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Welsh Health Specialised
Services Committee (WHSSC)

Specialised Services Policy Position Statement PP274

Everolimus for renal angiomyolipoma associated with tuberous sclerosis complex (TSC) in adults

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Contents

Policy Statement	4
1. Introduction	6
1.1 Plain language summary	6
1.2 Aims and Objectives	6
1.3 Epidemiology	6
1.4 Current Treatment.....	7
1.5 Proposed Treatment	7
1.6 What NHS Wales has decided.....	7
2. Criteria for Commissioning	8
2.1 Inclusion Criteria	8
2.2 Exclusion Criteria	8
2.3 Stopping Criteria	8
2.4 Continuation of Treatment.....	9
2.5 Acceptance Criteria.....	9
2.6 Pathway (Annex i)	9
2.7 Exceptions.....	9
2.8 Clinical Outcome and Quality Measures	9
2.9 Blueteq and reimbursement.....	10
2.10 Responsibilities	10
3. Documents which have informed this policy	12
4. Date of Review	13
5. Putting Things Right.....	14
5.1 Raising a Concern.....	14
5.2 Individual Patient Funding Request (IPFR)	14
6. Equality Impact and Assessment.....	15
Annex i Pathway.....	16
Annex ii Codes	17
Annex iii Abbreviations and Glossary	18

Policy Statement

Welsh Health Specialised Services Committee (WHSSC) will commission everolimus for people with renal angiomyolipoma associated with tuberous sclerosis complex (TSC) in accordance with the criteria outlined in this document.

In creating this document WHSSC has reviewed the relevant guidance issued by All Wales Medicine Strategy Group (AWMSG)¹ and NHS England² and has concluded that everolimus 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.

¹ [Provision of everolimus \(Votubia®\) for tuberous sclerosis complex in Wales, Advice Number 2322, October 2022](#)

² [Clinical Commissioning Policy Statement: Everolimus \(Votubia®\) for treatment of angiomyolipomas associated with tuberous sclerosis, B14X09, June 2016](#)

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.

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 has been developed for the planning and delivery of everolimus for renal angiomyolipoma associated with TSC for people 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.

1.1 Plain language summary

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.

TSC growths have a different name depending on which organ they develop in. Angiomyolipoma growths are normally found in the kidney but can also affect the liver. Though angiomyolipoma growths can be asymptomatic, they can also have life-threatening consequences due to their impact on kidney function and the risk of haemorrhage. Angiomyolipomas are the leading cause of morbidity and mortality in adult TSC patients³.

1.2 Aims and Objectives

This Policy Position aims to define the commissioning position of WHSSC on the use of everolimus for people with renal angiomyolipoma associated with TSC.

The objectives of this policy are to:

- ensure commissioning for the use of everolimus is evidence based
- ensure equitable access to everolimus
- define criteria for people with renal angiomyolipoma associated with TSC to access treatment
- improve outcomes for people with renal angiomyolipoma associated with TSC.

1.3 Epidemiology

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. Renal angiomyolipoma develops in approximately 80% of TSC patients.

³ [Dixon B, Hulbert J, Bissler J. Tuberous Sclerosis Complex Renal Disease. Nephron Experimental Nephrology. 2011;118\(1\):e15-e20.](#)

1.4 Current Treatment

The current commissioned first choice intervention for management of angiomyolipomas is percutaneous embolisation with surgical intervention second choice. For angiomyolipomas presenting with acute haemorrhage, first-line therapy is embolisation followed by treatment with corticosteroids.

1.5 Proposed Treatment

Everolimus, a rapamycin analogue, is a disease modifying drug in TSC. It can reverse the underlying abnormality in cells affected by the genetic mutation and has been shown to stop renal angiomyolipomas from growing and causing problems. It is licensed by the European Medicines Agency for the treatment of adult patients with renal angiomyolipoma associated with tuberous sclerosis complex (TSC) who are at risk of complications (based on factors such as tumour size or presence of aneurysm, or presence of multiple or bilateral tumours) but who do not require immediate surgery.

1.6 What NHS Wales has decided

WHSSC has carefully reviewed the relevant guidance issued by the All Wales Medicine Strategy Group (AWMSG) and NHS England. We have concluded that everolimus should be made available within the criteria set out in section 2.1.

2. Criteria for Commissioning

The Welsh Health Specialised Services Committee will approve funding of everolimus for adults with renal angiomyolipoma associated with TSC in line with the criteria identified in the policy.

2.1 Inclusion Criteria

- Angiomyolipomas which are 30mm or greater and which demonstrate interval growth.

2.2 Exclusion Criteria

Contraindications for the use of everolimus are:

- Acute bleeding. This should be treated with embolisation first to gain haemostasis.
- Females of childbearing potential must use a highly effective method of contraception while receiving everolimus, and for up to 8 weeks after ending treatment.
- Hypersensitivity to the active substance, to other rapamycin derivatives or to any of the excipients.

2.3 Stopping Criteria

Stabilisation and reduction in size of renal angiomyolipoma and the non-occurrence of renal bleeding; while preserving renal function are the main aims of treatment. This is monitored clinically and with MRI scan of the kidney. If the treatment with everolimus fails to deliver these outcomes it should be stopped. Progression was defined within EXIST 2 as $\geq 25\%$ increase from nadir in angiomyolipoma volume or $\geq 20\%$ increase from nadir in the volume of either kidney with a value greater than baseline, appearance of new angiomyolipoma $\geq 1\text{cm}$, or grade ≥ 2 angiomyolipoma-related bleeding).

If the renal angiomyolipoma(s) has not stabilised (i.e., ceased to grow) after 6 months of treatment with everolimus at the maximum tolerated dose of up to 10mg daily, the treatment will be deemed to have failed and must be discontinued. A renal MRI scan should be performed to assess whether the renal angiomyolipoma has ceased to grow.

Bleeding and/or the need for embolisation or surgical intervention indicate that treatment has failed and therefore must be discontinued. If a patient demonstrates a progressive fall in glomerular filtration rate (GFR) of below 30 mls/min, or a progressive increase in proteinuria of greater than 3g/L, despite dose adjustment, then treatment must be discontinued. Intractable unacceptable side effects despite dose adjustment will be deemed a reason to stop treatment. The rate of treatment discontinuation has been reported to be 12.5%.

2.4 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.

2.5 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.

2.6 Pathway (Annex i)

Patients should be discussed in TSC MDT with nephrologist and consideration for further discussion at an external TSC MDT should be given (e.g. St George's) if a more complex case. Decision made with regards to Everolimus treatment and patient seen by local nephrologist to discuss and commence treatment if consent given. Please see annex (i).

2.7 Exceptions

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 request will then be considered by the All Wales IPFR Panel.

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

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

2.8 Clinical Outcome and Quality Measures

The Provider must work to written quality standards and provide monitoring information to WHSSC.

The centre must enable the patient's, carer's and advocate's informed participation and to be able to demonstrate this. Provision should be made for patients with communication difficulties.

2.9 Blueteq and reimbursement

Everolimus for renal angiomyolipoma associated with TSC 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 list price for everolimus packs of 30 tablets is 2.5mg £1,200.00, 5mg £2,250.00, 10mg £2,970.00. 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 AWTTTC Vault for further information on the Patient Access Scheme (PAS) price.

2.10 Responsibilities

Health Boards and WHSSC are to circulate this Policy Position Statement to all Hospitals/MDTs to inform them of the conditions under which the treatment will be commissioned.

Referrers should:

- inform the patient that this treatment is not routinely funded outside the criteria in this policy, and
- refer via the agreed pathway.

Clinician considering treatment should:

- discuss all the alternative treatment with the patient
- advise the patient of any side effects and risks of the potential treatment

- inform the patient that treatment is not routinely funded outside of the criteria in the policy, and
- confirm that there is contractual agreement with WHSSC for the treatment.

In all other circumstances an IPFR must be submitted.

3. Documents which have informed this policy

The following documents have been used to inform this policy:

- **All Wales Medicine Strategy Group (AWMSG) guidance**
 - [Provision of everolimus \(Votubia®\) for tuberous sclerosis complex in Wales, Advice Number 2322, October 2022](#)
- **NHS England policies**
 - [Clinical Commissioning Policy Statement: Everolimus \(Votubia®\) for treatment of angiomyolipomas associated with tuberous sclerosis, B14X09, June 2016](#)

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. Date of Review

This document will be reviewed when information is received which indicates that the policy requires revision.

5. Putting Things Right

5.1 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.

5.2 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 request will then be considered by the All Wales IPFR Panel.

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.

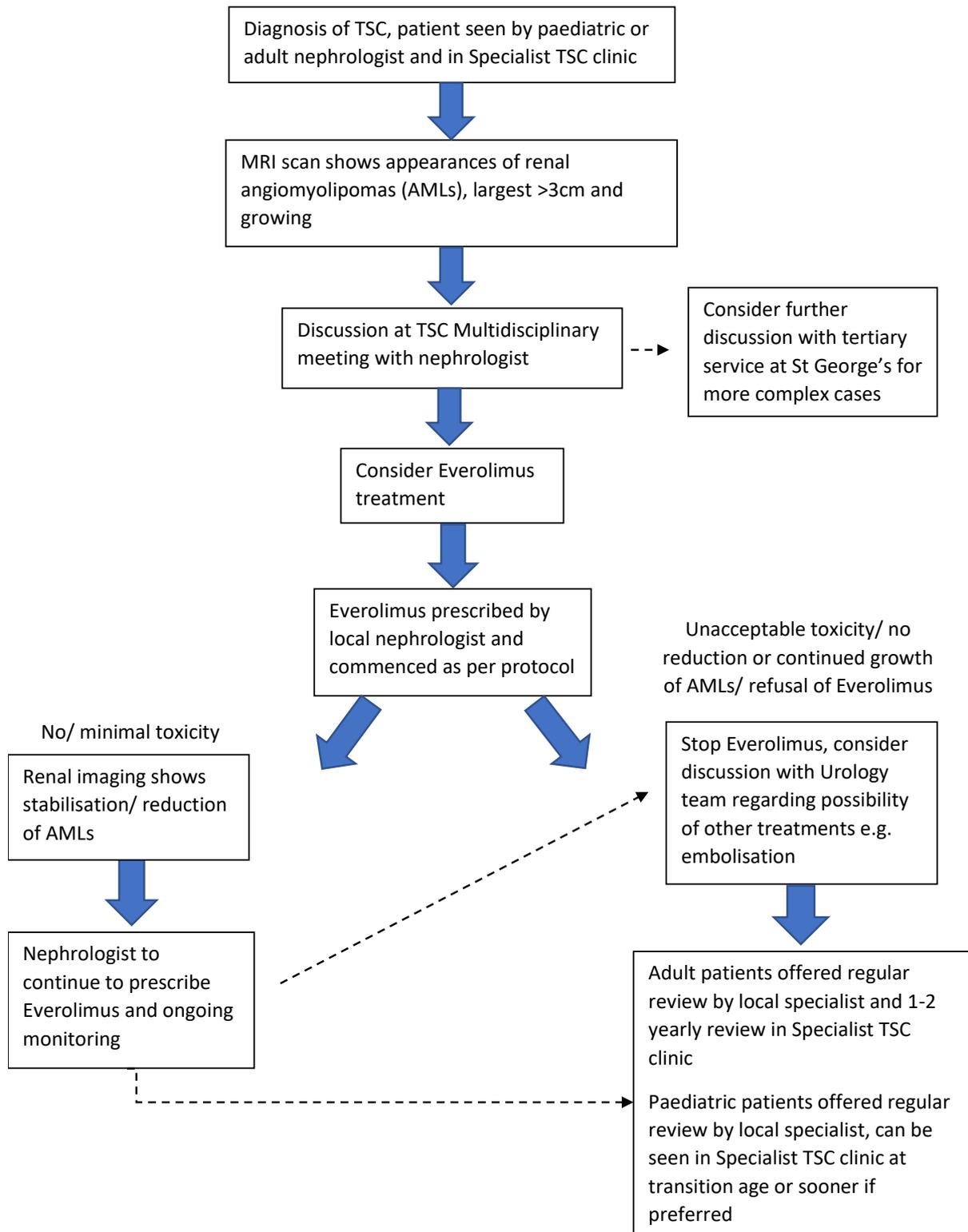
Further information on making IPFR requests can be found at: [Welsh Health Specialised Services Committee \(WHSSC\) | Individual Patient Funding Requests](#)

6. 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 subjected to an Equality Impact Assessment.

Annex i Pathway



Annex ii Codes

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

Annex iii Abbreviations and Glossary

Abbreviations

IPFR	Individual Patient Funding Request
TSC	Tuberous Sclerosis Complex
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.