NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Upadacitinib for treating active psoriatic arthritis after inadequate response to DMARDs

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of upadacitinib within its marketing authorisation for treating active psoriatic arthritis.

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] In around 70% of people psoriasis precedes psoriatic arthritis.[2] The prevalence of psoriatic arthritis in England in 2018 was estimated to be around 83,700 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.[2]

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. Axial inflammation might also occur in some cases. 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. Nail symptoms include swelling, discolouration and pitting.

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 and other non-conventional DMARDs (such as Janus kinase inhibitors and IL-17 inhibitors) may be used for treating people with active psoriatic arthritis. NICE recommends adalimumab, etanercept, infliximab, golimumab, certolizumab pegol, apremilast, ixekizumab, secukinumab or tofacitinib 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 (NICE technology appraisal 199, 220, 445, 433, 537, and 543). Certolizumab pegol is also recommended when the disease has stopped responding to a TNF-alpha inhibitor after the first 12 weeks (NICE technology appraisal 445). Ixekizumab, secukinumab and tofacitinib are also recommended in people whose disease has not responded within 12 weeks or stopped responding after 12 weeks of treatment with a TNF-alpha inhibitor or when TNF-alpha inhibitors are contraindicated but would otherwise be

considered (NICE Technology appraisal guidance 537, 445 and 543). Ustekinumab is recommended 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 (NICE technology appraisal 340). Biosimilar products for some of the biological therapies are available for use in the NHS.

The technology

Upadacitinib (Rinvoq, AbbVie) is a selective and reversible Janus-kinase (JAK) 1 inhibitor that blocks the JAK-signal transducer and activator of transcription (STAT) pathway and inflammatory responses. It is administered orally.

Upadacitinib 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 at least 1 DMARD. Inclusion criteria in an identified clinical trial specifies upadacitinib may be used alone, or in combination with up to 2 non-biological DMARDs. It has a marketing authorisation in the UK for treating moderate to severe active rheumatoid arthritis in adults who have responded inadequately to, or who are intolerant to one or more DMARDs.

Intervention(s)	Upadacitinib, alone or in combination with non-biological disease modifying anti-rheumatic drugs (DMARDs)
Population(s)	Adults with active psoriatic arthritis whose disease has not responded adequately to a previous DMARD therapy, or for whom DMARDs are not tolerated or contraindicated

Comparators	For people whose disease has not responded adequately to 1 conventional disease modifying anti-rheumatic drug (DMARD): • Conventional DMARDs For people whose disease has not responded adequately to at least 2 conventional DMARDs: • Biological DMARDs (with or without methotrexate, including etanercept, adalimumab, infliximab, golimumab, certolizumab pegol, ixekizumab and secukinumab) • Apremilast • Tofacitinib For those whose disease has not responded adequately to conventional DMARDs and 1 or more TNF-alpha inhibitors: • Ustekinumab • Secukinumab • Certolizumab pegol • Tofacitinib • Ixekizumab • Best supportive care For people in whom TNF-alpha inhibitors are contraindicated or not tolerated: • Ustekinumab • Secukinumab • Ixekizumab • Tofacitinib • Best supportive care
Outcomes	The outcome measures to be considered include: • disease activity • functional capacity • disease progression • periarticular disease (for example enthesitis, tendonitis, dactylitis) • axial outcomes (for example, spinal pain and fatigue) • 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. 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 or comparator technologies and subsequent treatments 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 previous treatment failure (for example due to lack of efficacy, intolerance or adverse events) • mechanism of action or number of previous treatments • presence or severity of concomitant psoriasis (no psoriasis, mild, moderate or severe psoriasis) • presence or severity of axial involvement 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** 'Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis (review of technology appraisal guidance 104 and 125)' (2010). NICE Technology Appraisal 199 (moved to the static list). 'Golimumab for the treatment of psoriatic arthritis' (2011). NICE Technology Appraisal 220 (moved to the static list). 'Ustekinumab for treating active psoriatic arthritis' (2015). NICE Technology Appraisal 340 (moved to the static list). 'Certolizumab pegol and secukinumab for treating active psoriatic arthritis following inadequate response to disease

	modifying anti-rheumatic drugs' (2017) NICE Technology Appraisals 445. Review date: 2020 'Apremilast for treating active psoriatic arthritis' (2017) NICE Technology Appraisal 433 'Ixekizumab for treating active psoriatic arthritis following inadequate response to disease-modifying anti-rheumatic drugs' (2018) NICE Technology Appraisals 537. 'Tofacitinib for treating active psoriatic arthritis after inadequate response to DMARDs' (2018) NICE Technology Appraisals 543. **Terminated appraisals** 'Abatacept for treating psoriatic arthritis after DMARDs' (terminated appraisal) (2019) NICE Technology Appraisals 568. **Appraisals in development (including suspended appraisals):** 'Guselkumab for treating active psoriatic arthritis after inadequate response to DMARDs' Proposed technology appraisal [ID1658]. Publication date to be confirmed. **Related Guidelines:** 'Psoriasis: assessment and management' (2012). NICE clinical guideline 153. Last updated: September 2017. 'Spondyloarthritis in over 16s: diagnosis and management' (NG65) Published in February 2017. Last updated: June 2017 **Related Quality Standards:** 'Spondyloarthritis' (2018). Quality Standard 170. Last updated June 2018 'Psoriasis' (2013). Quality Standard 40. Last updated: April 2017. **Related NICE Pathways:** NICE Pathway: musculoskeletal conditions, Pathway last updated 2018. NICE Pathway: psoriasis, Pathway last updated 2019
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) Chapter 5, Adult highly specialist rheumatology services Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 2 to 5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

References

[1]Psoriasis Association (2018) 'Psoriasis Arthritis' Accessed July 2020

[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 (2019) Population estimates mid-year 2018 Accessed July 2020