NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Certolizumab pegol for treating rheumatoid arthritis after inadequate response to a TNF inhibitor [ID824]

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of certolizumab pegol within its marketing authorisation for treating rheumatoid arthritis after inadequate response to a TNF inhibitor.

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.

Estimates of the number of people in England with rheumatoid arthritis vary between about 360,000 and about 690,000. Approximately 15% of people with rheumatoid arthritis have severe disease. Rheumatoid arthritis is about 2 to 3 times more prevalent in women than in men. It can develop at any age, but the usual age of onset in the UK is about 40–70 years.

There is no cure for rheumatoid arthritis and treatment aims to improve quality of life and to prevent or reduce joint damage. Treatment for rheumatoid arthritis usually includes: non-steroidal anti-inflammatory drugs which reduce pain, fever and joint swelling/inflammation, and disease modifying anti-rheumatic drugs (DMARDs). DMARDs may be broadly classed as either non-biological or biological. Non-biological DMARDs include methotrexate, leflunomide and sulfasalazine, while the latter group includes, but is not limited to, tumour necrosis factor (TNF) inhibitors. DMARDs slow the disease process and 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. In established disease, management should address complications, associated comorbidities; and quality of life.

Rituximab in combination with methotrexate is recommended as an option for people with severe rheumatoid arthritis who have had an inadequate response to DMARDs or are intolerant to DMARDs, including a TNF inhibitor (TA195). Abatacept (TA195), adalimumab (TA195), etanercept (TA195), golimumab (TA225), infliximab (TA195) and tocilizumab (TA247) each in combination with methotrexate are recommended as treatment options only if rituximab therapy is contraindicated or is withdrawn because of an adverse event. If the person cannot receive rituximab therapy because they have a contraindication to methotrexate or methotrexate is withdrawn because of an adverse event, adalimumab and etanercept can be given as monotherapy (TA195). If the disease does not respond adequately to 1 or more TNF inhibitors and rituximab, tocilizumab in combination with methotrexate can be given (TA247).

The technology

Certolizumab pegol (Cimzia, UCB Pharma) is an inhibitor of TNF alpha, a pro-inflammatory mediator that is partly responsible for damage to the joints in rheumatoid arthritis. It is administered subcutaneously.

Certolizumab pegol in combination with methotrexate, has a marketing authorisation in the UK for the treatment of moderate to severe, active rheumatoid arthritis in adult patients when the response to DMARDs, including methotrexate, has been inadequate. Certolizumab pegol can be given as monotherapy in case of intolerance to methotrexate or when continued treatment with methotrexate is inappropriate.

Intervention(s)	Certolizumab pegol monotherapy or in combination with methotrexate
Population(s)	Adults with moderate to severe, active rheumatoid arthritis whose disease has not responded adequately to a TNF inhibitor
Comparators	For adults previously treated with other DMARDs including at least 1 TNF inhibitor • Rituximab in combination with methotrexate For adults for whom rituximab is contraindicated or withdrawn • Abatacept, adalimumab, etanercept, golimumab, infliximab and tocilizumab each in combination with methotrexate For adults for whom rituximab therapy cannot be given because methotrexate is contraindicated or withdrawn • Adalimumab monotherapy, etanercept monotherapy or tocilizumab monotherapy

	For people with moderate to severe, active disease despite treatment with biological DMARDs recommended according to NICE guidance • Best supportive care
Outcomes	The outcome measures to be considered include: • disease activity • physical function • joint damage • pain • mortality • fatigue • radiological progression • extra-articular manifestations of the 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. 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 should be taken into account. The availability and cost of biosimilar products should be taken into account.

Other considerations	If evidence allows, the appraisal will consider subgroups of people identified as: • having had primary or secondary failure of response to the first TNF inhibitor; or • having seronegative or seropositive antibody status. If the evidence allows, the appraisal will include the costs of joint replacement therapy and hospital admissions. 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: Technology Appraisal in Preparation, 'Adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, abatacept and tocilizumab for the treatment of rheumatoid arthritis (review of TA guidance 130, 186, 224, 234 and part review of TA guidance 225 and 247)'. Earliest anticipated date of publication TBC. Technology Appraisal No. 247, Feb 2012, 'Tocilizumab for the treatment of rheumatoid arthritis (rapid review of technology appraisal guidance 198)'. Guidance being part reviewed as part of the multiple technology appraisal currently in development. Technology Appraisal No. 280, Apr 2013, 'Abatacept for treating rheumatoid arthritis after the failure of conventional disease-modifying anti-rheumatic drugs (rapid review of technology appraisal guidance 234). Guidance being reviewed as part of the multiple technology appraisal currently in development. Technology Appraisal No. 225, Jun 2011, 'Golimumab for the treatment of rheumatoid arthritis after the failure of previous disease-modifying anti-rheumatic drugs. Guidance being part reviewed as part of the multiple technology appraisal currently in development. Technology Appraisal No. 195, Aug 2010, 'Adalimumab, etanercept, infliximab, rituximab and abatacept for the treatment of rheumatoid arthritis after the failure of a TNF inhibitor'. Transferred to the static list in September 2013. Technology Appraisal No. 186, Feb 2010, 'Certolizumab

	pegol for the treatment of rheumatoid arthritis'. Guidance being reviewed as part of the multiple technology appraisal currently in development. Technology Appraisal No. 130, Oct 2007, 'Adalimumab, etanercept and infliximab for the treatment of rheumatoid arthritis'. Guidance being reviewed as part of the multiple technology appraisal currently in development. Related Guidelines: Clinical Guideline No. 79, Original publication date Feb 2009 (partially updated December 2015) 'Rheumatoid arthritis: The management of rheumatoid arthritis in adults'. Related Quality Standards: Quality Standard No. 33, Jun 2013, 'Quality standard for rheumatoid arthritis'. Review Proposal Date unknown. http://www.nice.org.uk/guidance/qualitystandards/qualitystandards.jsp Related NICE Pathways: NICE Pathway: Rheumatoid arthritis, Pathway created: Jun 2013. http://pathways.nice.org.uk/pathways/rheumatoid-arthritis
Related National Policy	NHS England: NHS England Manual for prescribed specialised services 2013/14. Section 5: Adult highly specialist rheumatology services. NHS England & BMJ Group. Shared Decision Making Sheets: Rheumatoid Arthritis. NHS England. A13. Specialised Rheumatology. National programmes of care and clinical reference groups. National Service Frameworks: Older People Department of Health: Department of Health (2013) NHS Outcomes Framework 2014-2015