

## Amifampridine

### Approved indication: Lambert-Eaton myasthenic syndrome

#### Ruzurgi (Lacuna) 10 mg tablets

Lambert-Eaton myasthenic syndrome can develop in some patients with cancer, particularly small cell lung cancer. There is also an autoimmune form of the syndrome and this sometimes affects children. Both forms are due to an abnormality in the release of presynaptic acetylcholine. This disorder of neuromuscular transmission results in muscle weakness that may present as an abnormal gait and autonomic dysfunction which can present as a dry mouth, constipation or erectile dysfunction.

Amifampridine has been used, through the Special Access Scheme, to manage the symptoms of Lambert-Eaton myasthenic syndrome. It is thought to work by blocking the potassium channels of the presynaptic neuron. This prolongs depolarisation and the influx of calcium ions resulting in the release of acetylcholine.

The dose of amifampridine is based on body weight. It is given in divided doses and titrated to find a balance between symptom relief and adverse effects. Lower doses may be required in patients with variants in the gene for N-acetyltransferase 2. As this enzyme metabolises amifampridine, patients who are 'slow acetylators' will have higher drug concentrations. The elimination half-life of amifampridine is around four hours, with most of the dose being excreted in the urine. The effects of renal and hepatic impairment have not been studied in clinical trials.

Lambert-Eaton myasthenic syndrome is very rare so trials of drug therapy are small. A phase II trial randomised 12 patients to take amifampridine and 14 to take a placebo for six days. Electromyography showed that the amplitude of action potentials increased in patients taking amifampridine. These patients also improved on a quantitative assessment of muscle function.<sup>1</sup>

Another randomised trial studied 32 patients who were already taking amifampridine. A group of 14 continued their usual dose, while 18 patients had their dose tapered to zero over several days and then resumed their usual dose. Tapering off the dose of amifampridine resulted in 72% (13/18) of the patients being at least 30% slower in getting up out of a chair. They also felt much weaker than the 14 patients who continued amifampridine. These effects reversed after the usual dose was resumed.<sup>2</sup>

Some of the adverse effects of amifampridine, such as abdominal pain, may be related to its cholinergic actions. These effects are more likely if the patient is taking other cholinergic drugs, such as cholinesterase inhibitors. As amifampridine can cause seizures, it is contraindicated if there is a history of seizures. The risk of seizures will be increased if the patient is also taking drugs known to lower the seizure threshold. Prolongation of the QT interval is a potential risk. The most frequent adverse events include dysaesthesia, abdominal pain, dyspepsia, dizziness and nausea.

While the evidence for the efficacy of amifampridine is limited, it is also limited for alternative therapies such as pyridostigmine or immunosuppression. Although the effect size is uncertain, amifampridine is recommended as the first-line drug treatment for managing the symptoms of Lambert-Eaton myasthenic syndrome. It has been approved for use in adults and in children at least six years old.

**T** [manufacturer provided relevant information](#)

### REFERENCES

1. Sanders DB, Massey JM, Sanders LL, Edwards LJ. A randomized trial of 3,4-diaminopyridine in Lambert-Eaton myasthenic syndrome. *Neurology* 2000;54:603-7. <https://doi.org/10.1212/wnl.54.3.603>
2. Sanders DB, Juel VC, Harati Y, Smith G, Peltier AC, Marburger T, et al. 3,4-diaminopyridine base effectively treats the weakness of Lambert-Eaton myasthenia. *Muscle Nerve* 2018;57:561-8. <https://doi.org/10.1002/mus.26052>

First published  
1 September 2022  
<https://doi.org/10.18773/austprescr.2022.056>



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The Transparency Score is explained in [New drugs: transparency, Vol 37 No 1, Aust Prescr 2014;37:27](#).

At the time the comment was prepared, information about this drug was available on the websites of the [Food and Drug Administration](#) in the USA, the [European Medicines Agency](#) and the [Therapeutic Goods Administration](#).