NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Filgotinib for treating moderate to severe rheumatoid arthritis

Final scope

Final remit/appraisal objective

To appraise the clinical and cost effectiveness of filgotinib within its marketing authorisation for treating moderate to severe rheumatoid arthritis.

Background

Rheumatoid arthritis is an inflammatory autoimmune disease that typically affects the synovial tissue of the small joints of the hands and feet but can affect any synovial joint, causing swelling, stiffness, pain and progressive joint destruction. It is a systemic disease and can affect the whole body, including the lungs, heart and eyes. Rheumatoid arthritis is usually a chronic relapsing condition which has a pattern of flare-ups followed by periods of lower disease activity; however, for some people, the disease is constantly progressive. Rheumatoid arthritis has a severe impact on quality of life and it is estimated that approximately one-third of people stop work within 2 years because of the disease, and this prevalence increases thereafter. Severity of disease can be classified into 4 categories, based on the disease activity score (DAS28) scoring system. A DAS28 greater than 5.1 indicates high disease activity or severe disease, between 3.2 and 5.1 indicates moderate disease activity, less than 3.2 indicates low disease activity, and less than 2.6 indicates disease remission.

The prevalence of rheumatoid arthritis in the UK is estimated to be 0.44% in males and 1.16% in females;[1] which is approximately 450,000 people in England (122,000 males and 328,000 females).[1,2] There are approximately 17,500 people diagnosed with rheumatoid arthritis every year in England.[2,3,4] It can develop at any age, but the peak age of onset in the UK is between 45 and 75 years.[4]

There is no cure for rheumatoid arthritis and treatment aims to improve quality of life and to prevent or reduce joint damage. The main aim of management in early disease is to suppress disease activity and induce disease remission, prevent loss of function, control joint damage, maintain pain control and enhance self-management. For people with newly diagnosed rheumatoid arthritis, NICE guideline 100 ('Rheumatoid arthritis in adults: management') recommends monotherapy with conventional disease modifying anti-rheumatic drugs (DMARDs; including methotrexate, leflunomide and sulfasalazine) as first-line treatment, ideally beginning within 3 months of the onset of persistent symptoms. When disease remission or low disease activity has not been achieved with DMARD monotherapy it is recommended that additional conventional DMARDs (oral methotrexate, leflunomide, sulfasalazine or hydroxychloroquine) are used in combination. Where the disease has not responded to intensive combination therapy with conventional DMARDs, NICE Technology appraisal guidance 375, 466, 480 and 485 recommend biological DMARDs (adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab, abatacept and sarilumab) or other immunomodulatory therapies (baricitinib and tofacitinib) each in combination with methotrexate for severe rheumatoid arthritis only. For those people with severe rheumatoid arthritis who

cannot take methotrexate because it is contraindicated or because of intolerance, the guidance recommends that adalimumab, etanercept, certolizumab pegol, tocilizumab, baricitinib, sarilumab or tofacitinib monotherapy can be used.

Where the disease has not responded adequately or in the case of intolerance to other DMARDs, including at least one TNF inhibitor (a therapy subset of biological DMARDs), rituximab in combination with methotrexate is recommended for severe active disease only (NICE Technology appraisal guidance 195). Where rituximab is contraindicated or withdrawn because of an adverse event, biological DMARDs (adalimumab, etanercept, infliximab, abatacept, golimumab, tocilizumab, certolizumab pegol and sarilumab) or other immunomodulatory therapies (tofacitinib and baricitinib) each in combination with methotrexate are recommended as options (NICE Technology appraisal guidance 195, 225, 247 ,415, 466, 480 and 485). Where rituximab therapy cannot be given because methotrexate is contraindicated or has been withdrawn due to an adverse event, biological DMARDs (adalimumab, etanercept, certolizumab pegol and sarilumab) or other immunomodulatory therapies (tofacitinib and baricitinib) each as a monotherapy, can be used (NICE Technology appraisal guidance 195, 415, 466, 480 and 485).

The technology

Filgotinib (brand name unknown, Gilead) is a selective Janus-kinase (JAK) 1 inhibitor that blocks the JAK-signal transducer and activator of transcription (STAT) pathway and inflammatory responses. It is administered orally.

Filgotinib does not currently have a marketing authorisation in the UK for rheumatoid arthritis. It has been studied in clinical trials for adults with moderate to severe rheumatoid arthritis:

- in combination with methotrexate, compared with placebo or adalimumab in combination with methotrexate; for rheumatoid arthritis that has not responded adequately to treatment with methotrexate

- in combination with conventional DMARDs, compared with placebo in combination with conventional DMARDs; for rheumatoid arthritis that has not responded adequately to therapy with at least 1 biological DMARD

Intervention(s)	Filgotinib (as monotherapy or in combination with other conventional DMARDs, including methotrexate)
Population(s)	Adults with moderate to severe, active rheumatoid arthritis, whose disease has responded inadequately to, or who are intolerant of conventional or biological DMARDs

Comparators	For moderate active rheumatoid arthritis that has not responded adequately to therapy with conventional DMARDs: • Combination of two or more conventional DMARDs (including methotrexate and at least one other DMARD, such as sulfasalazine and leflunomide) • Conventional DMARD monotherapy with dose escalation • Best supportive care For severe active rheumatoid arthritis that has not responded adequately to therapy with conventional DMARDs: • Biological DMARDs in combination with methotrexate (adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab, abatacept or sarilumab) • Adalimumab, etanercept, certolizumab pegol, tocilizumab or sarilumab (each as monotherapy) • Tofacitinib, baricitinib or upadacitinib (each as monotherapy or in combination with methotrexate) For severe active rheumatoid arthritis that has not responded adequately to therapy with DMARDs including at least one TNF inhibitor: • Rituximab in combination with methotrexate When rituximab is contraindicated or withdrawn due to adverse events: • Adalimumab, etanercept, infliximab, abatacept tocilizumab, certolizumab pegol, golimumab or sarilumab (each in combination with methotrexate) Tofacitinib, baricitinib, or upadacitinib (each in combination with methotrexate)When methotrexate is contraindicated or withdrawn due to adverse events: • Adalimumab, etanercept, certolizumab pegol or sarilumab (each as monotherapy) • Tofacitinib, baricitinib, or upadacitinib (each as monotherapy) When the disease has not responded adequately to therapy with rituximab in combination with methotrexate**:** • Tocilizumab, sarilumab (each in combination with methotrexate) • Upadacitinib (in combination with methotrexate)

Outcomes	The outcome measures to be considered include: • disease activity • physical function • joint damage, pain • mortality • fatigue • radiological progression • extra-articular manifestations of disease • 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 technologies and subsequent treatment technologies will be taken into account. The availability and cost of biosimilar products should be taken into account.
Other considerations	If the evidence allows the following subgroups will be considered. These include people with moderate disease activity (DAS28 between 3.2 and 5.1) and severe active disease (DAS28 greater than 5.1). 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**: Sarilumab for moderate to severe rheumatoid arthritis (2017) NICE Technology Appraisal 485.

	Tofacitinib for moderate to severe rheumatoid arthritis (2017) NICE Technology Appraisal 480. Baricitinib for moderate to severe rheumatoid arthritis (2017) NICE Technology Appraisal 466. Certolizumab pegol for treating rheumatoid arthritis after inadequate response to a TNF-alpha inhibitor (2016) NICE Technology Appraisal 415. Review Date October 2019 Adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept for rheumatoid arthritis not previously treated with DMARDs or after conventional DMARDs only have failed (2016) NICE Technology Appraisal 375 (previously TA130, TA186 and TA280). Tocilizumab for the treatment of rheumatoid arthritis (2012) NICE Technology Appraisal 247. Golimumab for the treatment of rheumatoid arthritis after the failure of previous disease modifying anti-rheumatic drugs. (2011) NICE Technology Appraisal 225. Adalimumab, etanercept, infliximab, rituximab and abatacept for the treatment of rheumatoid arthritis after the failure of a TNF inhibitor. (2010) NICE Technology Appraisal TA195. **Appraisals in development:** Upadacitinib for treating moderate to severe rheumatoid arthritis. NICE technology appraisals guidance [ID1400] Expected publication date: March 2020 Sirukumab for previously treated moderate to severe active rheumatoid arthritis NICE technology appraisals guidance [ID1002] (suspended appraisal) Rituximab for the treatment of rheumatoid arthritis after the failure of conventional disease-modifying anti-rheumatic drugs NICE technology appraisals guidance [ID333] (suspended appraisal) **Related Guidelines:** Rheumatoid arthritis in adults: management (2018) NICE guideline NG100. Review date to be confirmed. **Related Quality Standards:** Rheumatoid arthritis in over 16s (2017) NICE Quality Standard QS33. **Related NICE Pathways:** 'Rheumatoid arthritis' (2019). 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 30-32] Department of Health and Social Care, NHS Outcomes Framework 2016-2017 (updated 2020): Domains 1-5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 National Service Frameworks for Older People: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/198033/National_Service_Framework_for_Older_People.pdf

References

1 Symmons D et al. (2002) The prevalence of rheumatoid arthritis in the United Kingdom: new estimates for a new century. Rheumatology 41 (7): 793-800.

2.Office for National Statistics (2019) 'Population estimates for the UK, England and Wales, Scotland and Northern Ireland: mid-2018'. Accessed July 2019.

3. Symmons D et al. (2012) The incidence of rheumatoid arthritis in the UK: comparisons using the 2010 ACR/EULAR classification criteria and the 1987 ACR classification criteria. Results from the Norfolk Arthritis Register. Annals of the Rheumatic Diseases 72: 1315-1320.

4. Arthritis Research UK Musculoskeletal Calculator. Accessed July 2019.