GIG CYMRU NHS WALES

Pwyllgor Gwasanaethau Iechyd Arbenigol Cymru (PGIAC)

Welsh Health Specialised Services Committee (WHSSC)

Specialised Services Policy Position PP240

Risdiplam for Spinal Muscular Atrophy for people aged under 16 years

May 2022

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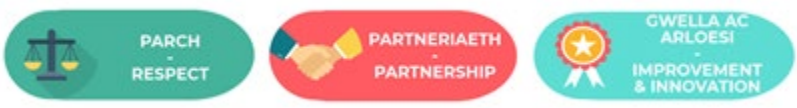

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Description	NHS Wales routinely commission this specialised service in accordance with the criteria described in this policy
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Policy Statement

Welsh Health Specialised Services Committee (WHSSC) commission risdiplam for children with spinal muscular atrophy from 2 months up until their 16th birthday in accordance with the criteria outlined in this document.

In creating this document WHSSC has reviewed the relevant guidance issued by National Institute of Health and Care Excellence (NICE)[1] and has concluded that risdiplam should be made available.

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] NICE, Technology appraisal guidance: Risdiplam for treating spinal muscular atrophy (TA755)

1. Introduction

This Policy Position Statement has been developed for the planning and delivery of risdiplam children with spinal muscular atrophy from 2 months up until their 16th birthday. 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. Commissioning of risdiplam for adults is the responsibility of Health Boards.

1.1 Plain language summary

Spinal muscular atrophy (SMA) is a rare, progressive neuromuscular disease caused by a genetic mutation in the SMN1 gene on chromosome 5q. People with the condition have a range of symptoms, including muscle weakness, and have worsening physical disability, mobility loss and respiratory dysfunction. SMA can be grouped into 5 main types (0 to 4), based on the age of onset and the maximum motor function reached.

SMA type 0, the most severe, affects babies before birth. The babies do not develop any motor skills and often survive for only a few weeks after birth.

Babies with type 1 SMA are unable to sit or roll because of severe muscle weakness, which gets worse over time. The muscle weakness also affects swallowing and breathing, and typically results in death within 2 years if respiratory support is not used.

In type 2 SMA, the onset of symptoms is between 7 months and 18 months. People with this condition can sit independently at diagnosis. However, progressive loss of motor function means they have a reduced life expectancy compared with the general population.

In type 3 SMA there are varying degrees of muscle weakness, which appear between 18 months and 18 years. People with this condition can have a normal lifespan and walk or sit unaided, but many lose mobility and other functions over time.

Type 4 SMA is the least severe and affects adults, who may have milder motor impairment and live a normal lifespan. Type 0 and type 4 SMA are rarely diagnosed in clinical practice in the NHS. SMA is a rare, progressive neuromuscular disorder, so all patients experience more severe symptoms over time and affects all aspects of daily life[2].

Risdiplam is a small molecule drug that targets the 'back up' survival motor neuron 2 (*SMN2*) gene to produce more SMN protein. Signals (called messenger RNAs) are made from *SMN2*, and risdiplam specifically interacts with these, resulting in more SMN protein being made in cells of the body. Risdiplam crosses the blood brain barrier and distributes throughout the

[2] https://www.nice.org.uk/guidance/TA755

body to many different types of cell, tissue and organ, including the brain, spinal cord and muscles. It is given daily in liquid form by mouth or feeding tube at the prescribed dose, at approximately the same time each day[3].

1.2 Aims and Objectives

This Policy Position Statement aims to define the commissioning position of WHSSC on the use of risdiplam for children with spinal muscular atrophy from 2 months old up until their 16th birthday.

The objectives of this policy are to:

- ensure commissioning for the use of risdiplam is evidence based
- ensure equitable access to risdiplam
- define criteria for people with spinal muscular atrophy to access treatment
- improve outcomes for people with spinal muscular atrophy.

1.3 Epidemiology

Approximately 1 in 40 people carry the faulty SMN1 gene15, that means there are around 1.67 million carriers in the UK.

Recent studies indicate that approximately one in every 10,000 babies worldwide are born with a type of SMA, and that SMA Type 1 accounts for approximately 60% of cases[4,5]. In 2015, there were 33,215 live births in Wales which suggests that in that year, approximately 3 babies were born in Wales with a type of SMA.

Recent studies suggest between 1 and 2 people in every 100,000 worldwide have a Type of SMA[3,4] which suggests a prevalence of between 31 and 62 in Wales.

1.4 Current Treatment

Most treatments for spinal muscular atrophy are based on symptom control and aim to maintain movement and function for as long as possible and to improve quality of life. This involves a multidisciplinary approach including respiratory, gastroenterology and orthopaedic care, as well as nutritional support, physiotherapy, assistive technologies, occupational therapy and social care.

Nusinersen is a disease-modifying treatment for 5q SMA, available under a Managed Access Agreement for patients with SMA types 1, 2 and 3. In

[3] https://smauk.org.uk/risdiplam
[4] Verhaart IEC et al. (2017) Prevalence, incidence and carrier frequency of 5q–linked spinal muscular atrophy – a literature review. *Orphanet J Rare Dis 12:* 124.
[5] Verhaart IEC, et al. (2017) A multi-source approach to determine SMA incidence and research ready population. J Neurol 264: 1465-1473.

some patients, intrathecal administration of nusinersen may require sedation and/or radiographic imaging; patients may also feel anxiety associated with lumbar puncture.

1.5 Proposed Treatment

Risdiplam is a survival of motor neuron 2 (SMN2) pre-mRNA splicing modifier designed to treat SMA caused by mutations of the SMN1 gene in chromosome 5q that lead to SMN protein deficiency. Functional SMN protein deficiency is directly linked to the SMA pathophysiology which includes progressive loss of motor neurons and muscle weakness. Risdiplam corrects the splicing of SMN2 to shift the balance from exon 7 exclusion to exon 7 inclusion into the mRNA transcript, leading to an increased production of functional and stable SMN protein. Thus, risdiplam treats SMA by increasing and sustaining functional SMN protein levels[6]. Risdiplam is taken orally once a day.

1.6 What NHS Wales has decided

WHSSC has carefully reviewed the relevant guidance issued by National Institute of Health and Care Excellence (NICE). We have concluded that risdiplam should be made available within the criteria set out in section 2.1.

[6] https://www.medicines.org.uk/emc/product/12582/smpc#gref

2. Criteria for Commissioning

The Welsh Health Specialised Services Committee approve funding of risdiplam for children with spinal muscular atrophy from 2 months up until their 16th birthday, in-line with the criteria identified in the policy.

2.1 Inclusion Criteria

- Risdiplam is recommended as an option for treating 5q spinal muscular atrophy (SMA) in people 2 months and older[7], with a clinical diagnosis of SMA types 1, 2 or 3 or with pre-symptomatic SMA and 1 to 4 SMN2 copies.
- It is recommended only if the conditions of the Managed Access Agreement (MAA) are followed.

2.2 Exclusion Criteria

- People aged 16 years and older[8].

2.3 Stopping Criteria

Stopping criteria are detailed in the MAA.

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 specification 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.

[7] This treatment is commissioned by WHSSC for people aged up to 16 years of age.
[8] Health Boards have the commissioning responsibility of risdiplam for people aged 16 years and older.

2.6 Patient Pathway (Annex i)

Patients should be referred for assessment of eligibility for treatment to a Paediatric Neurologist at the following centres:

- Children's Hospital for Wales
  University Hospital of Wales
  Heath Park Way
  Cardiff
  CF14 4XW

- Alder Hey Children's Hospital
  East Prescot Road
  Liverpool
  L14 5AB

Treatment cannot commence until the patient and/or their parent or guardian has signed the MAA.

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 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 manner in which 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.

2.9 Blueteq and reimbursement

Risdiplam will only be funded for patients registered via the Blueteq system and where an appropriately constructed MDT has approved its use within highly specialised paediatric endocrinology centres.

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 risdiplam is prescribed and administered in accordance with its marketing authorisation[9].

Risdiplam is available as a 0.75 mg/mL powder for oral solution. The cost per 80ml pack is £7,900 excluding VAT[10]. The company has a commercial access agreements. This makes risdiplam available to the NHS with a discount. The size of the discount is commercial in confidence. Health Boards in Wales should refer to the AWTTC Vault for further information on the Patient Access Scheme (PAS) price.

2.10 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.

[9] Evrysdi 0.75 mg/mL powder for oral solution - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)
[10] Medicinal forms | Risdiplam | Drugs | BNF | NICE

The Provider must comply with the requirements of the NICE MAA which includes mandated participation in the 'SMA reach' clinical outcome tool.

2.11 Responsibilities

Referrers should:

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

Clinicians 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.

2.12 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 risdiplam at the agreed discounted price.
- Health Boards are to ensure that all providers understand the need to approve risdiplam 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:

- **National Institute of Health and Care Excellence (NICE) guidance**
  - Risdiplam for treating spinal muscular atrophy, TA755, 16 December 2021

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 Codes

Code Category	Code	Description
ICD-10	G12	Spinal muscular atrophy and related syndromes.

Annex ii Abbreviations and Glossary

Abbreviations

IPFR Individual Patient Funding Request

MAA Managed Access Agreement

NICE National Institute for Health and Care Excellence

SMA Spinal Muscular Atrophy

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.

Appendix 1 Prior Approval Request Form

PRIOR APPROVAL REQUEST FORM

Details of clinician making the referral:	
Name:	
Designation:	
Address:	
Postcode:	
Telephone number:	
Email:	
Secretary name:	
Telephone:	Email:

Patient Details	
First name:	Last name:
Address:	Date of birth:
	NHS number:
Postcode:	Hospital number:

Urgency			
How urgent is the request? (tick as applicable)	**Urgent:** 24-48 hours	**Soon:** Within 3 weeks	**Non-urgent:** 4-6 weeks

Please note: *If a decision is required urgently, clinical reasons must be provided. Administrative reasons will not be considered.*

Reason for request
☐ NICE Approved Drugs
☐ NICE Technology Appraisals and Highly Specialised Technology Appraisals
☐ AWMSG Health Technology Appraisals (including the orphan and ultra-orphan status)

Clinical details
Details of treatment requested (including weight of patient, dosage and duration)
Medical history and current clinical status -: (**Please provide a copy of the latest clinical report**)
Additional information to support the referral: (e.g. relevant clinical letters/reports)
Cost of treatment:

I confirm that as the patient's Consultant, I have discussed this application and consent has been provided to obtain further clinical information pertinent to this funding request if required.

Clinicians signature:

Date:

Please return this form with a copy of the referral letter to:

Please return completed form to:

Patient Care Team
Welsh Health Specialised Services
Unit G1, The Willowford
Treforest Industrial Estate
CF37 5YL

Email: whssc.ipc@wales.nhs.uk or whssc.ipc@nhs.net

If you have any questions, please telephone 01443 443443 ext.78123