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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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Rasagiline

The treatment of Parkinson's disease often requires the use of multiple agents to achieve optimal symptom control with minimal side effects. The mainstay of treatment is levodopa, however the development of movement disorders occurs with long term treatment. In younger patients, therefore, it may be preferable to reserve levodopa for use later in the course of disease progression. Also, in patients taking long term levodopa, additional therapies may help to reduce motor fluctuations.

Rasagiline is a new Monoamine Oxidase Type B inhibitor (MAOI-B) and has recently been listed for subsidised supply through the Pharmaceutical Benefits Scheme on a cost minimisation basis against the existing MAOI-B inhibitor selegiline. It inhibits the breakdown of dopamine in the brain and is indicated as either monotherapy, or as adjunctive therapy with levodopa. As monotherapy, the efficacy and safety of rasagiline has been assessed in two randomized placebo-controlled trials, TEMPO (26 weeks) and ADAGIO (36 weeks). In both trials, patients with newly diagnosed Parkinson's disease showed significantly improved symptoms while treated with rasagiline, as determined by the Unified Parkinson's Disease Rating Scale (UPDRS). In the Adagio trial, the change in UPDRS scores was assessed between late start and early start groups taking rasagiline, with the aim to determine whether rasagiline has any effect on disease progression. Interestingly, there was a significant difference in the group treated with 1mg, daily, but not amongst those the group treated with 2mg daily. Further studies are needed to determine if rasagiline can slow progression of Parkinson's disease.

The LARGO (18 weeks) and PRESTO (26 weeks) trials were designed to investigate the utility of rasagiline as adjunctive therapy to levodopa, in patients with advanced Parkinson's disease. There was a significant reduction in "off time" for those treated with combined rasagiline and levodopa group compared with levodopa alone. No head to head trials of rasagiline compared with other Parkinson's disease therapies have been published, but a post hoc analysis of the LARGO study suggests that rasagiline may have similar efficacy to entacapone (although the treatments were not directly compared in this study). An indirect comparison suggests that rasagiline may be less effective than dopamine agonists in reducing motor symptoms.

The use of rasagiline was associated with an increase in dyskinesia when used as adjunctive therapy in the PRESTO study but not the LARGO trial. Other common side effects include gastrointestinal upset, headaches, flu like symptoms, depression, arthralgia, fatigue and dizziness. The incidence of impulse control disorders was not increased and therefore rasagiline may be an alternative for patients who have experienced this adverse effect with dopamine agonists.

The use of rasagiline is contraindicated with Monoamine Oxidase (MAO) inhibitors (non-selective and other selective MAO inhibitors), and potent inhibitors of CYP1A2, for example, fluvoxamine, St John's Wort, ciprofloxacin and cimetidine. Use of rasagiline is also contraindicated with other antidepressants due to the risk of serotonin syndrome. Due to the risk of hypertensive crisis, patients should avoid consuming high levels of tyramine, as found in aged cheeses, fermented foods and some beer, and also should avoid sympathomimetic drugs such as pseudoephedrine.

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