Leflunomide

Arava (Hoechst Marion Roussel)

10 mg, 20 mg and 100 mg tablets

Approved indication: rheumatoid arthritis

Australian Medicines Handbook Section 14

Disease modifying antirheumatic drugs, such as gold and methotrexate, are increasingly prescribed for patients with rheumatoid arthritis. These drugs are toxic and may not slow the progression of the disease. Leflunomide is an attempt to produce an effective, well tolerated treatment. It is an immunomodulating drug which inhibits the pyrimidine synthesis that is associated with cell proliferation. Leflunomide also has a weak anti-inflammatory action.

Patients begin taking leflunomide with a loading dose for three days. This is because the drug has a long half-life (2–3 weeks). There is extensive first pass metabolism which converts leflunomide to its active form. The active metabolite is slowly excreted into the urine and faeces. Smoking increases clearance.

Leflunomide has been compared with placebo and sulfasalazine, a drug with the capability of retarding disease progression. A total of 359 patients were randomised to be treated for 24 weeks. Although many patients did not complete the study, the arthritic symptoms and signs responded to treatment in 20% of the patients in the placebo group compared with 55% of the leflunomide group and 56% of the sulfasalazine group. X-rays revealed that there was less disease progression in the active treatment groups. The study did not have enough power to show a difference between leflunomide and sulfasalazine.[1] Other studies suggest the efficacy of leflunomide and methotrexate may be similar.

While 96 of the 133 patients taking leflunomide completed the trial, 19 (14%) had to withdraw because of adverse events.[1] Common problems were diarrhoea, nausea, rashes and alopecia. Other adverse effects include headache, dizziness, leucopenia and altered liver function. Regular white blood counts and liver function tests are recommended.

In October 1999 the European Medicines Evaluation Agency issued a statement warning the public about serious adverse reactions to leflunomide. There was particular concern about reports of pancytopenia and serious skin reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis.

Few significant drug interactions have emerged, but live vaccines are not recommended until six months after the conclusion of treatment. Leflunomide is contraindicated in pregnancy.

Until more information is available about leflunomide it will probably be reserved for patients with severe active rheumatoid arthritis who cannot tolerate or do not respond to other disease modifying drugs.

REFERENCE

1. Smolen JS, Kalden JR, Scott DL, Rozman B, Kvien TK, Larsen A, et al. Efficacy and safety of leflunomide compared with placebo and sulphasalazine in active rheumatoid arthritis: a double-blind, randomised, multicentre trial. Lancet 1999;353:259-66.

Temozolomide

Temodal (Schering-Plough)

5 mg, 20 mg, 100 mg and 250 mg capsules

Approved indication: brain tumours

Australian Medicines Handbook Section 14.1.3

The primary brain tumours include anaplastic astrocytoma and glioblastoma multiforme. Both of these tumours have a poor prognosis. Patients may be treated with surgery followed by radiotherapy and chemotherapy. Temozolomide has been developed as an option for treating patients who relapse after this therapy.

Temozolomide is an alkylating agent, with similarities to dacarbazine. It is taken once a day at least one hour before food for five days each month. The drug is rapidly absorbed and crosses the blood-brain barrier. Most of the drug is metabolised with less than 10% being excreted unchanged in the urine.

In 162 patients with anaplastic astrocytoma there was a response rate of 33% with temozolomide. The median survival time for these patients was 14.6 months. In the more common glioblastoma multiforme, the median survival time was much shorter. When the drug was compared with procarbazine in the treatment of 225 patients, the median progression-free survival was 2.7 months for temozolomide and 1.8 months for procarbazine.

In the few months that they survive, most patients will have adverse effects from the treatment. Myelosuppression is very common, so patients must have their blood count checked before each monthly treatment. Nausea and vomiting are also common and some patients will need antiemetic drugs.

While temozolomide has been approved for both types of tumour in Australia, the evidence of its effectiveness in glioblastoma multiforme was insufficient to warrant an accelerated approval in the U.S.A.

NEW FORMULATIONS

Loratadine/pseudoephedrine sulfate

Clarinase 24 Hour Relief (Schering-Plough)

10 mg loratadine/240 mg pseudoephedrine sulfate sustained-release tablets

Omeprazole magnesium

Acimax (AstraZeneca)

20 mg tablets

Losec (AstraZeneca)

10 mg and 20 mg tablets

Topiramate

Topamax (Janssen-Cilag)

15 mg and 25 mg sprinkle capsules