

RGH Pharmacy E-Bulletin

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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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T-cell co-stimulation blockade for rheumatoid arthritis

T-cell costimulation blockade represents the next major advance in the use of biologic agents for the management of rheumatoid arthritis (RA).

Since the late 1990s, the use of biologic agents in the management of RA has significantly altered the approach to treatment for this and a variety of other inflammatory illnesses. Therapies that inhibit tumour necrosis factor (etanercept, infliximab and adalimumab) or interleukin-1 (adalimumab) or which deplete circulating B-cells (rituximab) have become integral in the management of severe, refractory RA.

More recently, a further biologic approach has been investigated: prevention of T-cell activation by costimulation blockade. It is well understood that activated T-cells are involved in the autoimmune response that leads to inflammatory synovitis and joint destruction in RA. Abatacept (Orencia®) is a soluble fusion protein and is the first in a new class of agents called selective T-cell costimulation modulators. This agent blocks costimulation of lymphocytes and their complete activation by antigen-presenting cells.

Clinical evaluations of abatacept indicate that recommended doses of the agent are more effective than placebo for improving clinical manifestations of RA. In adults with persistently active RA despite methotrexate treatment, the addition of abatacept has resulted in significant improvement in efficacy compared with methotrexate alone. Treatment with abatacept in conjunction with at least one other Disease Modifying Anti-Rheumatic Drug (DMARD) has been effective in patients who had an inadequate response to therapy with a TNF blocking agent. Response may occur within 15 days following initiation of therapy and has been maintained for up to three years in one study.

Abatacept is generally well tolerated however, as with other biologic DMARDs, there is an increased risk of infection during treatment. Other adverse effects include headache, dizziness, nausea and infusion-related reactions. Abatacept is given by intravenous infusion and dosed according to body weight (approximately 10 mg/kg). Doses are administered at 0, 2 and 4 weeks, then every four weeks thereafter depending upon response.

Like other biologic agents, treatment with abatacept is expensive, costing between \$13,000 and \$26,000 per patient per year. From March 1st 2008, abatacept has been listed for subsidy under the auspices of the Pharmaceutical Benefits Scheme (PBS) in Australia, for use as initial biologic DMARD treatment for severe RA. Authority is required to prescribe abatacept for patients who are receiving methotrexate at a dose of at least 7.5 mg weekly and who have severe active disease. Patients must have failed to achieve an adequate response with methotrexate and leflunomide-based combination DMARD therapy.

There is limited experience with the use of abatacept in combination with other biologic DMARDs; patients receiving the combination in clinical trials experienced more frequent and more severe infections and concurrent therapy is not recommended at this time. As with other immunosuppressive therapy, live vaccines should not be given concurrently or within three months of stopping abatacept.

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FOR FURTHER INFORMATION – CONTACT THE PHARMACY DEPARTMENT ON 82751763 or email: chris.alderman@rgh.sa.gov.au
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