SPECIALISED COMMISSIONING - CLINICAL EVIDENCE EVALUATION CRITERIA FOR CLINICAL COMMISSIONING POLICY PROPOSITION
URN: 1810
TITLE: Idebenone for treating visual impairment in adults and young people with Leber's hereditary optic neuropathy (LHON)
CRG: Specialised Ear and Ophthalmology
NPOC: Trauma
Date: 16/01/19

This policy is being considered for:	For routine commissioning		Not for routine commissioning	X
Is the population described in the policy similar to that in the evidence reviewed, including subgroups?	Yes.			
Is the intervention described in the policy similar to the intervention for which evidence is presented in the evidence review?	Yes.			
Are the comparators in the evidence reviewed plausible clinical alternatives within the NHS and are they suitable for informing policy development?	Yes.			
Are the clinical benefits described in the evidence review likely to apply to the eligible population and/or subgroups in the policy?	No statistically significant benefit was demonstrated in visual acuity, the primary end point in the RHODOS randomised control trial. Panel noted that no statistically significant benefit was reported in terms of quality of life (using either the Visual Function (VF)-14 tool for patients or clinician reported based outcomes measured using the Clinician's Global Impression of Change (CGIC)). Panel noted that it was difficult to be certain about possible benefits from treatment given the small sample sizes. Panel noted that idebenone had been authorised under 'exceptional circumstances'. This means that due to the rarity of the disease it has not been possible to obtain complete information on this medicinal product. Panel recognised that there was a benefit demonstrated in colour vision and in visual acuity in patients with discordant visual acuity between eyes. Panel noted feedback from the PWG that the treatment may be more effective in recent onset disease. The benefit seen in patients with discordant vision (tends to occur earlier in the disease process) tend to support this view. However, no specific trial evidence was provided to support that view.			

	Panel acknowledged that evidence was provided from the extended access programme which was included as part of the European public assessment report (EPAR). Panel noted that there are conditions and requirements of the marketing authorisation that include the submission of the results of an external natural history controlled, open-label intervention study to assess the efficacy and safety of idebenone in the treatment of LHON patients, including long-term treatment. This reflects the uncertainty over the evidence base. Panel could not clearly identify criteria for treatment which could be linked back to the treatment and related to the benefit.
Are the clinical harms described in the evidence review likely to apply to the eligible and /or ineligible population and/or subgroups in the policy?	Yes – the market authorisation is also conditional on the provision of longer term safety data.
The Panel should provide advice on matters relating to the evidence base and policy development and prioritisation. Advice may cover: • Balance between benefits and harms • Quality and uncertainty in the evidence base • Challenges in the clinical interpretation and applicability of policy in clinical practice • Challenges in ensuring policy is applied appropriately • Likely changes in the pathway of care and therapeutic advances that may result in the need for policy review.	The Panel noted that this was a licensed product and noted the EPAR available for idebenone. Panel noted that 'clinically relevant recovery' in visual acuity appeared superior in treated patients compared with untreated patients in the follow-up study of RHODOS and the expanded access programme (EAP). Panel noted the comments from the PWG and understood that LHON is rare and that the main randomised control trail was relatively small with 55 patients receiving idebenone and 30 receiving placebo with outcomes measured at 24 weeks. The primary visual acuity outcomes favoured treatment but were not statistically significant. However, Panel recognised that there was a significant benefit in colour vision and discordant eyes. Panel noted that the extension study was referenced in the EPAR and that this provided some evidence of a clinically relevant response at 6 months. The magnitude of benefit is modest and that the clinically relevant recovery is described as 'improvement of at least logMAR 0.2 for patients with "on-chart" visual acuity at baseline, or an improvement from "off-chart" to at least logMAR 1.6 for patients with "off-chart" visual acuity at baseline' which may represent a relatively modest clinical improvement. Panel noted that there was a risk of over-estimating the effect of idebenone because of potential for spontaneous recovery in LHON. The Panel supported the not for routine commissioning policy proposition. Panel recognised the limitations of the evidence base and looked forward to receiving further feedback during stakeholder testing and public consultation.

	Panel did not consider that there was sufficient evidence to indicate that treatment could be restricted to a particular subgroup of patients where the benefit could be greater, for example, those with recent onset disease. This may include comments on the interpretation of the evidence with regards to sub-groups. Panel acknowledged that there was limited evidence that may suggest some benefit for patients however this benefit was uncertain and the magnitude of any benefit appeared limited and mainly derived from data gathered in non-randomised follow up and expanded access. Panel also recognised that there is no alternative active treatment of this condition. The Panel heard that the EPAR outlines that the licence is currently conditional based upon further evaluation on a longer term basis.		
Overall conclusion	This is a proposition for routine commissioning and	Should proceed for routine commissioning	
		Should be reversed and proceed as not for routine commissioning	
	This is a proposition for not routine commissioning and	Should proceed for not routine commissioning	X
		Should be reconsidered by the PWG	

Overall conclusions of the panel

Report approved by:
David Black
Clinical Panel Chair
25/01/19

Post meeting note:
[Input how actions requested by Clinical Panel have been addressed]