NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Certolizumab pegol for treating rheumatoid arthritis following inadequate response to a TNF inhibitor

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of certolizumab pegol within its marketing authorisation for treating rheumatoid arthritis after failure of 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.

Rheumatoid arthritis affects approximately 690,000 people in England. Of these, approximately 15% have severe disease. It is about two- to four-times more prevalent in women than in men. It can develop at any age, but the peak 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. Corticosteroids may also be used to control inflammation. 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 and associated comorbidity; and the impact of the condition on the patient's 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 alone or in combination with methotrexate
Population(s)	Adults with moderate to severe 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 previously treated with TNF inhibitors and rituximab • Tocilizumab in combination with methotrexate For adults for whom rituximab is contraindicated or withdrawn • Abatacept, adalimumab, etanercept, golimumab and infliximab each in combination with methotrexate For adults for whom rituximab therapy cannot be given

	because methotrexate is contraindicated or withdrawn • Adalimumab monotherapy, etanercept monotherapy
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 of comparator technologies 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. If evidence allows, the appraisal will consider subgroups of people identified as sero-negative or sero-positive. 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. 234, 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, Feb 2009 'Rheumatoid arthritis: The management of rheumatoid arthritis in adults'. Review Proposal Date Mar 2015. 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 (January 2014) "CCGs commission all other rheumatological services, including…Rheumatoid Arthritis." Manual for prescribed specialised services 2013/14. Page 24. 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

Questions for consultation

Have all relevant comparators for certolizumab pegol been included in the scope? Which treatments are considered to be established clinical practice in the NHS for rheumatoid arthritis? Are non-biological DMARDs (such as methotrexate, sulfasalazine, leflunomide) an appropriate comparator for certolizumab pegol in adults whose disease has not responded adequately to a TNF inhibitor?

Are biosimilars expected to be established clinical practice within the next 12 months for the treatment of rheumatoid arthritis?

Are the subgroups suggested in 'other considerations appropriate? Are there any other subgroups of people in whom certolizumab pegol is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider certolizumab pegol will fit into the existing NICE pathway, Rheumatoid Arthritis?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the

proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which certolizumab pegol is licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider certolizumab pegol to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of certolizumab pegol can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction)