

Myasthenia Gravis Association

A guide to the change from 3,4 DAP To Firdapse® for LEMS and CMS patients, but not MG patients

As at 30th July 2010, the Myasthenia Gravis Association understands that the current position of 3,4 DAP (3,4 diamino-pyridine) treatment for LEMS (Lambert Eaton Myasthenic Syndrome) and CMS patients (Congenital Myasthenic Syndromes) is as follows;

3,4 DAP

3,4 DAP provides a valuable short-term relief of symptoms for many LEMS and CMS patients. It is also known as 3,4 DAP **base**.

Until recently, it was made in the UK.

It was never specifically licensed for either LEMS or CMS, but has been used to treat hundreds of patients since the 1980s, supported by published evidence.

It had to be obtained by special arrangement and often subsidy from the Pharmacy at the John Radcliffe Hospital, Oxford. This used to be quite acceptable in the UK, but was awkward in some other countries.

Its production will now cease.

FIRDAPSE®

Encouraged by some European countries, BioMarin Pharmaceutical Inc has recently obtained an exclusive EU-wide and USA-wide licence for use in LEMS and CMS of its new variant product, Firdapse® [also known as 3,4 DAP phosphate salt]. This is classified as an Orphan Drug.

The licence was granted on the strength of the close similarity of Firdapse® to 3,4 DAP. Firdapse® is a salt with a longer storage time. As yet, there are no published reports on its efficacy in either LEMS or CMS patients.

The total annual cost of using Firdapse® is understood to be higher than that for 3,4 DAP.

There are ongoing discussions as to how the NHS will meet these costs.

HELP

If you are having problems obtaining your medication and need help, first consult your GP or Consultant. You can also contact us on 01332 290219 or email mg@mga-charity.org We are kept up-to-date by our medical experts and will do our best to help.

If you are having problems obtaining your medication and need our help, then please contact us on 01332 290219, or email mg@mga-charity.org.

We will endeavour on your behalf to seek advice from our medical experts and come back to you.

FURTHER INFORMATION

For further information on **What Should I do Next** and **Frequently Asked Questions**, please turn over



Myasthenia Gravis Association
The College Business Centre,
Uttoxeter New Road, Derby,
DE23 6UQ
Tel: 01332 290219

Freephone: 0800 919922 (UK)
1800 409672 (Eire)
Web Site: www.mgauk.org.uk
Email: mg@mga-charity.org

MGA is a Registered Charity No. 1046443

Myasthenia Gravis Association

WHAT SHOULD I DO NEXT?

If you are having problems obtaining your medication and need help, first consult your GP or Consultant. You can also contact us on 01332 290219 or email mg@mga-charity.org

FREQUENTLY ASKED QUESTIONS

BioMarin have supplied the following answers to frequently asked questions.

Is this new preparation safe? How can we be sure it will not adversely affect the children?

Firdapse® is licensed in Europe for the treatment of Lambert Eaton Syndrome in adults, and the safety and efficacy of the product have not been assessed in patients under 18 years of age.

While there were no formal safety studies for the compounded material previously used, there are 20 years of case reports of the use of this active ingredient in patients with neuromuscular diseases. **Indeed**, 3,4 DAP has been shown to be generally well tolerated. **Firdapse® contains the same active substance as compounded 3,4 DAP base, in the form of a phosphate salt, and has proven relative bioequivalence.**

Have any clinical trials been performed on this drug?

Yes, non clinical and clinical trials have been performed with Firdapse®, to establish the safety profile of the preparation. These include studies to observe any effect on the cardiac rhythm, and also the effect of taking the medication with food in healthy volunteers.

Will ALL individuals who require 3,4 DAP be able to continue to receive this medication?

Firdapse® is licensed for the treatment of LEMS in adults throughout the European Union member states, and is available to physicians to prescribe in the UK. It can be dispensed through community and hospital pharmacies, or delivered to the patients home, at no extra cost to the patient of NHS.

Will children be allowed to trial – and commence – this drug in future? (Or will the resulting cost to a local PCT mean that neurologists are less likely to suggest its use?)

If the prescriber feels that Firdapse® is the most appropriate treatment for their patients, the prescription will be able to be dispensed.

If Firdapse® is licenced for use in LEMS only, why can 3,4 DAP not still be prescribed and used for CMS? (It works very well as it is.)

To the best of our knowledge, there are no formal clinical trials with 3,4 DAP base or phosphate salt (Firdapse®) which looked specifically at the safety or efficacy of this compound in children. Compounded materials are created ad hoc, and are subject to significant variability in terms of active ingredient content, which may risk over or under dosing, which is of particular concern in paediatric populations where exact dose is of paramount

Myasthenia Gravis Association

importance. It is true that the dispensing pharmacist may wish to dispense an ad hoc preparation to fulfil certain prescriptions, such as those for liquids or suspensions, as there is no licensed medication of this form.

What does a parent/patient need to do, now, to ensure that they continue to receive supplies of this vital drug? (PCTs are unlikely to drive this – it will get stuck in the bureaucratic quagmire)

At present, we are not aware of any primary care organisation who have refused to fund Firdapse® for patients already receiving the treatment. BioMarin is working with all those government bodies responsible for paying for medications, either primary care groups in England, the All Wales Medicines Group in Wales and the Scottish Medicines Consortium in Scotland with the aim of ensuring that treatment is not withdrawn due to lengthy procedures.

What do neurologists from outside of the specialist centres need to do to ensure that their patients continue to have access to this drug?

Because Firdapse® is available by ordering from wholesalers, in the same manner as any other pharmaceutical product, if a physician wishes to prescribe the drug, it can be dispensed from any community or hospital pharmacy in the UK.

Who does a parent/patient contact, now, if they have concerns? (many are terrified of problems with the supply of this drug.)

If the patient or parents of any one affected are concerned about their prescription, they should speak to their prescriber about the most appropriate choice of treatment for their condition. If the concerns are surrounding the local funding arrangements in their area, they are very welcome to contact BioMarin who will work with their local funding body to aim to ensure that there is no break in therapy.

How can we compile information to provide a factsheet for parents/patients, reassuring them of the situation and explaining how to ensure continuity of supply?

Where questions are received that you would like BioMarin to answer, please forward them to medinfoeu@bmrn.com and our Medical Information department will look to answer them as quickly as possible.

Will Biomarin be putting any of the profits it will make on Firdapse® into research on better treatment and medications for CMS/LEMS/MG?

BioMarin has an extensive set of clinical trials either planned or on going with Firdapse®, in a variety of conditions. These are likely to include formal safety and efficacy studies in CMS.

Myasthenia Gravis Association

FURTHER INFORMATION ON SUPPLIES

Bio Marine have advised on the availability of supplies as follows:

With regard to reports of lack of availability in young patients with CMS, we are working with each individual hospital to establish which formulation of the medication is most suitable for that patient. For example, if a liquid preparation is being ordered, this is not possible for BioMarin to supply, as we manufacture solid tablet preparations only, and therefore there is no reason we are aware of, for the liquid manufacturer not being able to supply this. It is important to note that we can not speak for that manufacturer.

There is no shortage or lack of stock to supply Firdapse® to patients with LEMS, the pharmacist can order the product in the same manner as any other medication. Please let us know where a pharmacist has problems and we will follow it up with them.

There is no shortage or lack of stock to supply Firdapse® to adult patients, the pharmacist can order the product in the same manner as any other medication. Please let us know where a pharmacist has problems and we will follow it up with them.

THE MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AGENCY

What does the MHRA have to say?

Although the MHRA does not recommend "off label" (outside of the licensed indications) use of products, if the UK licensed product can meet the clinical need, even "off-label", it should be used in preference to an unlicensed product. Licensed products available in the UK have been assessed for quality safety and efficacy. If used "off-label" some of this assessment may not apply, but much will still be valid. This is a better risk position than in the use of an un-assessed, unlicensed product. The fact that the intended use is outside of the licensed indications is therefore not a reason to use an unlicensed product. It should be understood that the prescriber's responsibility and potential liability are increased when prescribing off-label.