SPECIALISED COMMISSIONING - CLINICAL EVIDENCE EVALUATION CRITERIA FOR A PROPOSITION FOR A CLINICAL COMMISSIONING POLICY FOR ROUTINE COMMISSIONING

URN: 1700
TITLE: Everolimus for refractory focal onset seizures associated with tuberous sclerosis complex
CRG: Paediatric neurosciences
NPOC: Women & Children via NICE CSP
Lead: [redacted]
Date: 18/10/17

This policy is being considered for:	For routine commissioning	X	Not for routine commissioning	
Is the population described in the policy the same as that in the evidence review including subgroups?	Yes. The license is for children aged 2 and over.			
Is the intervention described in the policy the same or similar as the intervention for which evidence is presented in the evidence review?	Yes as per the license.			
Is the comparator in the policy the same as that in the evidence review? Are the comparators in the evidence review the most plausible comparators for patients in the English NHS and are they suitable for informing policy development?	Yes. The Panel were anxious to ensure that surgery was included early in the pathway of care. Surgery can be curative for some patients.			
Are the clinical benefits demonstrated in the evidence review consistent with the eligible population and/or subgroups presented in the policy? Are the clinical harms demonstrated in the evidence review reflected in the eligible	Yes. The Panel noted the effectiveness of reducing seizure frequency. The evidence did not demonstrate significant improvement in specific measures of quality of life and in other measures relating to behavioural difficulties that can be associated with epilepsy. The main benefit demonstrated is reduction in seizure frequency. Yes. The panel noted the significant incidence of adverse effects. Some of these may be serious. There is a significant discontinuation rate. Panel noted the potential for long term use of everolimus and that adverse effects			

and /or ineligible population and/or subgroups presented in the policy?	for prolonged exposure to everolimus may not yet be clear.
Rationale Is the rationale clearly linked to the evidence?	Yes.
<u>Advice</u> The Panel should provide advice on matters relating to the evidence base and policy development and prioritisation. Advice may cover: • 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 the documents should be amended as outlined below: • The overall length of the document should be reduced and the table of diagnostic features removed. • Amendments are required throughout the document to ensure that the document is written from an NHS England perspective. • An adequate/inadequate response to anti-epileptic drugs should be defined as part of the clinical criteria. • The definition of 'refractory' needs to be consistent with that used in the vagal nerve stimulation policy • Significant editorial changes to remove sections that are not necessary for a clinical commissioning policy including sections with detailed descriptions of clinical features, diagnostic criteria and details on dosing and monitoring. The position of epilepsy surgery in the criteria needs to be made clear, this is correct in the flow chart. Much of the narrative in section 9 can be removed. • We need to see reference to neurosurgery, neurology and children's epilepsy surgery service specifications clearly outlined. • We also need to remove the section on continuation criteria but leave in the section on stopping criteria. • The stopping criteria need to be more specific and it is not sufficient to state that the MDT can determine continuation without listing the criteria that should be met. • The reference to SEGA in this section should be removed. • A definition is required for CYP. • The policy also needs to define more clearly what represents are inadequate response. The policy criteria need to be consistent with other relevant clinical commissioning policies (including VNS and Epilepsy surgery). The policy can progress as a routine commissioning policy. Once the relevant amendments have been made, this should be signed off by the Clinical Panel Chair outside of the meeting before proceeding to stakeholder

	testing. The panel discussed the unmet need for patients with refractory epilepsy. Panel noted that everolimus does appear to cause a mean reduction in seizure frequency, but only a very small proportion of patients are rendered seizure free. The measures of seizure response include a reduction in seizure frequency of about 25% compared to placebo. Response may increase over time. Panel advise that the degree of benefit, rate of adverse effects and the net costs will need to be carefully assessed in the prioritisation process.		
Overall conclusion	This is a proposition for routine commissioning and	Should proceed for routine commissioning	X
		Should reversed and proceed as not for routine commissioning	
	This is a proposition for not routine commissioning and	Should proceed for not routine commissioning	
		Should be reconsidered by the PWG	

Overall conclusions of the panel

Panel advice	**Response**
The panel were anxious to ensure that surgery was included in the pathway of care. Surgery can be curative for some patients.	The policy has been amended to ensure this. The policy now describes in the pathway, a statement regarding surgery linked to the starting criteria. This is that patients should have previously been considered for surgical resection as assessed by a designated Children's Epilepsy Surgery Service (CESS) or adult specialised epilepsy surgery service
The overall length of the document should be reduced and the table of diagnostic features removed.	Now shortened and diagnostic features removed
Amendments are required throughout the document to ensure that the document is written from an NHS England perspective.	Amendments made

An adequate/inadequate response to anti-epileptic drugs should be defined as part of the clinical criteria.	Clarified in policy
The definition of 'refractory' needs to be consistent with that used in the vagal nerve stimulation policy	Clarified as not responding to treatment
Significant editorial changes to remove sections that are not necessary for a clinical commissioning policy including sections with detailed descriptions of clinical features, diagnostic criteria and details on dosing and monitoring	Changes made
The position of epilepsy surgery in the criteria needs to be made clear, this is correct in the flow chart. Much of the narrative in section 9 can be removed.	Changes made
We need to see reference to neurosurgery, neurology and children's epilepsy surgery service specifications clearly outlined	Additions made
Remove the section on continuation criteria but leave in the section on stopping criteria.	These changes made
The stopping criteria need to be more specific and list the criteria that should be met.	Changes made
The reference to SEGA in this section should be removed	This has been removed
A definition is required for CYP	This was removed instead
The policy also needs to define more clearly what represents are inadequate response	Clarified
The policy criteria need to be consistent with other relevant clinical commissioning policies (including VNS and Epilepsy surgery).	'Read across' in place

Report approved by:
David Black
Clinical Panel Co-Chair