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Welsh Health Specialised
Services Committee (WHSSC)

Specialised Services Policy Position Statement PP250

**Everolimus for refractory focal onset seizures
associated with tuberous sclerosis complex (aged
2 years and above)**

December 2023

Version 1.0



Document information

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Policy Statement

Welsh Health Specialised Services Committee (WHSSC) will commission everolimus for refractory focal onset seizures associated with tuberous sclerosis complex for people aged 2 years and above in accordance with the criteria outlined in this document.

In creating this document WHSSC has reviewed the relevant guidance issued by AWMSG¹ and has concluded that everolimus for refractory focal onset seizures associated with tuberous sclerosis complex (aged 2 years and above) should be made available.

Welsh Language

WHSSC is committed to treating the English and Welsh languages on the basis of equality, and endeavour to ensure commissioned services meet the requirements of the legislative framework for Welsh Language, including the [Welsh Language Act \(1993\)](#), the [Welsh Language \(Wales\) Measure 2011](#) and the [Welsh Language Standards \(No.7\) Regulations 2018](#).

Where a service is provided in a private facility or in a hospital outside of Wales, the provisions of the Welsh language standards do not directly apply but in recognition of its importance to the patient experience the referring health board should ensure that wherever possible patients have access to their preferred language.

In order to facilitate this, WHSSC is committed to working closely with providers to ensure that in the absence of a Welsh speaker, written information will be offered and people have access to either a translator or 'Language-line' if requested. Where possible, links to local teams should be maintained during the period of care.

Decarbonisation

WHSSC is committed to taking assertive action to reducing the carbon footprint through mindful commissioning activities. Where possible and taking into account each individual patient's needs, services are provided closer to home, including via digital and virtual access, with a delivery chain for service provision and associated capital that reflects the WHSSC commitment.

Disclaimer

WHSSC assumes that healthcare professionals will use their clinical judgment, knowledge and expertise when deciding whether it is appropriate to apply this policy position statement.

¹ [everolimus \(Votubia®\) - All Wales Therapeutics and Toxicology Centre \(nhs.wales\)](#)

This policy may not be clinically appropriate for use in all situations and does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian, or Local Authority.

WHSSC disclaims any responsibility for damages arising out of the use or non-use of this policy position statement.

1. Introduction

This Policy Position Statement has been developed for the planning and delivery of everolimus for refractory focal onset seizures in people with tuberous sclerosis complex for people aged 2 years and above who are resident in Wales. This service will only be commissioned by the Welsh Health Specialised Services Committee (WHSSC) and applies to residents of all seven Health Boards in Wales.

In creating this document WHSSC has reviewed the relevant guidance issued by the All Wales Medicines Strategy Group (AWMSG)² and has concluded that everolimus should be made available.

1.1 Background

Tuberous sclerosis complex (TSC) is a genetic condition. It can lead to noncancerous growths developing in the brain, eye, heart, kidney, skin and lungs. The impact of TSC varies considerably. Some people are mildly affected and may not even know they have TSC, while others are much more severely affected.

Seizures are one of the most common neurological features of TSC and occur in approximately 84% of people³. Seizures are considered to be refractory when two different anti-epileptic drugs (AEDs) given at therapeutic doses have failed to control a person's seizures (also known as uncontrolled or intractable).

For people with TSC-related seizures, anti-seizure medication (known as antiepileptic drugs or AEDs) is the standard treatment. For an AED to be considered appropriate it must have previously been shown to be effective for the patient's epilepsy and seizure type.

For people whose TSC-related seizures have not adequately responded to treatment with at least two 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

² <https://awttc.nhs.wales/accessing-medicines/medicine-recommendations/everolimus-votubia3/>

³ <https://pubmed.ncbi.nlm.nih.gov/28057044/>

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 two 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 treated. In addition, some patients choose not to undergo surgery. However, children with TSC-related refractory seizures should be assessed for surgical resection in accordance with [WHSSC Policy CP174 Paediatric Epilepsy Surgery](#). Adults should be assessed under a specialised epilepsy surgery multidisciplinary team (MDT).

It is estimated that around 5.6 in 100,000 people are born with the condition, meaning there are approximately 185 people with TS in Wales, of whom 80 may have refractory seizures. TSC is primarily diagnosed in children and young adults (aged 20 or younger), although it may present in patients as late as age 40.

1.2 Equality Impact and Assessment

The Equality Impact Assessment (EQIA) process has been developed to help promote fair and equal treatment in the delivery of health services. It aims to enable Welsh Health Specialised Services Committee to identify and eliminate detrimental treatment caused by the adverse impact of health service policies upon groups and individuals for reasons of race, gender re-assignment, disability, sex, sexual orientation, age, religion and belief, marriage and civil partnership, pregnancy and maternity and language (Welsh).

This policy has been subject to an Equality Impact Assessment in line with guidance contained in CPL-026⁴.

The Assessment demonstrates the policy is robust and there is no potential for discrimination or adverse impact. All opportunities to promote equality have been taken.

⁴ [Equality Impact Assessment Policy \(EQIA\), WHSSC Corporate Policy \(2022\)](#)

2. Recommendation

The recommendations below represent the views of the AWMSG, arrived at after careful consideration of the evidence available. Health professionals are expected to take into account the relevant AWMSG guidance, alongside the individual needs, preferences and values of the patient.

2.1 Inclusion Criteria

Everolimus is recommended as an option for use within NHS Wales for the adjunctive treatment of patients aged 2 years and older who's refractory partial-onset seizures, with or without secondary generalisation, are associated with tuberous sclerosis complex (TSC).

This recommendation applies only in the circumstances where the approved Patient Access Scheme (PAS) is utilised or where the list/contract price is

2.2 Stopping Criteria

The frequency of TSC-related seizures should be assessed every six months, and everolimus should be stopped if the frequency is not at least 30% lower compared to six months before starting treatment.

2.3 Continuation of Treatment

Healthcare professionals are expected to review a patient's health at regular intervals to ensure they are demonstrating an improvement to their health due to the treatment being given.

If no improvement to a patient's health has been recorded, then clinical judgement on the continuation of treatment must be made by the treating healthcare professional.

2.4 Acceptance Criteria

The service outlined in this document is for patients ordinarily resident in Wales, or otherwise the commissioning responsibility of the NHS in Wales. This excludes patients who whilst resident in Wales, are registered with a GP practice in England, but includes patients resident in England who are registered with a GP Practice in Wales.

2.5 Patient pathway (Annex i)

Patients are reviewed in the TSC clinic and, if the patient meets criteria for everolimus, the patient is discussed in the TSC MDT where a decision to treat will be made. The patient should then be seen by a local specialist to discuss everolimus in more detail and, if consent is given, the local specialist will prescribe. Please see annex (i).

2.6 Transition arrangements

Transition arrangements should be in line with [Transition from children's to adults services for young people using health or social care services NICE guidance NG43](#) and the [Welsh Government Transition and Handover Guidance](#).

Transition involves a process of preparation for young people and their families for their transition to adulthood and their transition to adult services. This preparation should start from early adolescence 12-13-year olds. The exact timing of this will ideally be dependent on the wishes of the young person but will need to comply with local resources and arrangements.

The transition process should be a flexible and collaborative process involving the young person and their family as appropriate and the service.

The way this process is managed will vary on an individual case basis with multidisciplinary input often required and patient and family choice taken into account together with individual health board and environmental circumstances factored in.

2.7 Designated Providers

The TSC MDT, where the decision to treat is made, is hosted by The All Wales Medical Genomics Service:

[All Wales Medical Genomics Service](#)

University Hospital of Wales
Heath Park
Cardiff
CF14 4XW

2.8 Blueteq and reimbursement

Everolimus for treating refractory focal onset seizures associated with tuberous sclerosis complex will only be funded for patients registered via the Blueteq system and where an appropriately constituted MDT has approved its use within a highly specialised centre.

Where the patient meet the criteria in this policy and the referral is received by an agreed centre, a Blueteq form should be completed for approval. For further information on accessing and completing the Blueteq form please contact WHSSC using the following e-mail address: WHSSC.blueteq@wales.nhs.uk

If a non-contracted provider wishes to treat a patient that meets the criteria they should contact WHSSC (e-mail: WHSSC.IPC@wales.nhs.uk). They will be asked to demonstrate they have an appropriate MDT in place.

Funding is approved on the basis that the treatments selected is prescribed and administered in accordance with its marketing authorisation.

The list price for everolimus dispersible packs of 30 tablets is 2mg £960.00, 3mg £1,400.00, 5mg £2,250.00 (excluding VAT; company submission). The company has a commercial arrangement. This makes everolimus available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount. Health Boards in Wales should refer to the AW TTC Vault for further information on the Patient Access Scheme (PAS) price.

2.9 Action to be taken

- Health Boards are to circulate this Policy Position Statement to all Hospitals/MDTs to inform them of the conditions under which the technology will be commissioned.
- Health Boards are to ensure that all providers are purchasing the drug treatments listed in this policy at the agreed discounted price.
- Health Boards are to ensure that all providers understand the need to approve everolimus at the appropriate MDT and are registering use on the Blueteq system, and the treatment will only be funded where the Blueteq minimum dataset is fully and accurately populated.
- Providers are to determine estimated patient numbers and the current dose of any patient(s) who will transfer from any company compassionate use scheme or EAMS.
- The Provider should work to written quality standards and provide monitoring information to WHSSC on request.

3. Documents which have informed this policy

The following documents have been used to inform this policy:

- **WHSSC policies and service specifications**
 - [CP174 Paediatric Epilepsy Surgery](#)
- **National Institute of Health and Care Excellence (NICE) guidance**
 - [Epilepsies Diagnosis and Management CG137, published January 2012, updated May 2021](#)
- **All Wales Medicine Strategy Group (AWMSG) guidance**
 - [Final Appraisal Recommendation Advice No: 1121 – September 2021 Everolimus \(Votubia®\) 2 mg, 3 mg and 5 mg dispersible tablet](#)
- **Scottish Medicine Consortium (SMC) policies**
 - [Everolimus 2mg, 3mg and 5mg dispersible tablets \(Votubia®\) SMC No 1331/18](#)
- **NHS England policies**
 - [Clinical Commissioning Policy: Everolimus for refractory focal onset seizures associated with tuberous sclerosis complex \(ages 2 years and above\)](#)
- **Other published documents**
 - [Tuberous Sclerosis Association: UK guidelines for managing tuberous sclerosis complex 2019](#)

This document should be read in conjunction with the following documents:

- **NHS Wales**
 - All Wales Policy: [Making Decisions in Individual Patient Funding requests](#) (IPFR).

4. Putting Things Right

4.1 Raising a Concern

Whilst every effort has been made to ensure that decisions made under this policy are robust and appropriate for the patient group, it is acknowledged that there may be occasions when the patient or their representative are not happy with decisions made or the treatment provided.

The patient or their representative should be guided by the clinician, or the member of NHS staff with whom the concern is raised, to the appropriate arrangements for management of their concern.

If a patient or their representative is unhappy with the care provided during the treatment or the clinical decision to withdraw treatment provided under this policy, the patient and/or their representative should be guided to the LHB for [NHS Putting Things Right](#). For services provided outside NHS Wales, the patient or their representative should be guided to the [NHS Trust Concerns Procedure](#), with a copy of the concern being sent to WHSSC.

4.2 Individual Patient Funding Request (IPFR)

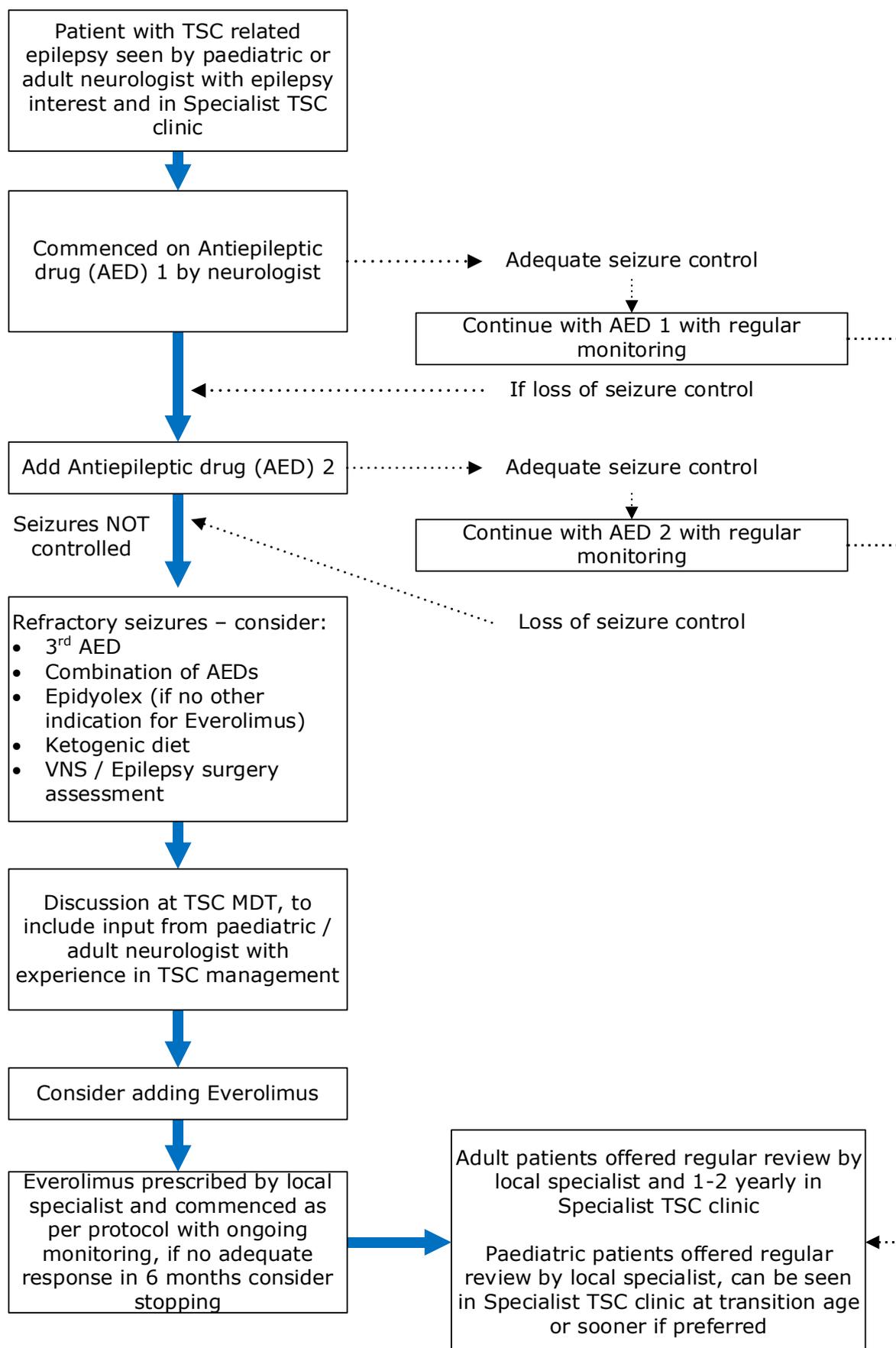
If the patient does not meet the criteria for treatment as outlined in this policy, an Individual Patient Funding Request (IPFR) can be submitted for consideration in line with the All Wales Policy: Making Decisions on Individual Patient Funding Requests. The All Wales IPFR Panel will then consider the request.

If an IPFR is declined by the Panel, a patient and/or their NHS clinician has the right to request information about how the decision was reached. If the patient and their NHS clinician feel the process has not been followed in accordance with this policy, arrangements can be made for an independent review of the process to be undertaken by the patient's Local Health Board. The ground for the review, which are detailed in the All Wales Policy: Making Decisions on Individual Patient Funding Requests (IPFR), must be clearly stated

If the patient wishes to be referred to a provider outside of the agreed pathway, an IPFR should be submitted.

Further information on making IPFR requests can be found at [Welsh Health Specialised Services Committee \(WHSSC\) | Individual Patient Funding Requests](#)

Annex i TSC Epilepsy Pathway



Annex ii Codes

Code Category	Code	Description
ICD-10	Q85.1	Tuberous sclerosis

Annex iii Abbreviations and Glossary

Abbreviations

AED	Antiepileptic Drugs
IPFR	Individual Patient Funding Request
MDT	Multi-disciplinary Team
TSC	Tuberous Sclerosis Complex
VNS	Vagal Nerve Stimulation
WHSSC	Welsh Health Specialised Services Committee

Glossary

Individual Patient Funding Request (IPFR)

An IPFR is a request to Welsh Health Specialised Services Committee (WHSSC) to fund an intervention, device or treatment for patients that fall outside the range of services and treatments routinely provided across Wales.

Welsh Health Specialised Services Committee (WHSSC)

WHSSC is a joint committee of the seven local health boards in Wales. The purpose of WHSSC is to ensure that the population of Wales has fair and equitable access to the full range of Specialised Services and Tertiary Services. WHSSC ensures that specialised services are commissioned from providers that have the appropriate experience and expertise. They ensure that these providers are able to provide a robust, high quality and sustainable services, which are safe for patients and are cost effective for NHS Wales.