Executive Summary

1.1 Background

Current evidence suggests that in Psoriatic Arthritis (PsA) patients, TNF-α inhibitors represent an efficacious and safe treatment. In the previous appraisal of TNF-α inhibitors in PsA patients (TA 104), the Appraisal Committee accepted that the true benefit of these drugs may have been underestimated due to the exclusion of the psoriasis component of the disease from the economic analysis. Schering-Plough in this appraisal has submitted an economic model that overcomes the limitations of previous work and captures this additional benefit of treatment with a TNF-α inhibitor in PsA patients.

Schering-Plough has presented an assessment of the clinical and cost effectiveness of infliximab and other TNF-α inhibitors based on the available published evidence. This analysis suggests that infliximab is cost effective and well within the NICE threshold of acceptability when compared with palliative care. When compared with other TNF-α inhibitors, infliximab dominates both etanercept and adalimumab in a significant proportion of PsA patients.

In addition, Schering-Plough is submitting new evidence regarding the practice of vial optimisation in the UK clinical practice. Market research suggests that 63% of patients treated in rheumatology departments receive infliximab which has been prepared using vial optimisation, demonstrating significant real-world uptake of a practice which reduces wastage and thereby increases cost-effectiveness.

1.2 Psoriatic arthritis

Psoriatic arthritis (PsA) is a chronic debilitating spondyloarthropathy characterised by inflammatory arthritis which affects the joints and connective tissue and is associated with psoriasis of the skin or nails. The annual incidence of PsA ranges between 0.1-23.1 per 100,000 and the prevalence is estimated to be 1.0-420.0 per 100,000 across the globe (Alamanos, 2008). The course of PsA can be variable and unpredictable, ranging from a mild and nondestructive disease to an erosive and deforming arthritis (seen in 40% to 60% of PsA patients) (Gottlieb, 2008). Untreated PsA patients may have persistent inflammation, progressive joint damage, severe physical limitations, disability, and increased mortality (Gottlieb, 2008). Nail psoriasis is a frequent and cosmetically disfiguring presentation of PsA, often causing functional impairment, pain, and emotional distress for many patients. Nonetheless, it is often under-recognised and under-treated (De jong, 1996; Williamson, 2004). Patients with PsA are also associated with a higher prevalence of cardiovascular risk factors, such as higher expression of inflammatory markers, hypertension, increased body mass index (BMI), and diabetes (Gladman, 2008; Tam, 2008). PsA has a significant economic burden with direct annual healthcare costs estimated to be as high as $1.9 billion in the US (Williams, 2002). As with most chronic conditions, the major cost drivers of direct costs in PsA are hospitalisations and drug treatment (Huscher, 2006; Javitz, 2002).

1.3 Infliximab in treatment of psoriatic arthritis

The goals of PsA treatment are to improve disease signs and symptoms, prevent loss of function and disability, prevent or control joint, tendon, and entheses inflammation and damage, and improve Quality of Life (QoL) (Kyle, 2005; Kavanaugh, 2006). The BSR guidelines recommend that biologic disease-modifying anti-rheumatic drug (DMARD) therapy should be used for those patients with active PsA (≥3 tender joints and ≥3 swollen joints) who fail to respond to adequate treatment (>6 months) of at least two nonbiologic DMARDs (eg, methotrexate, sulfasalazine, cyclosporine, or leflunomide) (Kyle, 2005).

Infliximab, a TNF-α inhibitor, has been shown to be efficacious in PsA patients who have previously failed at least two biologic DMARDs. Two Randonised Control Trials (RCTs) of infliximab in PsA patients, IMPACT and IMPACT 2, demonstrated significant improvements in the proportion of subjects achieving ACR 20, ACR 50 and ACR 70 responses at week 14 and 24. Patients treated with infliximab also achieved significantly better PsARC responses compared to placebo as early as week 2 and sustained it through week 24. A significantly higher proportion of infliximab patients achieved greater than 75% improvement in PASI from baseline at all time points through week 24 and showed significant improvement in quality of life compared to placebo group at weeks 14 and 24.

1.4 The cost-effectiveness of infliximab in Psoriatic Arthritis

The average cost of scheduled maintenance treatment with infliximab per patient is estimated to be in the range of £11,063 to £14,420 for the first year of treatment (8 infusions, 5mg/kg at weeks 0, 2 and 6 and every 8 weeks thereafter), decreasing to £8,988 or £11,716 respectively in a normal maintenance year (6.5 infusions) for a 60kg or 80kg patient, including the costs of administration.

An economic evaluation was performed to estimate the cost per Quality Adjusted Life Year (QALY) gained associated with each TNF-α inhibitor treatment compared to palliative care in moderate-severe PsA patients. A decision analysis model was constructed to simulate the progression of hypothetical cohorts of patients receiving each relevant treatment strategy. Efficacy estimates were derived through a network meta-analysis of published trials of infliximab and other TNF-α inhibitors with an attempt to capture their benefits on both the rheumatic and dermatologic component of the disease. Efficacy estimates were then converted into appropriate QALYs using published algorithms whilst other model parameters were obtained from the literature or expert opinion as appropriate.

For a 60kg patient, infliximab scheduled maintenance treatment derived 2.55 additional QALYs at an additional cost of £43,250 compared to palliative care without infliximab. The resultant incremental cost effectiveness ratio (ICER) for a maintenance treatment strategy with infliximab was £16,942 compared to palliative care. The ICER increased to £19,982/QALY and £23,022/QALY for a 70kg patient (with vial optimisation) and 80kg patient, respectively. In comparison with etanercept and adalimumab, infliximab scheduled maintenance treatment derived 0.03 and 0.76 additional QALYs. In a 60kg patient, these additonal QALYs were derived at a cost saving of £527 compared to etanercept and at an addtional cost of £8,676 compared to adalimumab. Thus for a 60kg patient infliximab dominated etanercept and extended dominated adalimumab. The corresponding ICERs were higher for a 70kg and an 80kg patient. Due to the weight based dosing of infliximab, for any patient weighing less than 62kg, infliximab is the most cost effective TNF-α inhibitor treatment. This would account for between a quarter and one third of patients according to the weight distribution observed in the BSRBR cohort.

1.5 Conclusion

Infliximab is a highly effective and well-tolerated therapy for the management of moderate-to-severe PsA patients and provides significant clinical benefit over palliative care. Economic analyses demonstrate that the incremental costs associated with achieving these clinical benefits are reasonable, and that infliximab represents a cost-effective treatment option well within the NICE threshold compared to palliative care without biologic DMARDs. The network meta-analysis indicated that infliximab is comparable to other TNF-α inhibitors in terms of its efficacy and safety. Infliximab is likely to be the most cost effective treatment alternative in a substantial proportion of PsA patients.