GIG CYMRU NHS WALES

Pwyllgor Gwasanaethau Iechyd Arbenigol Cymru (PGIAC)

Welsh Health Specialised Services Committee (WHSSC)

Specialised Services
Policy Position Statement PP273

Everolimus for subependymal giant cell astrocytoma (SEGA) associated with tuberous sclerosis complex (TSC) (all ages)

December 2023

Version 1.0

PARCH - RESPECT

PARTNERIAETH - PARTNERSHIP

GWELLA AC ARLOESI - IMPROVEMENT & INNOVATION

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Description	NHS Wales will routinely commission this specialised service in accordance with the criteria described in this policy
Document No	PP273
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Contents

Policy Statement

Welsh Health Specialised Services Committee (WHSSC) will commission everolimus for people of all ages with subependymal giant cell astrocytoma (SEGA) 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 England[2] 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.

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] AWMSG, everolimus (Votubia®)
[2] NHS England Clinical commissioning Policy: Everolimus for subependymal giant cell astrocytoma (SEGA) associated with tuberous sclerosis complex

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 SEGA associated with TSC for people of all ages 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.

Subependymal giant cell astrocytomas (SEGAs) are a type of non-cancerous growth in the brain that can be caused by TSC. They can be solitary or multiple and usually form within the ventricles near the foramen of Monro, an opening deep in the brain that drains cerebrospinal fluid. They are usually asymptomatic until they grow large enough to block circulation of the cerebrospinal fluid (CSF), leading to hydrocephalus (a build-up of fluid on the brain). Common symptoms of SEGAs include headaches, nausea, vomiting, seizures, behavioural changes, and visual problems.

Surgery is the standard treatment for SEGAs. However, they are often found deep in the brain and this can mean that they can be difficult or impossible to remove. Surgery may lead to complications. It is also possible that surgery fails to remove all of the growth.

For patients with TSC who develop SEGAs that cannot be removed by surgery, they can be given a medicine to reduce the size of the SEGA, such as everolimus. Everolimus works by reducing the size and slows the growth of the SEGA.

1.2 Aims and Objectives

This Policy Position aims to define the commissioning position of WHSSC on the use of everolimus for people with SEGA 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 SEGA associated with TSC to access treatment
- improve outcomes for people with SEGA 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. SEGAs develop in 5-20% of TSC patients usually during childhood and adolescence.

1.4 Current Treatment

Surgery is the standard treatment for SEGAs; however, due to their deep location they can be difficult or impossible to resect, leading to complications or incomplete clearance. The risk of mortality or permanent serious post-operative complications increases in parallel to the difficulty of the surgery.

1.5 Proposed Treatment

Everolimus, a rapamycin analogue, is a disease modifying drug in TSC. It reduces tumour volume with respect to SEGAs and reports benefits on the distressing facial rash (facial angiofibromatosis). It acts by inhibiting mTOR (a major cell growth and proliferation controller), which is over-activated in individuals with TSC.

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 patients of all ages with SEGA associated with TSC in line with the criteria identified in the policy.

2.1 Inclusion Criteria

Patient presents with SEGA lesion(s) and has at least one lesion of baseline longest diameter 1cm as assessed by multiphase MRI and is considered not amenable to surgery as assessed by a properly constituted neuro-oncology multi-disciplinary team (MDT). Specifically, if the MDT decides that:

- the SEGA is too difficult to remove surgically; OR
- SEGA needs reduction in size prior to surgery; OR
- SEGA lesion(s) are multiple or infiltrative; OR
- surgery has been performed and there is residual SEGA (i.e. it was not possible to completely excise) that needs treating.

AND
The patient presents with:

- significant growth in target SEGA lesion(s) (as decided by a properly constituted neuro-oncology MDT since patient's last annual MRI); OR
- unequivocal worsening of non-target lesions of SEGA; OR
- the appearance of new lesion(s) of baseline longest diameter 1cm; OR
- symptoms of new or worsening hydrocephalus (but where urgent surgery is not required); OR
- patient presents for the first time with lesion(s) of baseline longest diameter 1cm (accounting for patients not cared for in a surveillance programme); OR
- partially excised SEGA lesion(s) known to be growing before surgery.

2.2 Exclusion Criteria

Any patient presenting with raised intracranial pressure (a surgical solution would be necessary as it would not be possible to wait for mTOR inhibition to take effect).

2.3 Stopping Criteria

- Evidence of continued growth in volume of the target SEGA lesion (any, assessed by bi-annual MRI); OR
- Evidence of appearance of one or more new SEGA lesions with a minimum longest diameter of 1cm; OR
- Serious adverse effects; OR(iv) Acute worsening of hydrocephalus necessitating a surgical solution; OR
- Non-compliance indicated by blood levels despite reasonable efforts to educate patients/parents and/or secure regular drug administration.

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 following discussion at the TSC MDT.

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 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 Welsh Government: The 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 Patient Pathway (Annex i)

Tuberous sclerosis is primarily diagnosed amongst children and young adults (<20), although patients may present as late as 40. Patients with TSC are monitored with annual multiphase MRI scans. If a SEGA lesion is detected, a neurologist should discuss patient in neuro-oncology MDT and TSC MDT, and a decision made whether to continue to monitor the lesion through regular scans or perform surgery to remove the lesion.

Any patient presenting with raised intracranial pressure will need a surgical solution (either removal of SEGA or shunt insertion) as it would not be possible to wait for mTOR inhibition to take effect.

If the patient is not amenable to surgery (as defined in 2.1 above, the MDT can decide to treat with everolimus which is prescribed by the local neurologist and commenced as per protocol. Everolimus will not be used first-line in patients who have acute symptoms.

Treatment is prescribed with an initial dose (a starting dose of 7mg/m² body surface area is recommended for ages 1 to less than 3 and 4.5 mg/m² for ages 3+) and titrated. Trough levels of everolimus should be monitored by the prescribing consultant after initiation of treatment, following dose changes, addition of concomitant medications or change in liver function. Primary care services may need to be involved in performing some routine blood tests (e.g. liver function tests) and treating any minor adverse events (such as mouth ulcers and stomatitis).

Everolimus is not curative and patients are likely to remain on the drug for many years.

2.8 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

2.9 Clinical Outcome and Quality Measures

The Provider must work to written quality standards and provide monitoring information to the lead commissioner.

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 and for children, teenagers and young adults.

2.10 Blueteq and reimbursement

Everolimus for SEGA associated with TSC for people of all ages 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 meets 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 AWTTC Vault for further information on the Patient Access Scheme (PAS) price.

2.11 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 and/or their parent or guardian 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 and/or their parent or guardian
- advise the patient and/or their parent or guardian of any side effects and risks of the potential treatment
- inform the patient and/or their parent or guardian 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: Everolimus for subependymal giant cell astrocytoma (SEGA) associated with tuberous sclerosis complex, 16066/P, December 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

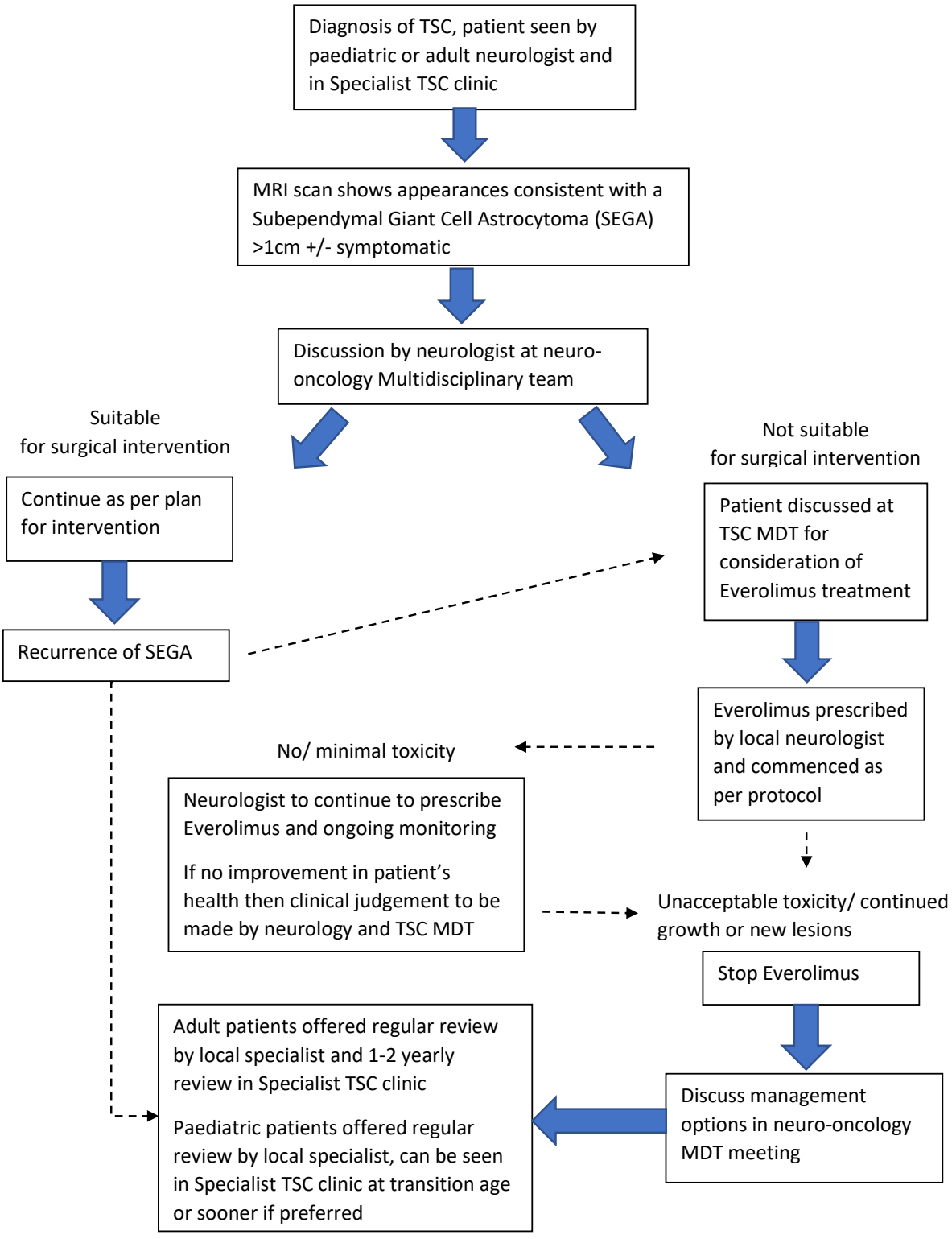
6. Equality Impact and Assessment

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.

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.

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.