GIG CYMRU NHS WALES

Pwyllgor Gwasanaethau Iechyd Arbenigol Cymru (PGIAC)

Welsh Health Specialised Services Committee (WHSSC)

Specialised Services Policy Position Statement PP187

Treatment options for Transthyretin Amyloidosis in Adults

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	For action Chief Pharmacists, Clinical Leads, Lead Consultant Neurology, All Wales Medical Genetic Services, lead consultant clinical and laboratory genetics, lead metabolic consultant, The National Amyloidosis Centre, UCL
Description	NHS Wales propose to 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) will commission inotersen, patisiran and vutrisiran for adults with stage 1 and stage 2 polyneuropathy with hereditary transthyretin amyloidosis in accordance with the criteria outlined in this document.

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.

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 inotersen, patisiran and vutrisiran for stage 1 and stage 2 polyneuropathy in adults with hereditary transthyretin amyloidosis for people resident in Wales. These treatments 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 National Institute of Health and Care Excellence (NICE)[1] and has concluded that inotersen, patisiran and vutrisiran should be made available.

1.1 Background

Hereditary transthyretin (hATTR) amyloidosis

Hereditary transthyretin (hATTR) amyloidosis is an ultra-rare condition caused by inherited mutations in the transthyretin (TTR) gene. The mutation causes the liver to produce abnormal TTR protein which accumulates as deposits in body tissues (amyloidosis). These deposits can disrupt the structure and damage the function of affected tissues.

Hereditary transthyretin (hATTR) amyloidosis can affect tissues throughout the body, and people may have a range of symptoms relating to 1 or more systems. These can include the:

- autonomic nervous system
- peripheral nerves
- heart
- gastrointestinal system
- eyes
- central nervous system.

The effects and complications of the condition can lead to death within 3 to 15 years of symptoms developing. There are approximately 150 people with hATTR amyloidosis in the UK[2].

Scoring systems for evaluating hATTR amyloidosis include scores based on disability due to peripheral neuropathy, for example, the polyneuropathy disability (PND) score and the familial amyloidotic polyneuropathy (FAP) stage)[3] (See table 1).

[1] https://www.nice.org.uk
[2] NICE STA. Vutrisiran for treating hereditary transthyretin-related amyloidosis [ID5074]. Final scope.
[3] Coutinho et al. (1980) Forty years of experience with type I amyloid neuropathy. Review of 483 cases. In: Glenner, G., Costa, P. and de Freitas, A. (eds), Amyloid and Amyloidosis. Amsterdam: Execerpta Medica, pp. 88–98

Table 1: Description and relationship between PND scores and FAP stages

PND score	PND score description	FAP stage	FAP stage description
0	No impairment	0	No symptoms
I	Sensory disturbances, preserved walking capability	1	Unimpaired ambulation; mostly mild sensory and motor neuropathy in the lower limbs
II	Impaired walking capability but ability to walk without a stick or crutches	2	Assistance with ambulation needed; mostly moderate impairment progression to the lower limbs, upper limbs and trunk
IIIA	Walking only with the help of 1 stick		
IIIB	Walking with the help of 2 sticks or crutches		
IV	Confined to a wheelchair or bedridden	3	Wheelchair-bound or bedridden; severe sensory and motor neuropathy of all limbs
Abbreviations: FAP, familial amyloidotic polyneuropathy; PND, polyneuropathy disability.			

Neuropathy in hATTR amyloidosis can be classified according to walking ability[4]:

- Stage 1: people do not need help with walking and have mostly mild sensory, motor neuropathy in the lower limbs, and autonomic neuropathy
- Stage 2: people need help with walking, there is progression in the lower limbs and symptoms develop in the hands (weakness and muscle wasting).
- Stage 3: people are wheelchair bound or bedridden and have severe sensory and motor neuropathy of all limbs, and autonomic neuropathy

People mainly have symptoms of polyneuropathy or cardiomyopathy, most patients seen in the NHS will have symptoms of both over the course of the condition.

In the UK, the most common genetic mutations associated with both polyneuropathy and cardiac involvement are Val122Ile (39%), Thr60Ala (25%) and Val30Met (17%). The Val30Met mutation is associated with higher survival rates. Val122Ile is primarily associated with cardiomyopathy.

[4] Coutinho et al. (1980) Forty years of experience with type I amyloid neuropathy. Review of 483 cases. In: Glenner, G., Costa, P. and de Freitas, A. (eds), Amyloid and Amyloidosis. Amsterdam: Execerpta Medica, pp. 88–98

1.2 Current Treatment

Current treatment options for hereditary transthyretin amyloidosis are limited and focus on supportive care, symptom relief such as pain management and nutritional and mobility support and lessening the effects of the condition on other organs, such as pacemakers and arrhythmia management.

Liver transplant, which prevents the formation of additional amyloid deposits, might be an option for some people. However, a transplant can only be done early in the course of the condition, and outcomes are poor in people with cardiac involvement, so this procedure is rarely done.

Inotersen

Inotersen (Tegsedi, Akcea Therapeutics) is a novel, first-in-class 2'-O-2-methoxyethyl phosphorothioate antisense oligonucleotide that inhibits production of transthyretin (TTR) in adults with hereditary transthyretin (hATTR) amyloidosis.

Patisiran

Patisiran (Onpattro, Alnylam) is a ribonucleic acid interference agent that inhibits TTR production by the liver (including abnormal TTR).

Vutrisiran

Vutrisiran (Amvuttra, Alnylam) is a ribonucleic acid interference agent that inhibits TTR production by the liver (including abnormal TTR).

1.3 Equality Impact 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-026[5].

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.

[5] https://whssc.nhs.wales/publications/corporate-policies-and-procedures/corp-026-eqia-policy/

An EQIA was also carried out by NICE during the evaluations of inotersen, patisiran and vutrisiran. For further details, please refer to the NICE website at:

- Inotersen: https://www.nice.org.uk/guidance/hst9
- Patisiran: https://www.nice.org.uk/guidance/hst10
- Vutrisiran https://www.nice.org.uk/guidance/ta868

2. Recommendations

The recommendations below represent the views of NICE, arrived at after careful consideration of the evidence available. Health professionals are expected to take into account the relevant NICE guidance[6], alongside the individual needs, preferences and values of the patient.

2.1 Inclusion Criteria

Inotersen

Inotersen is recommended, within its marketing authorisation, as an option for treating stage 1 and stage 2 polyneuropathy in adults with hereditary transthyretin amyloidosis. It is recommended only if the company provides inotersen according to the commercial arrangement[7].

Patisiran

Patisiran is recommended, within its marketing authorisation, as an option for treating hereditary transthyretin amyloidosis in adults with stage 1 and stage 2 polyneuropathy. It is recommended only if the company provides patisiran according to the commercial arrangement[8].

Vutrisiran

Vutrisiran is recommended, within its marketing authorisation, as an option for treating hereditary transthyretin amyloidosis in adults with stage 1 and stage 2 polyneuropathy. It is recommended only if the company provides vutrisiran according to the commercial arrangement[9].

If people with the condition and their clinicians consider vutrisiran to be 1 of a range of suitable treatments, discuss the advantages and disadvantages of the available treatments. After that discussion, if more than 1 treatment is suitable, choose the least expensive. Take account of administration costs, dosage, price per dose and commercial arrangements.

2.2 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.

[6] NICE | The National Institute for Health and Care Excellence
[7] Overview | Inotersen for treating hereditary transthyretin amyloidosis | Guidance | NICE
[8] Overview | Patisiran for treating hereditary transthyretin amyloidosis | Guidance | NICE
[9] Overview | Vutrisiran for treating hereditary transthyretin-related amyloidosis | Guidance | NICE

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.

2.3 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.

2.4 Designated Providers

NHS National Amyloidosis Centre
Centre for Amyloidosis & Acute Phase Proteins
Division of Medicine (Royal Free Campus)
University College London
Rowland Hill Street
London NW3 2PF

2.5 Patient Pathway (See Annex i)

2.6 Blueteq and reimbursement

Inotersen, patisiran and vutrisiran 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 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.

Inotersen is self-administered once weekly by subcutaneous injection. The price of inotersen per weekly dose (284 mg) is £5,925 (excluding VAT)[10].

Patisiran is administered once every 3 weeks by intravenous infusion at a dose of 0.3 mg/kg. The price of patisiran is £7,676.47 per 10-mg vial (excluding VAT)[10].

[10] https://bnf.nice.org.uk/

Vutrisiran is administered at a dose of 25 mg every three months by subcutaneous injection. The price of vutrisiran is £95,862.36 per 0.5 ml solution for injection containing 25 mg of vutrisiran (excluding VAT)[10].

The companies for each of these medicines has a commercial arrangement. This makes them 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.

2.7 Action to be taken

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

- WHSSC are to ensure that all providers are purchasing inotersen, patisiran and vutrisiran at the agreed discounted price.

- Providers are to ensure the need to approve inotersen, patisiran and vutrisiran 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. Putting Things Right

3.1 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.

3.2 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.

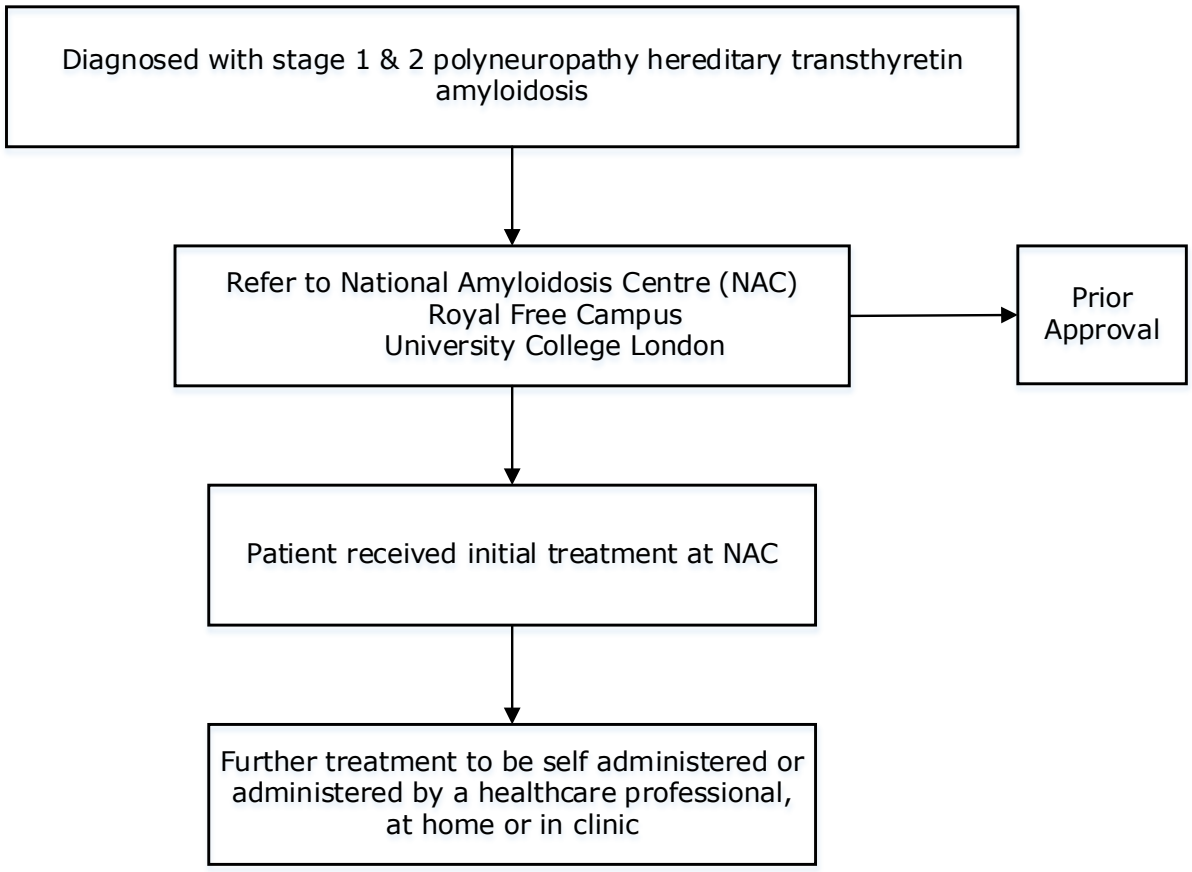
If an IPFR is declined by the Panel, a patient and/or their NHS clinician has the right to request information about how the decision was reached. If the patient and their NHS clinician feel the process has not been followed in accordance with this policy, arrangements can be made for an independent 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 Patient Pathway

Pathway for adults with stage 1 and stage 2 polyneuropathy



Annex ii Codes

Code Category	Code	Description
ICD-10	E85.1	Neuropathic heredofamilial amyloidosis