Pharmacoeconomic Issues in Psoriatic Arthritis

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Abstract. Therapies for psoriatic arthritis were inadequate until a short time ago. Nonsteroidal antiinflammatory drugs are helpful in relieving symptoms but do not prevent joint damage. Traditional disease-modifying antirheumatic drugs are used to control symptoms, but there is no evidence that they prevent or significantly slow the progression of structural damage in peripheral joints. The introduction of tumor necrosis factor-α (TNF-α) blocking agents has opened new horizons. These drugs lessen signs and symptoms of inflammation, enhance functional capacity and quality of life, and inhibit structural joint damage. On the other hand, TNF-α blockers are very costly and not easily available to all patients, whether they rely on a national health system or on private insurance. Pharmacoeconomic studies on these drugs so far have shown that they are cost-effective on both the musculoskeletal and skin manifestations of psoriatic disease, offering good value for money.

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Psoriatic arthritis (PsA) is a heterogeneous chronic disease involving the skin and nails and musculoskeletal structures such as entheses, joints, the synovial sheaths of tendons, and the axial skeleton. Patients can also have eye and gut involvement. In addition, compared with controls, patients with PsA or psoriasis have a significantly higher rate of insulin resistance, type 2 diabetes, obesity, metabolic syndrome, hypertension, hyperlipidemia, and cardiovascular disease. A label has been proposed to include all these clinical conditions: psoriatic disease (PsD).

PsA was once believed to be a mild disease. A growing body of evidence has emphasized that PsA is erosive and deforming in 40-60% of patients who have joint damage in the first years of the disease. Patients with PsA experience decreased quality of life (QOL), functional impairment, psychosocial disability, and a significant rise in mortality compared with the general population.

Therapies for PsA were unsatisfactory until a short time ago. Nonsteroidal antiinflammatory drugs help relieve symptoms but do not prevent joint damage. Local corticosteroid injections may be of great benefit in treating patients with persistent monoarthritis or oligoarthritis, but systemic glucocorticoid usage is not supported by evidence. Traditional disease-modifying antirheumatic drugs (DMARD) are used in PsA to control symptoms but there is no evidence that they prevent or significantly slow the progression of structural joint damage. The introduction of tumor necrosis factor-α (TNF-α) blocking agents (etanercept, infliximab, adalimumab, and golimumab) has opened new horizons. These drugs lessen signs and symptoms of inflammation, improve functional capacity and QOL, and inhibit structural damage in peripheral joints. However, TNF-α blockers are very expensive and not easily available to all patients, whether they rely on a national health system or on private insurance.

The most important questions are the illness costs of PsA, and whether anti-TNF-α agents are cost-effective. Illness costs in PsA are high even without these drugs. Costs are also high for patients with skin lesions only. In 2006, Javitz, et al estimated the direct cost of medical care for psoriasis (including PsA) for adults living in the United States, from a societal perspective. The total direct cost for about 1.4 million patients with psoriasis or PsA was $649.6 million: Outpatient physician visits amounted to $86.6 million and hospitalizations to $30.5 million; other costs included dermatologic prescription drugs, $147.9 million; photochemotherapy, $27.4 million; and over-the-counter medications, $357.2 million. Earlier on, Kraning and Odland estimated higher costs of $1.09 billion, in 1979; and in 1984, Krueger, et al estimated costs at $4.32 billion. The major reason for Javitz’ lower estimates in 2006 is the lower number of hospitalization days compared with previous years, which was the result of the availability of better drugs for improving symptoms and the higher use of day treatment clinics.
In 2006, Huscher, et al evaluated indirect and direct per-patient costs of illness of rheumatoid arthritis (RA), ankylosing spondylitis (AS), systemic lupus erythematosus (SLE), and PsA in Germany. Mean direct costs were €4737 per year in RA, €3676 in AS, €3191 in SLE, and €3156 in PsA. Taking into account indirect costs applying the human capital approach, total costs increased to €15,637 in RA, €13,513 in AS, €14,411 in SLE, and €11,075 in PsA annually. With the friction cost approach, values were €7,899, €7,204, €6,518, and €5,570, respectively. Costs were strongly dependent on functional status and rose with disease duration. The authors concluded that costs were high in all 4 diseases and deeply influenced by functional capacity. In the Psoriatic Arthritis Cost Evaluation (PACE) study, an Italian cost-of-illness study of TNF-α inhibitors for patients with PsA who do not respond to traditional DMARD, the cost per patient in the 6 months prior to the start of anti-TNF-α therapy was £1519.17. Brodzsky, et al determined total costs of PsA as €5574/patient/year in Hungary. Mean direct medical costs accounted for €1876; direct nonmedical costs for €794; and indirect costs for €2904.

Zhu, et al studied direct and indirect costs of PsA in Hong Kong. The average annual direct and indirect costs per patient were $4141 and $3127 (2006 US$), respectively. They found that pain and function were significantly associated with costs and suggested that treatments aiming to reduce pain and to restore function are highly likely to reduce the costs incurred by patients with PsA. However, no patient participating in the study was treated with TNF-α blockers because those drugs are not within the Hong Kong government’s reimbursement system.

As far as the question of cost-effectiveness, studies of anti-TNF-α blocking agents in PsA have demonstrated that these drugs are cost-effective on both the cutaneous and musculoskeletal manifestations of PsD. Most of those studies were carried out using data obtained from published international clinical trials, and 1 was done in a clinical practice setting. Bansback, et al estimated the potential long-standing benefits on health status of the TNF-α antagonist etanercept and evaluated its long-term effectiveness in comparison with conventional DMARD. Over a 10-year period, etanercept had a cost per quality-adjusted life-year (QALY) gained of €30,000 in comparison with lefunomide or combination therapy of methotrexate and cyclosporine.

Eandi and Salvarani compared cost-effectiveness and cost-utility of adalimumab, etanercept, and infliximab through the development of a single Markov model, using data obtained from phase III trials demonstrating the clinical efficacy of the 3 anti-TNF agents. Adalimumab was found to be cost-effective for the treatment of PsA. Bravo Vergel, et al evaluated the cost-effectiveness of etanercept, infliximab, and so-called “palliative care” (i.e., no active therapy, equivalent to placebo) from a UK National Health Service perspective. The study was performed on behalf of the National Institute for Health and Clinical Excellence. The authors used Bayesian statistical methods to synthesize evidence from 3 phase III trials identified through a systematic review, which allowed estimation of the relative efficacy of etanercept and infliximab despite the absence of head-to-head trials. Over 10 years, the incremental cost-effectiveness ratio (ICER) for etanercept compared with palliative care was £26,361 per QALY gained for the best-case (equal to gain) rebound scenario and £30,628 for the worst-case scenario (equal to natural progression). Infliximab demonstrated a higher ICER compared to etanercept, ranging from £165,363 per QALY gained for the best case to £205,345 for the worst case. These results are due to the higher acquisition and administration costs of infliximab compared with etanercept, with only a marginal increase in effectiveness. The results for etanercept in this study are, similar to those of the study by Bansback, et al, in the cost-effectiveness range of £20,000–£40,000 per QALY, which is considered cost-effective in the UK setting. Recently, Cummins, et al found that at the willingness-to-pay threshold of £30,000, the probability of golimumab being cost-effective for the treatment of active PsA is 89%.

Kavanaugh, et al examined the effect of infliximab on employment status, time lost from work, and productivity in 200 patients with active PsA enrolled in the double-blind, placebo-controlled, IMPACT-2 (Infliximab Multinational Psoriatic Arthritis Controlled Trial) study. Patients treated with infliximab had significantly improved productivity in comparison to those treated with placebo. They also showed a positive trend toward reduced time lost from work and increased employment despite the short trial period.

Sizto, et al evaluated the cost-effectiveness and optimal treatment sequence for moderate to severe psoriasis by combining costs and estimates of long-term efficacy obtained by available clinical evidence. They considered the Psoriasis Area and Severity Index response from 22 randomized trials on biologic (adalimumab, etanercept, infliximab, efalizumab) and nonbiologic (cyclosporine, methotrexate) systemic drugs. Adalimumab was the most cost-effective per QALY (ICER £30,000), followed by etanercept (ICER £37,000), efalizumab (ICER £40,000), and infliximab (ICER £42,000).

In the PACE study, 107 patients from 9 Italian rheumatology centers with different forms of PsA showing insufficient response to conventional treatment were given anti-TNF-α agents, mainly etanercept. Cost (expressed in 2007 euros) and usefulness (measured using EuroQoL) before and after the start of TNF-α therapy were assessed with the objective of calculating the incremental QALY gained and the cost-effectiveness acceptability curve. The study was executed from the perspective of the community, the largest entity that can have a point of view, and including the Italian third-party payer (the National Health Service), patients, and their families. At the end of the 12 months of anti-TNF-α therapy, there was a significant rise.
of direct cost because of an increase in the cost of the drug that was only partially counterbalanced by the decrease in indirect costs. In the last 6 months of the 12 months of anti-TNF-α therapy, the direct cost increased by €5052, the cost to the Italian National Health Service by €5044 and the social cost by €4638. However, a gain of 0.12 QALY produced a cost per QALY gained of €40,876 for the Italian National Health Service and of €37,591 for the society. The acceptability curve revealed that there would be a 97% likelihood that anti-TNF-α therapy would be estimated cost-effective at the willingness-to-pay threshold of €60,000 per QALY gained proposed for Italy. One of the values of the Italian study was the demonstration that anti-TNF-α therapy is cost-effective in the short term in clinical practice. A short-term advantage was also observed in a 24-week clinical trial on active PsA in which etanercept significantly reduced health-care resource use, absenteeism, and caregiver assistance.27

The cost-effectiveness studies of TNF-α inhibitors carried out to date have shown that these drugs are cost-effective on both the musculoskeletal and skin manifestations of PsD and offer good value for the money. It is desirable that other studies be done in the near future. Because most of the pharmacoeconomic investigations are supported by the companies producing the anti-TNF-α agents, methodological transparency is crucial. In addition, these drugs need to be less costly. The expected introduction of new drugs together with the effect of market forces could lower their cost.

REFERENCES