

# RGH Pharmacy E-Bulletin

Volume 37 (12): April 26, 2010

A joint initiative of the Patient Services Section and the Drug and Therapeutics Information Service of the Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia. The RGH Pharmacy E-Bulletin is distributed in electronic format on a weekly basis, and aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications.

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## Ustekinumab

Psoriasis is a chronic inflammatory disease which involves hyperproliferation of the skin, resulting in scaling and erythema. The affected areas are called psoriatic plaques and frequently occur on the extensor aspect of the elbows and knees. Thought to be a hereditary autoimmune condition, psoriasis may be aggravated by environmental factors. It is present in 2- 3% of the population, and usually in people aged 16 - 22 or 57 - 60. Pharmacological management varies, depending on the severity of inflammation, and site involved. Topical agents are used for mild disease and as an adjunct to other therapies in more severe disease. For severe disease phototherapy and systemic therapy are commonly used.

Biologic therapies are the newest option for treating psoriasis. There are currently four approved agents: infliximab, etanercept, adalimumab and ustekinumab. Ustekinumab (Stelara™) is a human monoclonal antibody that blocks the inflammatory effects of interleukin (IL)-12 and IL-23. These factors are over expressed in psoriasis plaques.

The efficacy of ustekinumab in patients with moderate to severe psoriasis has been assessed in a phase 2 placebo-controlled trial and two crossover trials. The first study involved 320 patients randomly assigned to treatment with ustekinumab at doses of 45 mg or 90 mg, or placebo. There was at least 75% improvement in a significantly greater percentage of patients who received active treatment.

PHOENIX 1 was a phase 3 double-blind, placebo-controlled trial, involving 766 patients with moderate to severe psoriasis. Patients randomly received ustekinumab 45 mg or 90mg at weeks 0 and 4, and then repeated every 12 weeks; or placebo at weeks 0 and 4, then crossed-over to active treatment at week 12. In both treatment groups, a significantly greater percentage of patients achieved 75% improvement at week 12. This improvement was maintained with 12 weekly dosing for at least 12 months. PHOENIX 2 was designed to assess if dosing intensification would improve skin response rates in patients who partially responded to initial treatment. Patients who had a 50 - 75% response to treatment were re-randomised at week 28 to continue dosing every 12 weeks or to escalate to dosing every 8 weeks. At week 52, more patients who received ustekinumab 90 mg every 8 weeks had responded to treatment, compared to those who continued the same dose every 12 weeks. In the PHOENIX trials, rates of adverse events were similar between active treatment and placebo. The most common side effects were upper respiratory tract infections, arthralgia, and headache. Due to the immunosuppressant effects of biologic agents, there is a theoretical increase in risk of infection and malignancy in patients receiving ustekinumab. In the PHOENIX trials there was no significant difference in risk of serious infection or malignancy.

In January 2010, a study comparing ustekinumab and etanercept was published in the *New England Journal of Medicine*. Patients were randomly assigned to receive 45 or 90 mg of ustekinumab at weeks 0 and 4, or etanercept 50 mg twice weekly for 12 weeks. The primary endpoint was the proportion of patients who achieved at least 75% improvement at week 12. This was achieved in 67.5% of patients who received 45 mg ustekinumab, 73.8% who received 90 mg, and 56.8% who received etanercept. Patients not responding to etanercept within 12 weeks were crossed over to ustekinumab, and almost half of these patients had significant improvement within 12 weeks after changing to ustekinumab.

Subsidised supply of ustekinumab through the Australian Pharmaceutical Benefits Scheme has recently been approved for treatment of moderate to severe plaque psoriasis in patients who have not responded to other systemic treatments, or cannot tolerate them.

This E-Bulletin is based on work by Heather Forbes, Clinical Pharmacist, RGH

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