Appendix A

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Scope: **Etanercept, infliximab, adalimumab and golimumab for the treatment of psoriatic arthritis**

Document cover sheet
Remove before consultation

Timing	Action	Who	Initials	Date
pre-referral				
	Pre-referral draft scope forwarded to TA for comment	TL	JV	18032009
	Pre-referral draft scope updated following TA review	TL/TA	JV	26032009
	Pre-referral draft scope updated following CD review	TL/TA		
	Pre referral draft scope updated with **tracked changes** following consultation and scoping workshop	TL		
post-referral				
	Scope reviewed and updated if necessary	TL/IS		
If necessary	second consultation on scope	TL		
	scope updated following consultation	TL		
7 weeks before invitation to participate	Scope sign off report completed	TL/TA/ PM		
5 weeks before invitation to participate	Final scope signed off	AD		

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NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Etanercept, infliximab, adalimumab and golimumab for the treatment of psoriatic arthritis (incl. review of TA104 and TA125)

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost-effectiveness of etanercept, infliximab, adalimumab and golimumab, within their licensed indications, for the treatment of psoriatic arthritis.

Background

Psoriatic arthritis (PsA, psoriatic arthropathy) is an inflammatory arthritis closely associated with psoriasis. An estimated 5–7% of all people with psoriasis, and approximately 40% of those with extensive skin disease, have PsA. The prevalence of psoriatic arthritis in the UK is estimated to be around 0.1% to 0.3% of the total population (50,000 to 156,000 people in England and Wales). It affects men and women equally and its incidence peaks between the ages of 30 and 55 years.

Although PsA is a chronic progressive condition, its course may be erratic, with flare-ups and remissions. Arthritis symptoms can range from mild inflammation of the synovial membrane surrounding a joint (synovitis) to severe progressive erosion of the joints. When the spine is affected the condition may be indistinguishable from ankylosing spondylitis.

The relationship between the skin and joint manifestations is unclear. In 60% of people with the condition the psoriasis precedes the arthritis, in 25% of people the arthritis appears first and in 15% of people the symptoms occur simultaneously. People with severe arthritis can have little or no skin disease, and vice versa. Flare-ups of symptoms do not necessarily coincide.

PsA can significantly impair a person's quality of life and cause disability; both skin and joints can be affected and people with PsA report more 'role limitation' and body pain than people with rheumatoid arthritis.

Treatment for PsA aims to improve the psoriasis, arthritis or both. Mild PsA can be managed with non-steroidal anti-inflammatory drugs (NSAIDs) and physical therapy, with intra-articular corticosteroid injections when necessary. Disease modifying anti-rheumatic drugs (DMARDs), including azathioprine, methotrexate, sulphasalazine, ciclosporin and leflunomide, are additionally used in individuals with severe or progressive disease. Gold compounds and anti-malarial drugs are also used to treat psoriatic arthritis, but less commonly, and photochemotherapy may be used to treat peripheral arthritis.

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In addition, a tumour necrosis factor alpha (TNF-α) inhibitor may currently be used for the treatment of people with severe active PsA. NICE technology appraisal guidance recommended etanercept or adalimumab (TA104 and TA125 respectively) when a person has peripheral arthritis with three or more tender joints and three or more swollen joints, and the PsA has not responded to at least two other DMARDs, given on their own or together. Guidance no 104 also recommended infliximab if the person satisfies the criteria for treatment with etanercept, but is either intolerant of, or has contraindications to, treatment with etanercept, or has major difficulties with self administered injections.

The technologies

Etanercept (Enbrel, Wyeth Pharmaceuticals), infliximab (Remicade, Schering-Plough Ltd), adalimumab (Humira, Abbott Laboratories Ltd) and golimumab (CNTO – 148, Schering-Plough Ltd) all inhibit the activity of TNF alpha, one of the factors responsible for the damaging processes that affect articular cartilage and bone.

Etanercept, infliximab and adalimumab have marketing authorisations for the treatment of active and progressive PsA in patients who have responded inadequately to DMARDs. Etanercept and adalimumab are administered via subcutaneous injection. Infliximab can be administered by intravenous infusion either in combination with methotrexate or alone in patients who show intolerance to methotrexate or for whom methotrexate is contraindicated.

Golimumab does not have a marketing authorisation for the treatment of psoriatic arthritis. Golimumab has been studied in clinical trials compared with placebo in people with active PsA despite DMARD or NSAID therapy (and permitting doses of methotrexate, low-dose corticosteroids, and NSAIDs).

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Interventions	• Etanercept • Infliximab (mono and combination therapy) • Adalimumab • Golimumab
Population(s)	People with active and progressive psoriatic arthritis who have responded inadequately to previous DMARDs
Comparators	• Alternative TNF inhibitors • Conventional management strategies for active and progressive psoriatic arthritis that has responded inadequately to previous DMARD therapy excluding TNF inhibitors

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Outcomes	The outcome measures to be considered include: • pain and other symptoms • functional capacity • effect on concomitant skin condition • disease progression (e.g. imaging) • 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.
Other considerations	Where the evidence allows, sequencing of different drugs may be considered. Guidance will only be issued in accordance with the marketing authorisation.
Related NICE recommendations	Related published Technology Appraisals: NICE Technology Appraisal guidance No. 104 - Etanercept and infliximab for the treatment of psoriatic arthritis, July 2006 NICE Technology Appraisal guidance No. 125 – Adalimumab for the treatment of psoriatic arthritis, Aug 2007 Related Technology Appraisals in development: Leflunomide for the treatment of psoriatic arthritis. Expected date of issue: TBC Related Guidelines: None

Questions for consultation

Are there any issues that require special attention in light of the duty to have due regard to the need to eliminate unlawful discrimination and promote equality?

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Are there any subgroups of patients in whom these drugs are expected to be more clinically effective and cost effective or other groups that should be examined separately?