Executive Summary

Psoriatic arthritis (PsA) affects approximately 0.3% of the general population. The anti-TNF-α drug, adalimumab (Humira®), represents an effective treatment option for patients with active, progressive PsA in England and Wales. The BSR guidelines and NICE guidance for adalimumab (TA125) indicate that adalimumab is recommended as an option for the treatment of adults with active and progressive psoriatic arthritis only when the following criteria are met:

- The person has peripheral arthritis with three or more tender joints and three or more swollen joints.
- The psoriatic arthritis has not responded to adequate trials of at least two standard disease-modifying anti-rheumatic drugs (DMARDs), administered either individually or in combination.

In randomised clinical studies of patients who had previously had an inadequate response to NSAIDs (study M02-518) or DMARDs (study M02-570), adalimumab (40mg every other week) successfully improved the multiple manifestations of PsA, yielding statistically significant improvement in:

- Arthritic manifestations – ACR / PsARC
- Joint destruction – Modified Total Sharp Score (mTSS)
- Skin manifestations – Psoriasis Area and Severity Index (PASI) / Physician's Global Assessment (PGA)
- Disability – Health Assessment Questionnaire Disability Index (HAQ-DI) Score
- Quality of life – Short Form 36 (SF−36), Dermatology Life Quality Index (DLQI), and Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F)

Long-term radiographic data from the ADEPT (M02-518) study provided evidence for a licence extension issued in 2007 to highlight that “adalimumab has been shown to reduce the rate of progression of peripheral joint damage as measured by X-ray in patients with polyarticular symmetrical subtypes of the disease and to improve physical function”.

The evaluated study population had characteristics comparable to patients with active PsA in England and Wales, and responses were similar for patients treated with adalimumab monotherapy or in combination with conventional DMARDs.

Currently, there are two other licensed anti-TNF agents to treat PsA (etanercept and infliximab). There are no head-to-head trials of any anti-TNF-alpha agents for the treatment of PsA. Randomised controlled trials have shown all three anti-TNF-α agents to be effective in the treatment of PsA. It is therefore important to consider the advantages that adalimumab provides over etanercept and infliximab.

The psoriasis component of PsA is sometimes deemed to have less impact on the patient’s quality of life than the arthritic manifestations of the disease, however in the ADEPT study (M02-518), the PASI composite scoring system was found to independently affect the total utility scores in PsA patients, suggesting skin involvement is important. In ADEPT, the proportion of patients achieving 50%, 75% and 90% improvement in the PASI was statistically significantly higher in patients treated with adalimumab than those treated with placebo. In addition, responses were seen as early as week 2, were statistically significant at week 12 and were maintained over the long term (week 104). Although pooled results from the etanercept PsA clinical trials at 12 weeks showed statistically significant responses in favour of etanercept compared to placebo for most outcomes, a statistically significant difference from placebo was not reported for PASI 75[1]. This is in accordance with the conclusions of Heiberg et al. “*Although no head to head comparisons have been performed between the different TNF-blocking agents, similar magnitude of clinical response has been observed*

across trials with the different agents with respect to joint symptoms, whereas improvements in skin manifestations seem to be somewhat greater with the monoclonal antibodies."

Adalimumab is provided in a pre-filled syringe for subcutaneous self-administration at home, obviating the inconvenience of drug reconstitution by patients or the burden of administering and monitoring intravenous infusions by health care providers (*e.g.* infliximab). Abbott provides the home delivery of adalimumab as a free of charge service. Adalimumab is a fully human monoclonal antibody. As such, immunogenicity may be reduced when compared to antibodies that contain non-human sequences, *e.g.* infliximab. In addition, the antibody construction of adalimumab has a long half-life that facilitates eow dosing (26 injections per year), compared to either once or twice-weekly dosing with etanercept (52 or 104 injections per year).

The annual acquisition cost of adalimumab to the NHS is £9,295 per patient. This annual cost is the same as for etanercept. Assuming the average patient with PsA receives the licensed dose of 5mg/kg, the first-year annual cost of infliximab would be £13,847, due to the need for additional loading doses, and £10,910 for subsequent years. In a cost-utility model assessing the combined treatment impact on both joint and skin, which was developed by the University of British Columbia, adalimumab demonstrated an incremental cost per QALY gained of £29,827, compared to conventional DMARDs when used according to the BSR treatment guidelines. The model also demonstrated that adalimumab was dominant relative to etanercept (adalimumab provided a greater QALY benefit at a lower cost than etanercept), and adalimumab has a much lower cost than infliximab with comparable QALY benefit. Improvement in arthritic symptoms was modelled based on estimated ACR response rather than PsARC response and improvement in psoriasis was modelled based on estimated PsARC response. It is important to note that the modelling assumes patients discontinue if they are not a PsARC responder in line with the BSR guidelines. However, in the adalimumab clinical trials there was a disconnect between ACR and PsARC response rates, meaning some patients achieving benefit would be stopped prematurely and some patients receiving minimal benefits would continue anti-TNF therapy with a PsARC stopping rule. As the ACR20 response is a more stringent assessment of joint response a sensitivity analysis was conducted using this measure for the 12 week stopping rule. This sensitivity analysis gives a cost per QALY of £26,213 for adalimumab versus conventional DMARDs.

Observational data including the British Society for Rheumatology Biologics Register and registries from other countries indicate that patients with PsA being given adalimumab achieve major improvements in physical functioning and health related quality of life, which in some cases are greater than the improvements observed for patients with rheumatoid arthritis. These data highlight the devastating impact that PsA can have on patients and the value of adalimumab therapy in the treatment of PsA.

This submission demonstrates that the use of adalimumab for the treatment of active progressive PsA represents a clinically-effective and cost-effective option for the NHS in England and Wales.