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Leflunomide

Leflunomide is an isoxazole immunomodulating agent. It is one of the newer disease-modifying antirheumatic drugs (DMARDs) and works in a similar way to other DMARDs, such as [methotrexate](#), [ciclosporin](#) and sulfasalazine, in the treatment of [rheumatoid arthritis](#) and [psoriatic arthritis](#). It has also shown promise in the treatment of [psoriasis](#).

In New Zealand leflunomide is available as 10mg, 20mg and 100mg tablets, trade name Arava®. It is currently only indicated for the treatment of rheumatoid arthritis, to improve signs and symptoms, to retard joint destruction and to improve functional ability and quality of life. In the United Kingdom leflunomide was also licensed for the treatment of psoriatic arthritis in 2004.

Treatment with leflunomide is considerably more expensive than treatment with other DMARDs, hence its use is usually restricted to patients that have not responded to other DMARDs.

Mechanism of action

Leflunomide is an isoxazole immunomodulatory agent, which inhibits dihydroorotate dehydrogenase (an enzyme involved in de novo pyrimidine synthesis) and has antiproliferative activity. This is a particularly useful property in psoriasis because skin cells are proliferating more quickly than normal. Several studies also show leflunomide to have anti-inflammatory effects.

Dosage and administration

Leflunomide is a tablet given orally. The starting dose is 100mg/day for 3 days and then reduced and maintained at 10–20mg/day. Tablets should be swallowed whole with a large glass of water.

Improvements in rheumatoid arthritis and psoriatic arthritis may be seen as early as 4 weeks after starting treatment, however full benefits may not be obvious until 4–6 months of continuous therapy.

Precautions

Leflunomide has been associated with potentially serious toxicity, particularly when used in combination with other hepatotoxic and haematotoxic agents. Regular monitoring of liver function tests, blood cell count and blood pressure is required. It is recommended that liver enzymes ALT and AST are checked before the start of therapy and monitored at monthly or more frequent intervals for at least the first 6 months. Once stable, monitoring every 6–8 weeks is usually sufficient.

The metabolised active drug of leflunomide (A771726) has a prolonged half-life (usually 1–4 weeks) which means it stays in the body for long periods. If patients are switching to another hepato- or haematotoxic medication, a washout period is recommended. Where necessary, cholestyramine may be used to help with the washout.

Side effects

Leflunomide has been associated with significant and serious adverse effects to multiple organ systems including the liver, blood, dermatological, respiratory and immune systems.

Some of the more common side effects that patients may experience when taking leflunomide are:

- Gastrointestinal effects (stomach pains, diarrhoea)
- Pruritus ([itch](#))
- Rash
- Hypertension (high blood pressure)
- Respiratory infections
- Liver enzyme elevations (leading to liver failure)
- Alopecia ([hair loss](#))

Early warning signs of toxicity may include:

- Bruising easily
- Tiredness, pallor
- Skin lesions or rashes
- Shortness of breath
- Increased susceptibility to infection

If any of these symptoms or signs are severe or do not go away you should contact your doctor immediately.

Blood disorders reported include pancytopenia (low count of all blood cells), agranulocytosis (low count of white cells) and thrombocytopenia (low count of platelets). These are usually rare and most often occur in patients receiving concomitant treatment with methotrexate or other immunosuppressive agents.

Related information

References:

On DermNet NZ:

- [Psoriatic arthritis](#)
- [Psoriasis](#)
- [Rheumatoid arthritis](#)

Other websites:

- [Arava](#) information from Medsafe

Books about skin diseases:

See the [DermNet NZ bookstore](#)

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DermNet does not provide an on-line consultation service.

If you have any concerns with your skin or its treatment, see a [dermatologist](#) for advice.

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