New Immunomodulating Drugs in Treating Moderate to Severe Psoriasis

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Summary and Conclusions

TECHNOLOGY AND TARGET GROUP Psoriasis is an inflammatory skin disease. An estimated 250 000 people in Sweden have the disease, of which there are 5 different forms. Plaque psoriasis is the most common form, accounting for more than 80% of all cases. Severe plaque psoriasis has substantially negative effects on patients' quality of life. Standard therapy usually consists of a combination of ultraviolet A light waves and psoralen tablets (PUVA)[1] and/or immunosuppressive systemic treatment. Methotrexate and ciclosporine are established systemic drugs that offer effective therapy and, after 12 to 16 weeks of treatment, reduce psoriatic lesions by 75% or more (PASI 75)[2] in 60% to 70% of the patients. However, these drugs are associated with a risk for serious side effects. This risk increases as the duration of treatment is increased, and may limit their use. Since some patients do not tolerate, or do not respond to, the established methods, new treatment options are needed. Three new immunomodulating drugs – infliximab (Remicade®), etanercept (Enbrel®), and efalizumab (Raptiva®) – were approved in 2004/2005 for treating moderate to severe plaque psoriasis in adults when other systemic therapies have had inadequate effects or cannot be given for other reasons. The target group includes approximately 1000 patients per year.

PRIMARY QUESTION What are the patient benefits and costs associated with using the new immunomodulating drugs – infliximab, etanercept, and efalizumab – in treating moderate to severe plaque psoriasis?

PATIENT BENEFIT Results from 3- and 6-month followup of randomized trials, where control groups received placebo, showed that infliximab, etanercept, and efalizumab all had favorable effects on skin lesions and quality of life. No studies have compared the new drugs against each other. The percentages of patients that achieved PASI 75 after approximately 3 months of treatment were: 82% for infliximab, 33% for etanercept, and 29% for efalizumab. After 10 to 12 weeks of treatment the mean improvements in total DLQI[3] scores (a validated quality of life scale) were: 79% for infliximab, 59% for etanercept (25 mg x 2), and 46% for efalizumab.

Only one large trial (efalizumab) specifically designed to investigate the patient group having the approved indications for the drug (patients demonstrating an inadequate response, side effects, or contraindications in established therapy) has been published. The limited data available suggest that the new immunomodulating drugs have similar effects in this group of patients as in other patients.

The mechanisms of action of these drugs carry a potentially increased risk for serious immune-related side effects, including severe infections.

ECONOMIC ASPECTS The drug costs per patient treated for a period of 24 weeks vary between 65 000 and 105 000 Swedish kronor (SEK), depending on the drug and dose. Information related to cost effectiveness is based on a British model study. The analysis showed that the healthcare costs per quality-adjusted life-year (QALY) were high with the new immunomodulating drugs. Compared to the alternative of no treatment, the costs of treating patients who have responded inadequately to treatment, or who cannot receive established therapy for other reasons, were estimated at 400 000 to 1 100 000 SEK per QALY, depending on the drug and dose. The study also presented another estimate, where the indications for treatment were expanded to include all patients with moderate to severe plaque psoriasis. In this scenario, the cost per QALY for the new immunomodulating drugs was extremely high compared to the established treatment options.

SBU's appraisal of the evidence

Favorable effects on skin lesions and quality of life in patients with moderate to severe plaque psoriasis have been shown after treatment with infliximab, etanercept and efalizumab for 3 to 6 months (Evidence Grade 1)*. The scientific evidence is insufficient* to assess the long-term effects of the 3 drugs, as well as the potential, uncommon and long-term, side effects.

Treatment costs per quality-adjusted life-year are high, or very high, even when the drugs are used within the approved indications (patients who respond inadequately to treatment, or who cannot receive established therapy for other reasons). Utilization beyond the scope of the approved indications would generate extremely high costs.

Criteria for Evidence Grading SBU's Conclusions, see page 2

1 *PUVA = Psoralen + Ultraviolet A*
2 *PASI = Psoriasis Area and Severity Index*
3 *DLQI = Dermatology Life Quality Index*

Criteria for Evidence Grading SBU's Conclusions

Evidence Grade 1 – Strong Scientific Evidence. The conclusion is corroborated by at least two independent studies with high quality and internal validity, or a good systematic overview.

Evidence Grade 2 – Moderately Strong Scientific Evidence. The conclusion is corroborated by one study with high quality and internal validity, and at least two studies with medium quality and internal validity.

Evidence Grade 3 – Limited Scientific Evidence. The conclusion is corroborated by at least two studies with medium quality and internal validity.

Insufficient Scientific Evidence. No conclusions can be drawn when there are not any studies that meet the criteria for quality and internal validity.

Contradictory Scientific Evidence. No conclusions can be drawn when there are studies with the same quality and internal validity whose findings contradict each other.

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