthropathy) is an inflammatory arthritis closely associated with psoriasis. It is estimated that around 1 in 5 people with psoriasis develop psoriatic arthritis[1], although this figure may be higher in people who have severe psoriasis[1]. In around 70% of people psoriasis precedes psoriatic arthritis[1]. The prevalence of psoriatic arthritis in England in 2014 was estimated to be around 81,177 adults[2,3]. Men and women are equally likely to develop psoriatic arthritis with the peak onset being between the ages of 30 and 50 years[1].

Although psoriatic arthritis is a chronic condition that progresses in the joints, its course may be erratic, with flare-ups and remissions. Arthritis symptoms can range from inflammation of the synovial membrane surrounding a joint (synovitis), ligaments and tendons (enthesitis and tendonitis), and inflammation of digits (dactylitis) to severe progressive erosion of the joints. Skin symptoms include the presence of patchy, raised, red areas of skin inflammation with scaling, which can affect any part of the body but is most commonly found on the extensor surfaces of the elbows and knees, the scalp and ears, the navel, and around the genital areas or anus.

The aim of treatment is to suppress joint, tendon and ligament inflammation, and to manage the skin symptoms of the disease. Current practice involves early diagnosis and early use of non-biological disease modifying anti-rheumatic drugs (DMARDs), including methotrexate, sulfasalazine and leflunomide, in order to minimise damage to joints. Non-steroidal anti-inflammatory drugs (NSAIDs), physiotherapy and intra-articular corticosteroid injections may also be used.

In addition, biological tumour necrosis factor (TNF)-alpha inhibitors may be used for treating people with active psoriatic arthritis. NICE technology appraisal guidance 199 and 220 recommend etanercept, infliximab, adalimumab or golimumab when a person has peripheral arthritis with 3 or

more tender joints and 3 or more swollen joints, and the psoriatic arthritis has not responded to at least 2 standard DMARDs, given on their own or together. Ustekinumab is recommended in NICE technology appraisal guidance 340 when treatment with TNF-alpha inhibitors are contraindicated but would otherwise be considered or the person has had treatment with 1 or more TNF-alpha inhibitors. Apremilast, certolizumab pegol and secukinumab are also recommended as options in NICE technology appraisal guidance 433 and 445, respectively; for people whose disease has not responded to at least 2 standard DMARDs. Certolizumab pegol is also recommended when a tumour necrosis TNF-alpha inhibitor stopped responding after the first 12 weeks and secukinumab is also recommended when TNF-alpha inhibitor has not responded within the first 12 weeks or has stopped responding after 12 weeks or contraindicated.

Biosimilar products of the biological therapies are available for use in the NHS.

The technology

Ixekizumab (Taltz, Eli Lilly) is a humanised monoclonal antibody that neutralises interleukin-17A, which is a key T-cell-derived cytokine involved in inducing and mediating inflammation. It is administered subcutaneously.

Ixekizumab does not currently have a marketing authorisation in the UK for treating psoriatic arthritis. It has been studied in clinical trials compared with placebo and adalimumab in adults with active psoriatic arthritis whose disease has not responded adequately to conventional DMARDs.

Intervention(s)	Ixekizumab alone or in combination with conventional disease modifying anti-rheumatic drug
Population(s)	Adults with active psoriatic arthritis whose disease has not responded adequately to previous disease-modifying anti-rheumatic drug therapy, or for whom DMARDs are not tolerated or contraindicated

Comparators	For people whose disease has not responded adequately to 1 non-biological disease modifying anti-rheumatic drug • Non-biological DMARDs For people whose disease has not responded adequately to at least 2 non-biological DMARDs: • Biological DMARDs (with or without methotrexate, including etanercept, adalimumab, infliximab, golimumab, certolizumab pegol, secukinumab) • Apremilast For people whose disease has not responded adequately to non-biological DMARDs and 1 or more TNF-alpha inhibitors: • Ustekinumab • Certolizumab pegol • Secukinumab • Best supportive care For people in whom TNF-alpha inhibitors are contraindicated: • Ustekinumab • Secukinumab • Best supportive care
Outcomes	The outcome measures to be considered include: • disease activity • functional capacity • disease progression • periarticular disease (for example enthesitis, tendonitis, dactylitis) • mortality • adverse effects of treatment • health-related quality of life.

Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any patient access schemes for the intervention or comparator technologies will be taken into account. For the comparators the availability and cost of biosimilars should be taken into consideration.
Other considerations	If evidence allows the following subgroups will be considered: • the reason for treatment failure (for example due to lack of efficacy, intolerance or adverse events) • presence or severity of concomitant psoriasis (no psoriasis, mild to moderate psoriasis, moderate to severe psoriasis) Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: 'Certolizumab pegol and secukinumab for treating active psoriatic arthritis after inadequate response to DMARDs' (2017). NICE Technology Appraisal 445. Review date May 2020. 'Apremilast for treating active psoriatic arthritis' (2017). NICE Technology Appraisal 433. Review date February 2020. 'Ustekinumab for treating active psoriatic arthritis' (2015). NICE Technology Appraisal 340. Guidance on static list. 'Golimumab for the treatment of psoriatic arthritis' (2011). NICE Technology Appraisal 220. Guidance on static list.

	'Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis (review of technology appraisal guidance 104 and 125)' (2010). NICE Technology Appraisal 199. Guidance on static list. Related Guidelines: 'Psoriasis: assessment and management' (2012). NICE clinical guideline 153. Review Proposal Date February 2017. 'Spondyloarthritis in over 16s: diagnosis and management' (2017). NICE clinical guideline 153. Review Proposal Date TBC 'The diagnosis and management of spondyloarthritis'. Last updated: March 2017. Related Quality Standards: 'Psoriasis' (2013). Quality Standard 40. Review Proposal Date TBC Related NICE Pathways: NICE Pathway: musculoskeletal conditions, Pathway last updated March 2017.
Related National Policy	NHS England (2016) 'Manual for Prescribed Specialised Services'. Chapter 5, Adult highly specialist rheumatology services Department of Health, NHS Outcomes Framework 2016-2017, April 2016. Domains 2 to 5. https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/06/pss-manual-may16.pdf

References

[1]Psoriasis Association (2014) 'Psoriatic Arthritis' Accessed March 2017

[2] Ogdie, A., Langan, S., Love, T., Haynes, K., Shin, S., Seminara, N., Mehta, N., Troxel, A., Choi, H., Gelfand, J. (2013) 'Prevalence and treatment patterns of psoriatic arthritis in the UK'. Rheumatology (Oxford) Mar 52(3): 568-75

[3] Office for National Statistics (2015) 'Population estimates mid-year 2014'