Consultation Report

Topic details

Title of policy or policy statement:	Everolimus for refractory partial-onset seizures associated with tuberous sclerosis complex (aged 2 years and above)
Programme of Care:	Women and Children
Clinical Reference Group:	Paediatric Neurosciences
URN:	170093P

1. Summary

This report summarises the outcome of a public consultation that was undertaken to test the policy proposal for the routine commissioning of Everolimus as an adjunct treatment for refractory seizures associated with tuberous sclerosis complex.

2. Background

NHS England has held a 30 day public consultation on the policy proposition to routinely commission Everolimus as an adjunctive treatment for the management of refractory seizures in children and adults with Tuberous Sclerosis Complex (TSC).

TSC is a genetic condition that can lead to non-cancerous growths developing in the brain, eye, heart, kidney, skin and lungs. Seizures are one of the most common neurological features of TSC and occur in approximately 84% of people.

For people with TSC-related seizures, anti-seizure medication (known as anti-epileptic drugs or AEDs) is the standard treatment. For people whose TSC-related seizures have not adequately responded to treatment with at least 2 different AEDs given at therapeutic doses, other treatment options are available. This includes:

- the additional use of 1 or more AED added on to their currently prescribed AED or the use of a different AED which has not been previously prescribed; and the following treatments:
    - a ketogenic diet (a diet low in carbohydrates) usually for infants and young children (because it is difficult for adolescents and adults to remain on a strict diet); and/or
    - vagus nerve stimulation (a device which stops seizures by sending regular, mild pulses of electrical energy to the brain and is implanted under the skin in the chest and connected to the vagus nerve, which is

the main nerve that connects the brain to the heart, lungs, upper digestive tract, and other organs of the chest and abdomen); and/or

- surgical resection (surgical resection may not be suitable for everyone with TSC-related seizures that have not adequately responded to treatment with at least 2 different AEDs given at therapeutic doses. This is because many patients with TSC-related seizures will not have a single type of seizure which is clearly related to one location in the brain that can safely be removed. In addition, some patients choose not to undergo surgery.

Everolimus is a drug that targets a pathway that regulates cell growth and multiplication. In patients with TSC, the mechanistic target of rapamycin (mTOR*) is over-activated, leading to uncontrolled growth of brain cells. This can result in tumours as well as elevated excitability of the brain cells which can lead to seizures. It has a marketing authorisation in England as add-on treatment for patients aged 2 years and older with TSC-related seizures that have not adequately responded to treatment with at least 2 different AEDs given at therapeutic doses.

Access to this treatment is proposed to be via MDT review involving specialised adult epilepsy services (or the CESS services for children) following consideration of all other alternative treatments first. Treatment is lifelong unless seizures remain/ become uncontrolled again or if toxicity levels reach an unacceptable level.

3. Publication of consultation

The policy was published and sign-posted on NHS England's website and was open to consultation feedback for a period of 30 days from 2nd March 2018 to 1st April 2018. Consultation comments have then been shared with the Policy Working Group to enable full consideration of feedback and to support a decision on whether any changes to the policy might be recommended.

Respondents were asked the following consultation questions:

1) Has all the relevant evidence been taken into account?
2) Does the impact assessment fairly reflect the likely activity, budget and service impact? If not, what is inaccurate?
3) Does the policy proposition accurately describe the current patient pathway that patients experience? If not, what is different?
4) Please provide any comments that you may have about the potential impact on equality and health inequalities which might arise as a result of the proposed changes that have been described?
5) Are there any changes or additions you think need to made to this document, and why?

* mTOR is a protein kinase that in humans is encoded by the MTOR gene and mediates processes involved in cell growth

4. Results of consultation

169 responses were received to this public consultation, the majority of whom were from family members of individuals living with TSC. There were consistent themes from the consultation responses as outlined below.

1) All relevant evidence has been taken into account

57% of respondents (96 of 169 responses) felt that whilst the evidence review fully considered the evidence of TSC-related epilepsy and Everolimus treatment for this, the impact of TSC on the physical and mental health of people living with TSC and the impact on the health and wellbeing of the families caring for people living with TSC had not been properly considered in the evidence review. Specific areas cited that were not included in the evidence review were: behavioural issues, learning disability, autism, sleep issues, education, medication side effects and independence. The cost of the ketogenic diet was also raised as something not considered in the evidence review.

Two respondents felt there was further evidence that could be considered from unpublished trail observations.

2) Impact assessment fairly reflects the likely activity, budget and service impact

98% of the responses either agreed that this was appropriate or did not comment on this question. There were responses that flagged the need to consider the workforce implications for the monitoring of everolimus. There were also responses that flagged a potential underestimation of the adult population who may currently be lost to follow up but may come forward for treatment now further options are available, and that the cost of uncontrolled seizures was not appropriately demonstrated in the model.

3) The policy proposition accurately describe the current patient pathway that patients experience

98% of respondents agreed that the current pathway was accurately described. Two respondents flagged the need to amend the policy document and pathway within this to show that specialised MDT discussion was required for adults with refractory TSC-related seizures, as they would not be able to access children's epilepsy specialised services (CESS).

4) Potential impact on equality and health inequalities which might arise as a result of the proposed changes that have been described

73% of respondents commented on this, with 72 of these respondents citing the high incidence in learning disability in this population (1 in 2 people with TSC believed to have a learning disability, with 30% of these being profound learning disabilities), and the impact uncontrolled epilepsy is believed to have on intellectual development. This group of respondents felt that access to Everolimus would reduce health inequalities associated with uncontrolled epilepsy, and improve the health outcomes of the broader family.

Other respondents cited the increased behavioural and mental health issues experienced by patients with epilepsy and a learning disability as a further health inequalities access to Everolimus would address.

97 respondents flagged concern over the accessibility of the documents for people with a Learning Disability, which was particularly significant given that 50% of people living with TSC have a Learning Disability. There were also a number of people who raised concern that they were not aware of the consultation being launched despite being registered stakeholders.

5. How have consultation responses been considered?

Responses have been carefully considered and noted in line with the following categories:

- Level 1: Incorporated into draft document immediately to improve accuracy or clarity
- Level 2: Issue has already been considered by the CRG in its development and therefore draft document requires no further change
- Level 3: Could result in a more substantial change, requiring further consideration by the CRG in its work programme and as part of the next iteration of the document
- Level 4: Falls outside of the scope of the specification and NHS England's direct commissioning responsibility

The majority of the responses fell into levels 2 and 4, as related to issues already considered by the PWG or out of scope of the policy. The responses that fell into level 1 were those relating to the clarification required over adult specialised epilepsy MDTs, monitoring, and the query over the presentation of information within the Integrated Impact Assessment.

The other level 1 feedback pertained to the format of the consultation and the consultation process itself. This has been fed back to the internal NHS England teams and will be discussed with the Programme of Care Board.

6. Has anything been changed in the policy as a result of the consultation?

Additional sentences have been included in the written description of the pathway on page 16 of the policy proposition document that clarifies that for adult patients, they should be considered by an adult specialised epilepsy multidisciplinary team (MDT), as the document previously related to the children's pathway only.

Changes have also been made to the exclusion numbers in the integrated impact assessment to ensure there is clarity over the anticipated cohort.

7. Are there any remaining concerns outstanding following the consultation that have not been resolved in the final policy proposal?

No.