

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.

Editor: Assoc. Prof. Chris Alderman, University of South Australia – Director of Pharmacy, RGH
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Natalizumab for multiple sclerosis

Multiple Sclerosis (MS) is an immune-mediated disorder where demyelination of the nerve cells occurs within the central nervous system. Motor, sensory and cognitive deficits can occur to varying degrees. There are four subtypes of MS: relapsing remitting, secondary progressive, primary progressive and progressive relapsing. Symptoms of MS include paraesthesia, muscle weakness and spasms, ataxia, dysarthria, dysphagia, depression, visual loss/blurring or diplopia, bowel/bladder incontinence etc.

MS relapses are usually treated symptomatically with oral or intravenous steroids, depending on the severity and disability. At present there is no known cure for MS, but immunomodulators (interferons such as beta-1a, beta-1b) and glatiramer are usually considered first-line therapy. Immunosuppressants (e.g. azathioprine, methotrexate, mitoxantrone etc) are second-line therapy. These drugs may slow progression and reduce the frequency of symptomatic episodes from MS.

Natalizumab (Tysabri) is a new drug that has recently become available for the treatment of MS. It is a humanized monoclonal antibody and it binds to α_4 subunit of $\alpha_4\beta_1$ -integrins on the surface of leucocytes, inhibiting their migration to the brain and therefore reducing inflammation. Leucocyte migration across the blood brain barrier is an important step in the formation of inflammatory lesions in MS.

In the AFFIRM study, 942 patients with relapsing MS were randomly assigned to Natalizumab (300mg given intravenously every 4 weeks) or placebo, for a treatment period of up to 116 weeks. After one year, the clinical relapse rate was lower in the natalizumab group (0.27 relapses per year vs. 0.78 with placebo, $p < 0.001$). This difference was maintained after two years. Natalizumab-treated patients were 42% less likely than those on placebo to have experienced sustained progression of disability.

Adverse effects of natalizumab include allergic and infusion-related reactions and impaired liver function. The formation of antibodies to natalizumab may occur, which may result in a reduced response. The use of natalizumab is associated with an increased risk of progressive multifocal leucoencephalopathy (PML) which is a rare and fatal brain infection.

In Australia, the supply of natalizumab for the treatment of MS is subsidised through the Pharmaceutical Benefits Scheme (section 100) with the following criteria: for relapsing remitting MS in ambulatory patients, two or more attacks in two years and confirmation of diagnosis by MRI. At present, neurologists prescribing natalizumab must register with the Tysabri Australian Prescribing Program.

Natalizumab is recommended for use only if other immunomodulators have failed or not tolerated. It is not to be used in conjunction with other immunomodulators (e.g. interferons or glatiramer) due to the increased risk of PML. There are no direct comparative studies with other immunomodulators for MS, and the safety and efficacy of natalizumab treatment beyond two years duration is as yet unknown.

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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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