NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Ixekizumab for treating axial spondyloarthritis after NSAIDs

Final scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of ixekizumab within its marketing authorisation for treating axial spondyloarthritis.

Background

Axial spondyloarthritis belongs to a clinically heterogeneous group of inflammatory rheumatologic diseases which share common genetic, histological and clinical features (also including psoriatic arthritis, arthritis associated with inflammatory bowel disease, reactive arthritis and undifferentiated spondyloarthritis). Axial spondyloarthritis involves inflammation of the sacroiliac joints and spine. If inflammation is visible on x-ray (as erosions, thickening of the bone, or fusion of joints), the disease is classified as radiographic axial spondyloarthritis (also known as ankylosing spondylitis). If x-rays of the sacroiliac joints and spine are normal, but there are other objective signs of inflammation (elevated C-reactive protein or evidence on magnetic resonance imaging) the disease is classified as non-radiographic axial spondyloarthritis.

The clinical symptoms of axial spondyloarthritis can vary from person to person, but usually develop slowly over several months or years. The main symptoms can include back pain, arthritis (inflammation of the joints in other parts of the body), enthesitis (inflammation where a bone is joined to a tendon), and fatigue. Extra-articular manifestations include uveitis, inflammatory bowel disease and psoriasis. The onset of symptoms typically occurs in the third decade of life, but it can be 7–10 years before a diagnosis is made.

Non-radiographic axial spondyloarthritis affects approximately equal numbers of men and women, but there are limited data on the prevalence of the condition. Some people with non-radiographic axial spondyloarthritis will develop radiographic axial spondyloarthritis (about 10% of people over 2 years, and 50% over 10 years[1]). Around 200,000 people have been diagnosed with axial spondyloarthritis in the UK.[2,3]

Conventional therapy for radiographic axial spondyloarthritis includes anti-inflammatory treatment with non-steroidal anti-inflammatory drugs (NSAIDs) and physiotherapy. NICE technology appraisal 383 recommends the tumour necrosis factor alpha (TNF-alpha) inhibitors, adalimumab, certolizumab pegol, etanercept, golimumab and infliximab as treatment options for adults with severe active ankylosing spondylitis in adults whose disease has responded inadequately to, or who cannot tolerate NSAIDs. Biosimilar versions of

adalimumab, etanercept and infliximab are available. Infliximab is only recommended if the least expensive infliximab product is used. NICE technology appraisal 407 recommends the interleukin-17A (IL-17A) inhibitor secukinumab as an alternative to, or after inadequate response to TNF-alpha inhibitors.

Conventional therapy for non-radiographic axial spondyloarthritis also includes anti-inflammatory treatment with NSAIDs and physiotherapy. NICE technology appraisal guidance 383 and 497 recommend TNF-alpha inhibitors adalimumab, certolizumab pegol, etanercept and golimumab as treatment options in people with disease that does not respond adequately to or cannot tolerate NSAIDs.

The technology

Ixekizumab (Taltz, Eli Lilly) is a human monoclonal antibody which specifically inhibits the IL-17A receptor (both IL-17A and IL-17A/F). Ixekizumab is administered by subcutaneous injection.

Ixekizumab does not have a marketing authorisation in the UK for axial spondyloarthritis. It has been studied in clinical trials compared with placebo in adults with spondyloarthritis whose disease had responded inadequately to or who are intolerant to non-steroidal anti-inflammatory drugs (radiographic and non-radiographic spondyloarthritis) or TNF alpha inhibitors (radiographic spondyloarthritis only).

Intervention(s)	Ixekizumab
Population(s)	People with axial spondyloarthritis for whom non-steroidal anti-inflammatory drugs or TNF-alpha inhibitors have been inadequately effective or not tolerated, or are contraindicated.
Comparators	**Radiographic axial spondyloarthritis** • TNF-alpha inhibitors (adalimumab, certolizumab pegol, etanercept, golimumab, infliximab) • IL-17A inhibitors (secukinumab) • Established clinical management without biological treatments **Non-radiographic axial spondyloarthritis** • TNF-alpha inhibitors (adalimumab, certolizumab pegol, etanercept, golimumab) • Established clinical management without biological treatments

Outcomes	The outcome measures to be considered include: • disease activity • functional capacity • disease progression • pain • peripheral symptoms (including enthesitis, peripheral arthritis and dactylitis) • symptoms of extra-articular manifestations (including uveitis, inflammatory bowel disease and psoriasis) • 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. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost-comparison may be carried out. 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 commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.
Other considerations	If the evidence allows the subgroups of people who have had or not had TNF-alpha inhibitors will be considered. The availability and cost of biosimilar products should be taken into account. 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:** 'Golimumab for treating non-radiographic axial spondyloarthritis' (2018) NICE technology appraisal 497. Review date December 2020. 'TNF-alpha inhibitors for ankylosing spondylitis and non-radiographic axial spondyloarthritis' (2016) NICE technology appraisal 383. Review date June 2021. 'Secukinumab for active ankylosing spondylitis after treatment with non-steroidal anti-inflammatory drugs or TNF-alpha inhibitors' (2016) NICE technology appraisal 407. Review date 2019. **Appraisals in development:** 'Secukinumab for treating non-radiographic axial spondyloarthritis' Proposed NICE technology appraisal [ID 1419]. Expected publication date August 2020.. **Related Guidelines:** 'Spondyloarthritis in over 16s: diagnosis and management' (2017) NICE guideline 65. Review date to be confirmed. **Related Quality Standards:** 'Spondyloarthritis'. NICE quality standard 170. **Related NICE Pathways:** 'Spondyloarthritis' (2017) NICE pathway
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Adult highly specialist rheumatology services [section 5, page 30]. Department of Health and Social Care, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1,2,4 and 5.

References

1 Siper J and Heijde van der D (2013) Non-radiographic axial spondyloarthritis. Arthritis and Rheumatism 65: 543–51

2 National Ankylosing Spondyloarthritis Society: Facts & Figures. Available at https://nass.co.uk/about-as/as-facts-and-figures/ Accessed November 2018

3 Department of Health (2006) The musculoskeletal services framework. Accessed November 2018