Pharmacotherapeutic report on amifampridine (Firdapse®) for the 'symptomatic treatment of ' Lambert Eaton myasthenic syndrome (LEMS) in adults'

Medicine. Amifampridine (in the form of a phosphate salt), tablet 10 mg

Summary of the therapeutic value

Intended effects. In cases of LEMS, amifampridine (=3,4-DAP) improves muscle strength scores and the resting compound muscular action potential (CMAP) amplitudes. It seems to be more effective than pyridostigmine. All controlled studies have a very short follow-up of max. 8 days, and they were carried out using preparations of amifampridine base. In general, the effect on motor parameters was retained for up to 15 months in the open follow-up studies. Bio-equivalence is documented the for the extent of absorption (AUC) between preparations of amifampridine phosphate salt and amifampridine base. In comparison with the base formulation, the phosphate salt was absorbed more rapidly, with a higher Cmax and a smaller Tmax. Due to this difference in absorption profile, the EMA has decided that the max. daily dose should be 60 mg. In the Netherlands a number of patients are currently taking 100 mg/day of preparations of amifampridine base in a regulated release formulation. Literature has indicated that the upper limit of this product should be 100 mg due to the occurrence of epileptic attacks. This side effect is more likely to occur with a higher Cmax. In some patients the lower daily dose of 60 mg may prove insufficient for achieving a good therapeutic effect throughout the day.

Unintended effects. The most frequent side effect of amifampridine is digital or perioral paraesthesia. This occurs with doses exceeding 10 mg. Severe side effects have rarely been reported. The most severe side effect is convulsion, which particularly occurs at high doses. Due to the limited data, the registration-holder is obliged to keep patient registration data on efficacy and to monitor side effects and collect data that are lacking on, for example, cardiovascular safety and carcinogenic potential.

Experience. Less experience has been obtained with amifampridine phosphate than with pyridostigmine and with the basic amifampridine.

Applicability. Pyridostigmine can be given to a larger group of patients. The use of amifampridine phosphate does not have any advantages over using pyridostigmine or amifampridine base.

Ease of use. The fact that only a short-acting 10 mg tablet is available means that the ease of use of amifampridine phosphate is more limited than that of the base product, which is also available in a formulation with regulated release.

Specific details. Amifampridine phosphate is registered as an orphan drug under exceptional circumstances.

Final conclusion. For the treatment of LEMS, amifampridine phosphate has an added therapeutic value in comparison with pyridostigmine. For the treatment of LEMS, the therapeutic value of amifampridine phosphate is comparable with that of amifampridine base.

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