

## LHON Society perspective on the European Commission authorisation of Raxone

At the society's AGM some short presentations were made about recent developments in treatment options for LHON and in particular the recent approval by the European Commission for the first ever approved treatment for the condition, namely Raxone (formerly known as Catena, both of which are trade names for the drug Idebenone).

Idebenone is not a new substance for the LHON community, with the RHODOS trial having been completed around 5 years now and reported publicly more than 4 years ago. A sizeable number of LHON patients took part in the trial or have taken idebenone subsequently either via official channels (eg "Named Patient" prescription) or unofficially via internet purchases of generic versions of idebenone. Consequently, and not surprisingly, many people have formed a view already about the treatment's effectiveness and these views range from broadly positive to completely dismissive, due mainly to its real or perceived benefits in each case.

Regardless of any individual views on idebenone's effectiveness, the LHON Society proposed at the AGM that we should view this development positively and celebrate the fact that for the first time in almost 150 years since the condition was first diagnosed there is now an approved treatment. We as a patient community need to consider how to take advantage of this landmark decision both in terms of making Raxone available to patients in the UK and as a means of raising the profile of LHON generally so that the next and subsequent treatment options take place with the minimum of delay.

Idebenone was developed more than 30 years ago by the Japanese Pharmaceutical group Takeda, initially as a treatment for Alzheimer's Disease, and the compound itself is now out of its initial patent protection. As a treatment for Alzheimer's it was not a commercial success and it has been dropped as treatment for that condition in most territories.

As is often the case with treatments that are not successful at first, there have been a number of attempts to "repurpose" idebenone for application in other conditions - an approach that in other drugs has sometimes been spectacularly successful. These efforts in idebenone have been targeted at conditions that are impacted by a malfunction in mitochondria and the three that have shown a degree of success in controlled trials are Friedreich's Ataxia (FDA), Duchenne Muscular Dystrophy (DMD) and Leber's Hereditary Optic Neuropathy (LHON).

In each case the malfunction in mitochondria is known to be caused by a deficiency of CoQ10 and early attempts were made to correct this via supplementation of naturally occurring CoQ10 itself but these have been largely ineffective due to the large molecule size of CoQ10 which makes it difficult to absorb through the mitochondrial membrane. Idebenone was developed as a synthetic molecule that is very similar to CoQ10 but is much more readily absorbed and this has been demonstrated in laboratory models.

While idebenone is now out of patent protection, there are a set of provisions established by the European Medicine's Agency (EMA) to encourage development of treatments for rare conditions which have been designated "Orphan" conditions. LHON has been given Orphan status by EMA and consequently any approved treatment for LHON will receive 10 years patent protection regardless of whether the compound is out of patent or not.

The RHODOS trial was commissioned to provide the clinical evidence that the effect of idebenone was significant enough to support an application for idebenone to be approved for treatment of LHON. Unfortunately, however, although there were some positive outcomes from the trial, the main endpoints were not achieved to a statistically significant level.

Initially, therefore, the application for Catena (the previous name for Raxone) was rejected due to lack of evidence, although no concerns were raised over the safety profile of the treatment, which is regarded as very safe with a history of more than 30 years of use, albeit in generally lower dosage levels. Following the submission of further evidence by the company the EMA issued a recommendation for approval in July under their “Exceptional Circumstances” programme and their recommendation was adopted by the European Commission in September this year. The Exceptional status is essentially a recognition by EMA that the normal trial data required for approval is unlikely to be available for such a rare condition. However, EMA has stipulated that the company must over the next few years still provide a substantial amount of supporting information regarding the efficacy of the treatment.

So, technically speaking, as of September this year Raxone is available on prescription for LHON anywhere within the EU. Things are not as simple as that in real life, however, and actual availability will vary markedly according to which country the patient is residing. As of the time of the AGM it was formally available in only one EU market, Germany, although others will no doubt follow in due course as the local payment details are worked out. In the meantime, some interim measures still exist in some countries, including France and Italy, pending a decision by the payment authorities in those countries.

Here in the UK the landscape is much less clear. We have all heard stories of NICE and their assessment of new treatments but they have limited capacity to assess new drugs in any year and, given the rare status of LHON, it is not clear yet whether NICE will have jurisdiction over a decision on whether the NHS will pay for idebenone. If not, there is a very complex structure within the NHS where the treatment could be approved elsewhere, but this is a lengthy, complex and thankless procedure.

For those with (very) deep pockets, idebenone is available on private prescription right now but it seems unlikely it will be available for most UK patients for at least another year or two, other than through some existing programmes which exist where the company makes the treatment available via certain specialist centres in return for the collection of data supporting their regulatory position. It is unclear how long these “loopholes” will continue, although the requirement on the company to furnish additional data to EMA does hold out some hope.

We apologise if this is a complicated explanation but unfortunately it is a complicated situation. If you have any questions on the above or any other aspects of Raxone’s approval (or suggestions how we as a society might improve the situation or otherwise benefit from it) then please don’t hesitate to contact us.

You can find more information about the authorisation and product information here:

<http://ec.europa.eu/health/documents/community-register/html/h1020.htm>