

National Horizon Scanning Centre

Golimumab (CNTO-148) for rheumatoid arthritis

December 2007



This technology summary is based on information available at the time of research and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes.

Golimumab (CNTO-148) for rheumatoid arthritis

Target group

- Rheumatoid arthritis (RA) - adults:
 - Naive to methotrexate (MTX);
 - Active disease despite MTX and/or anti-tumour necrosis factor- α (TNF α) therapy.

Technology description

Golimumab (CNTO-148) is a high affinity, fully humanised anti-TNF α monoclonal antibody that is being developed for intravenous (iv) and subcutaneous (sc) administration¹. Golimumab is intended to be used as monotherapy or in combination with methotrexate to reduce signs and symptoms, and to reduce structural damage.

Golimumab is also in phase III clinical trials for ankylosing spondylitis and psoriatic arthritis.

Innovation and/or advantages

Golimumab is the first anti-TNF agent with both sc and iv formulations with less frequent administration compared to current anti-TNF products.

Developer

Centocor (Marketing Authorisation holder); Schering-Plough (Distributor).

Place of use

- | | | |
|---|---|--|
| <input checked="" type="checkbox"/> Home care: sc for patient self-administration in the home | <input type="checkbox"/> Community or residential care e.g. district nurses, physio | <input type="checkbox"/> Primary care e.g. used by GPs or practice nurses |
| <input checked="" type="checkbox"/> Secondary care e.g. general, non-specialist hospital | <input checked="" type="checkbox"/> Tertiary care e.g. highly specialist services or hospital | <input type="checkbox"/> Emergency care e.g. paramedic services, trauma care |
| <input type="checkbox"/> General public e.g. over the counter | <input type="checkbox"/> Other: | |

Availability, launch or marketing dates, and licensing plans:

In phase III clinical trials.

NHS or Government priority area:

This topic is relevant to the Long-term (Neurological) Conditions National Service Framework and the Musculoskeletal Services Framework.

Relevant guidance

NICE guidance – published

- NICE Technology Appraisal. Rituximab for the treatment of rheumatoid arthritis (refractory). August 2007².
- NICE Technology Appraisal. Anakinra for the treatment of rheumatoid arthritis. November 2003³.
- NICE Technology Appraisal. Etanercept and infliximab for the treatment of rheumatoid arthritis and juvenile poly-articular idiopathic arthritis. 2002⁴.

NICE guidance – in development

- NICE Clinical Guideline. Rheumatoid arthritis in adults. Expected December 2008⁵.
- NICE Technology Appraisal. Adalimumab, etanercept and infliximab for the treatment of rheumatoid arthritis. Expected December 2007⁶.

- NICE Technology Appraisal. Abatacept for the treatment of rheumatoid arthritis. Expected December 2008⁷.

Other guidance

- The British Society of Rheumatology (BSR) updated guidelines for prescribing TNF α in adults with rheumatoid arthritis (2004)⁸.
- The British Society of Rheumatology guidelines on standards of care for persons with rheumatoid arthritis (2004)⁹.
- Scottish Intercollegiate Guidelines Network (SIGN): Management of early rheumatoid arthritis. Publication 48, December 2000¹⁰.

Clinical need and burden of disease

Rheumatoid arthritis is the most common inflammatory polyarthropathy in the UK, affecting around 1% of the population (over 400,000 people in England and Wales)¹¹, with the disease being severe in about 15% of patients. It is 2 to 3 times more common in women than in men and usually develops between the ages of 40 and 60 years^{12,13,14}.

Existing comparators and treatments

The clinical management of RA includes physical therapy, surgical interventions, and a range of pharmacological treatments including:

Non-biologic therapies

- Analgesics
- Corticosteroids
- Non-steroidal anti-inflammatory drugs (NSAIDs)
- Disease modifying anti-rheumatic drugs (DMARDs), including methotrexate (MTX), sulphalazine, leflunomide and cyclophosphamide (CTX). Usually administered within three months of diagnosis to stabilise joint function, either as monotherapies or in combination with biologic agents.

Biologic therapies

- Anti TNF α agents such as etanercept (enbrel), infliximab (remicade), adalimumab (humira).
- Anakinra (an interleukin-1 antagonist)
- Rituximab (MabThera), a genetically engineered chimeric monoclonal antibody selective B-cell therapy, is used in combination with MTX for patients with severe active RA who have failed one or more anti-TNF therapy
- Abatacept (Orencia), a genetically engineered fusion protein of human CTLA4 and the IgG1 FC region, is used in combination with MTX for patients with severe active RA who have failed one or more anti-TNF therapy.

Approximately 60% of RA patients respond sufficiently to MTX in combination with biologics¹⁵.

Efficacy and safety

Trial name or code	C0524T02: Active RA; phase III.	C0524T05: Active RA; MTX-naïve; phase III.	C0524T06: Active RA despite MTX therapy; phase III.
Sponsor	Centocor, Schering Plough	Centocor, Schering Plough	Centocor, Schering Plough
Status	Completed, unpublished	Ongoing	Ongoing
Location	International	Austria, Belgium, Hungary, Poland, Spain, UK, Russia,	Germany, Hungary, Poland

		Ukraine.	
Design	Randomised, double-blind, placebo-controlled.	Randomised, double-blind, placebo-controlled.	Randomised, double-blind, placebo-controlled.
Participants in trial	n=172; adults; active RA. Randomised to golimumab 50 mg or 100 mg sc at either 2 or 4 week intervals with MTX; or placebo + MTX + infusion of infliximab 3 mg/kg at week 20, 22, 28, 36 and 44.	n=600; adults. Randomised to golimumab 50 mg or 100 mg, or placebo every 4 weeks until week 52 with MTX or placebo. At week 52, subjects on MTX alone with joint pain or swelling given golimumab 50 mg.	n=400; adults. Randomised to golimumab 50 mg or 100 mg, or placebo every 4 weeks to week 20. MTX or placebo also given. At week 24, all patients receive golimumab 50 mg or 100 mg
Follow-up	Duration of treatment 48 weeks with follow-up at 68 weeks	Duration of treatment 252 weeks	Duration of treatment 252 weeks
Primary outcome	ACR ^a 20 at week 16.	ACR 50 at week 24; van der Heijde Modified Sharp (vdH-S) score at week 52.	ACR 20 at week 14. HAQ at week 24
Secondary outcomes	ACR improvement at week 16; safety and tolerability.	Health Assessment Questionnaire (HAQ) at week 52; ACR20 at week 24; vdH-S score at week 52; ACR at week 24.	vdH-S score at week 24; Disease Activity Score (DAS) 28 (using C-reactive protein) at week 14; ACR20 at week 24; HAQ at week 14
Results	ACR 20 at week 16 61.3% golimumab plus MTX vs 37.1% placebo plus MTX (p=0.010). ACR 50 at week 16 was 30.7% and 5.7% in golimumab plus MTX and placebo plus MTX group (p=0.003).	-	-
Adverse effects	Clinically relevant adverse events with golimumab MTX (8% vs 5.9%) include: pneumonia, cardiac tamponade, and cardiac failure.	-	-

Trial name or code	C0524T11: Active RA; despite anti-TNF α agent(s); Phase III	C0524T12: Active RA despite MTX therapy (iv); Phase III
Sponsor	Centocor, Schering Plough	Centocor, Schering Plough
Status	Ongoing	Ongoing
Location	Europe	Europe
Design.	Randomised, double-blind, placebo-controlled.	Randomised, double-blind, placebo-controlled.
Participants in trial	n=420; adults; at least one dose of etanercept, adalimumab, or infliximab. Randomised to golimumab (50 mg or 100	n=625; adults; on MTX for at least 4 weeks. Golimumab 2 mg/kg or 4 mg/kg (given with or without MTX) every 12

^a ACR: the American College of Rheumatology criteria comprise a core set of six outcome variables for the assessment of clinically important improvement: physical global assessment of disease activity; patient/parent global assessment of overall well-being; functional ability; number of joints with active arthritis; number of joints with limited range of motion; erythrocyte sedimentation rate. ACR20, ACR50, and ACR70 represent a 20%, 50%, and 70% improvement in at least three response criteria (and with no more than one response variable worse by greater than 30%).

	mg) or placebo sc at week 0 and every 4 weeks through week 20. A long-term extension starts week 24; golimumab (50 mg or 100 mg) sc every 4 weeks through to week 252.	weeks for at least 48 weeks. Patients participating in the long-term extension will be switched from iv to sc golimumab after 48 weeks.
Primary outcome	ACR 20 at week 14.	ACR 50 at week 14
Secondary outcomes	ACR 50 at week 14; DAS 28 (using C-reactive protein) at week 14. ACR 20 week 24; HAQ score at week 24.	ACR 50 at week 24; ACR 20 at week 14; DAS 28 using CRP at week 14.

Estimated cost and cost impact

The unit cost of golimumab is yet to be determined. The costs of other licensed biologic treatments are^b:

Drug	Cost	Administration
Adalimumab	£358	40 mg pre-filled syringe, given on alternate weeks
Etanercept	£89	25 mg vial, given twice weekly
Infliximab	£420	100 mg vial, given every 8 weeks as maintenance
Rituximab	£1746	2x 500 mg vials, given twice (infusion) two weeks apart.
Abatacept ^c	£756	3x 250 mg vials, given at week 1, 2, 4 and 4-weekly thereafter (by infusion).

Potential or intended impact – speculative

Patients

- | | | |
|---|--|---|
| <input checked="" type="checkbox"/> Reduced morbidity | <input type="checkbox"/> Reduced mortality or increased survival | <input checked="" type="checkbox"/> Improved quality of life for patients and/or carers |
| <input type="checkbox"/> Quicker, earlier or more accurate diagnosis or identification of disease | <input type="checkbox"/> Other: | <input type="checkbox"/> Non identified |

Services

- | | | |
|--|--|---|
| <input type="checkbox"/> Increased use | <input type="checkbox"/> Service reorganisation required | <input type="checkbox"/> Staff or training required |
| <input type="checkbox"/> Decreased use | <input type="checkbox"/> Other: | <input checked="" type="checkbox"/> Non identified |

Costs

- | | | |
|---|--|---|
| <input type="checkbox"/> Increased unit cost compared to alternative | <input type="checkbox"/> Increased costs: more patients coming for treatment | <input type="checkbox"/> Increased costs: capital investment needed |
| <input checked="" type="checkbox"/> New costs: If used in people who have already received anti-TNF agents. | <input type="checkbox"/> Savings: | <input type="checkbox"/> Other: |

References

- ¹ Zhou H, Jang H, Fleischmann RM *et al.* Pharmacokinetics and safety of golimumab, a fully human anti-TNF-alpha monoclonal antibody, in subjects with rheumatoid arthritis. *Journal of Clinical Pharmacology* 2007; 47 (3); 383-96.
- 2 National Institute for Health and Clinical Excellence Technology Appraisal. Rituximab for the treatment of rheumatoid arthritis (refractory). August 2007: TA126.

^b British National Formulary (BNF) No. 54. September 2007.

^c Monthly Index of Medical Specialties (MIMS), July 2007. Cost for abatacept based on a 750 mg dose required for patients weighing 60-100kg.

- ³ National Institute for Clinical Excellence Technology Appraisal. Anakinra for the treatment of rheumatoid arthritis. November 2003: TA72.
- ⁴ National Institute for Clinical Excellence Technology Appraisal. Etanercept and infliximab for the treatment of rheumatoid arthritis and juvenile poly-articular idiopathic arthritis. 2002. TA36.
- ⁵ National Institute for Health and Clinical Excellence Clinical Guideline. Rheumatoid arthritis: the management and treatment of rheumatoid arthritis in adults. Expected Dec 2008.
- ⁶ National Institute for Health and Clinical Excellence Technology Appraisal. Adalimumab, etanercept and infliximab for the treatment of rheumatoid arthritis. Expected Dec 2007.
- ⁷ National Institute for Health and Clinical Excellence Technology Appraisal. Abatacept for the treatment of rheumatoid arthritis. Expected Dec 2008.
- ⁸ The British Society of Rheumatology (BSR) updated guidelines for prescribing TNF α in adults with rheumatoid arthritis (2004).
- ⁹ The British Society of Rheumatology guidelines on standards of care for persons with rheumatoid arthritis (2004).
- ¹⁰ Scottish Intercollegiate Guidelines Network (SIGN): Management of early rheumatoid arthritis. Publication 48, December 2000.
- ¹¹ National Institute for Health and Clinical Excellence Clinical Guideline (in preparation). Rheumatoid arthritis: the management and treatment of rheumatoid arthritis in adults. Final scoping document dated Feb 2007.
- ¹² Lawrence RC, Helmick CG, Arnett FC *et al*. Estimates of the prevalence of arthritis and selected musculoskeletal disorders in the United States, *Arthritis and Rheumatism* 1998; 41: 778-781.
- ¹³ Symmons DP, Barrett EM, Bankhead CR *et al*. The incidence of rheumatoid arthritis in the United Kingdom: results from the Norfolk Arthritis Register. *British Journal of Rheumatology* 1994; 33: 735-739.
- ¹⁴ National Rheumatoid Arthritis Society. What is Rheumatoid Arthritis? Available at: http://www.rheumatoid.org.uk/index.php?page_id=36 (accessed 3 Oct 2007).
- ¹⁵ Rindfleisch JA, Muller D. Diagnosis and management of rheumatoid arthritis. *American Family Physician* 2005; 15, 72 (6); 1037-47.

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