motor neurone disease association

Withdrawal of marketing authorisation for Nuedexta

Introduction

The European Medicines Agency (EMA) has withdrawn its marketing authorisation for Nuedexta, a drug that treats emotional lability (the 'pseudo-bulbar affect', or PBA) in MND and other neurological conditions. The withdrawal has been made at the request of the manufacturer of Nuedexta, Avanir Pharmaceuticals, and confirmed publicly by the EMA on 15 March. Marketing authorisation gives the approval for drugs to be used for specific conditions or symptoms.

This briefing explains what has happened and why, and what it might mean for people affected by MND.

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What is Nuedexta?

Nuedexta, or dextromethorphan, is a drug that treats emotional lability in MND and other neurological conditions. It is only approved to treat this symptom, and not to slow the progression of MND.

Nuedexta was developed by Avanir Pharmaceuticals Inc, a subsidiary of Otsuka America Inc, which in turn is wholly owned by the global healthcare company Otsuka Pharmaceutical Co. Ltd.

What is emotional lability?

Emotional lability is a symptom of MND, though it is not experienced by everyone with the disease. It is an abnormal motor response caused by the effects of MND on the pathway between the outer layer of the brain and the brain stem. This means a person's outward responses may not match how

they feel: they may laugh or cry uncontrollably, but not feel correspondingly happy or sad. In many cases this is a temporary symptom that reduces over time.

Why has the manufacturer decided not to market Nuedexta in the EU?

Avanir wrote to us to explain the reasons for their decision, and set out why they did not feel they could not market the drug profitably in the EU. Causes of this are the cost of the post-marketing monitoring required of any new medicine in the EU, and the prices paid for drugs by health systems across Europe. Taken together, Avanir judges that these factors mean that it cannot market Nuedexta commercially in Europe. The withdrawal is not related to any safety or therapeutic issues.

Was the manufacturer planning to market Nuedexta in the EU?

The EMA authorised Nuedexta in July 2013, and Avanir subsequently spent time evaluating whether to sell the drug in Europe, and if so how. No announcement was ever made that it would definitely be available for supply to patients.

What does this mean for people living with MND?

This decision means that the management of emotional lability in people with MND will continue as before. It is commonly treated with antidepressants such as citalopram, which are well known to doctors and easy to prescribe. Some people with MND manage their emotional lability without drugs, once they've been supported to understand it.

Leading MND neurologists have indicated a range of views to us about whether they would have been likely to use Nuedexta. Some expressed interest in trying it for patients whose emotional lability was notably hard to treat, while others expressed satisfaction with existing approaches. It seems likely that it would have become, at best, a second line drug. This may explain why Avanir have felt unable to sell it successfully in Europe: it treats symptoms that are already managed using relatively cheap drugs that doctors are very familiar with.

What does the NICE guideline on MND say about emotional lability?

The NICE guideline contains information on emotional lability as a symptom of MND, but the management of emotional lability was not included in the guideline's scope. Accordingly, it does not offer advice on approaches to management. However, emotional lability also occurs in multiple sclerosis, and the NICE guideline on MS recommends treating it with antidepressants, of which citalopram is an example.[1] Current best practice in MND is in line with this approach.

[1] https://www.nice.org.uk/guidance/cg186/evidence/full-guideline-193254301 - page 224 onwards

Is there any other way of obtaining Nuedexta?

Because Nuedexta is a patented medicine, Avanir has the sole right to produce and distribute it; it will not be possible for another company to make it or for it to be imported into the EU – although it remains available in the USA.

Authorisation was granted by the European Medicines Agency – so would things change if the United Kingdom left the European Union?

No – the price paid by the NHS for new drugs would not be altered by an exit from the European Union, and it is hard to imagine that there would be any relaxation of post-marketing monitoring requirements either, so the factors that made Avanir unwilling to market the drug in the EU would remain in place.

Could Nuedexta be used to treat MND in any other way?

Research presented at the International Symposium on ALS / MND in 2015 suggested that Nuedexta may also have an impact on other bulbar symptoms in MND. However, this is a very tentative conclusion, and needs to be reproduced on a larger scale before we know whether or not the drug is genuinely effective in addressing other symptoms. Some researchers have expressed scepticism about these findings.

What has the MND Association done about this?

We have been in contact with Avanir for some time, and advised them in 2013 on possible approaches to bringing the drug to market in the UK. We have approached them for up-to-date information on their progress since then, but have not been asked to assist further.

We are writing to Avanir asking for an assurance that, should the drug be shown to treat other bulbar symptoms, they will seriously consider bringing it back to market in the EU.

Links to more information

Living with Motor Neurone Disease : emotional impact (includes information on emotional lability)

Research Development Information Sheet D: clinical trials (includes information on drug licensing)

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