GIG CYMRU NHS WALES

Pwyllgor Gwasanaethau Iechyd Arbenigol Cymru (PGIAC)

Welsh Health Specialised Services Committee (WHSSC)

# Specialised Services Policy Position PP187

## Treatment options for Transthyretin Amyloidosis in Adults

*June 2020*

*Version 1.0*

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| **Description** | NHS Wales will routinely commission this specialised service in accordance with the criteria described in this policy |
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# Contents

# Policy Statement

Welsh Health Specialised Services Committee (WHSSC) in accordance with the criteria outlined in this document will commission the following treatments for Transthyretin Amyloidosis:

- Inotersen for stage 1 and stage 2 polyneuropathy in adults with hereditary transthyretin amyloidosis
- Patisiran for stage 1 and stage 2 polyneuropathy in adults with hereditary transthyretin amyloidosis

In creating this document WHSSC has reviewed the relevant guidance issued by National Institute of Health and Care Excellence (NICE) and has concluded that Inotersen and Patisiran 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.

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 for stage 1 and stage 2 polyneuropathy in adults with hereditary transthyretin amyloidosis, **and**
- Patisiran for stage 1 and stage 2 polyneuropathy in adults with hereditary transthyretin amyloidosis

This service will only be commissioned by the Welsh Specialised Services Committee (WHSSC) and applies to residents of all seven Health Boards in Wales.

## 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[1].

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)[2] (See table 1).

[1] At the time of evidence submission to NICE.
[2] Coutinho et al. 1980

**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[3]:

- 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.

[3] Coutinho et al.1980

## 1.2 Aims and Objectives

This Policy Position Statement aims to define the commissioning position of WHSSC on the use of:

- Inotersen for stage 1 and stage 2 polyneuropathy in adults with hereditary transthyretin amyloidosis, **and**
- Patisiran for stage 1 and stage 2 polyneuropathy in adults with hereditary transthyretin amyloidosis

The objectives of this policy are to:

- ensure commissioning for the use of Inotersen or Patisiran is evidence based
- ensure equitable access to Inotersen or Parisian
- define criteria for people with transthyretin amyloidosis to access treatment
- improve outcomes for people with transthyretin amyloidosis

## 1.3 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.

## 1.4 Proposed Treatment

### 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.

Inotersen is self-administered once weekly by subcutaneous injection and has a marketing authorisation for the treatment of stage 1 or stage 2 polyneuropathy in adults with hATTR amyloidosis.

### Patisiran

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

Patisiran is administered once every 3 weeks by intravenous infusion at a dose of 0.3 mg/kg. It has a marketing authorisation in the UK for treating hereditary transthyretin-mediated amyloidosis in adult patients with stage 1 or stage 2 polyneuropathy.

## 1.5 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 Inotersen and Patisiran should be made available within the criteria set out in section 2.1.

# 2. Criteria for Commissioning

The Welsh Health Specialised Services Committee in-line with the criteria identified in the policy approve funding of:

- Inotersen for stage 1 and stage 2 polyneuropathy in adults with hereditary transthyretin amyloidosis, **and**
- Patisiran for stage 1 and stage 2 polyneuropathy in adults with hereditary transthyretin amyloidosis

## 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[4].

### 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[5].

## 2.2 Exclusion Criteria

Inotersen or Patisiran are only for treating stage 1 and stage 2 polyneuropathy in adults with hereditary transthyretin amyloidosis within the criteria listed in section 2.1.

## 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 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

[4] Overview | Inotersen for treating hereditary transthyretin amyloidosis | Guidance | NICE
[5] Overview | Patisiran for treating hereditary transthyretin amyloidosis | Guidance | NICE

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)

Adults with stage 1 and stage 2 polyneuropathy hereditary transthyretin amyloidosis will be managed at:

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

The treating clinician will complete a prior approval form for commencing Inotersen or Patisiran, (annex v). This form will need to be submitted to the Individual Patient Funding Request team at WHSSC.

## 2.6 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

## 2.7 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.

## 2.8 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.

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:

- **National Institute of Health and Care Excellence (NICE) guidance**
  - Inotersen for treating hereditary transthyretin-related amyloidosis, Highly Specialised Technologies Guidance, HST9. May 2019.
  - Patisiran for treating hereditary transthyretin amyloidosis, Highly Specialised Technologies guidance, HST10. August 2019

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

- **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

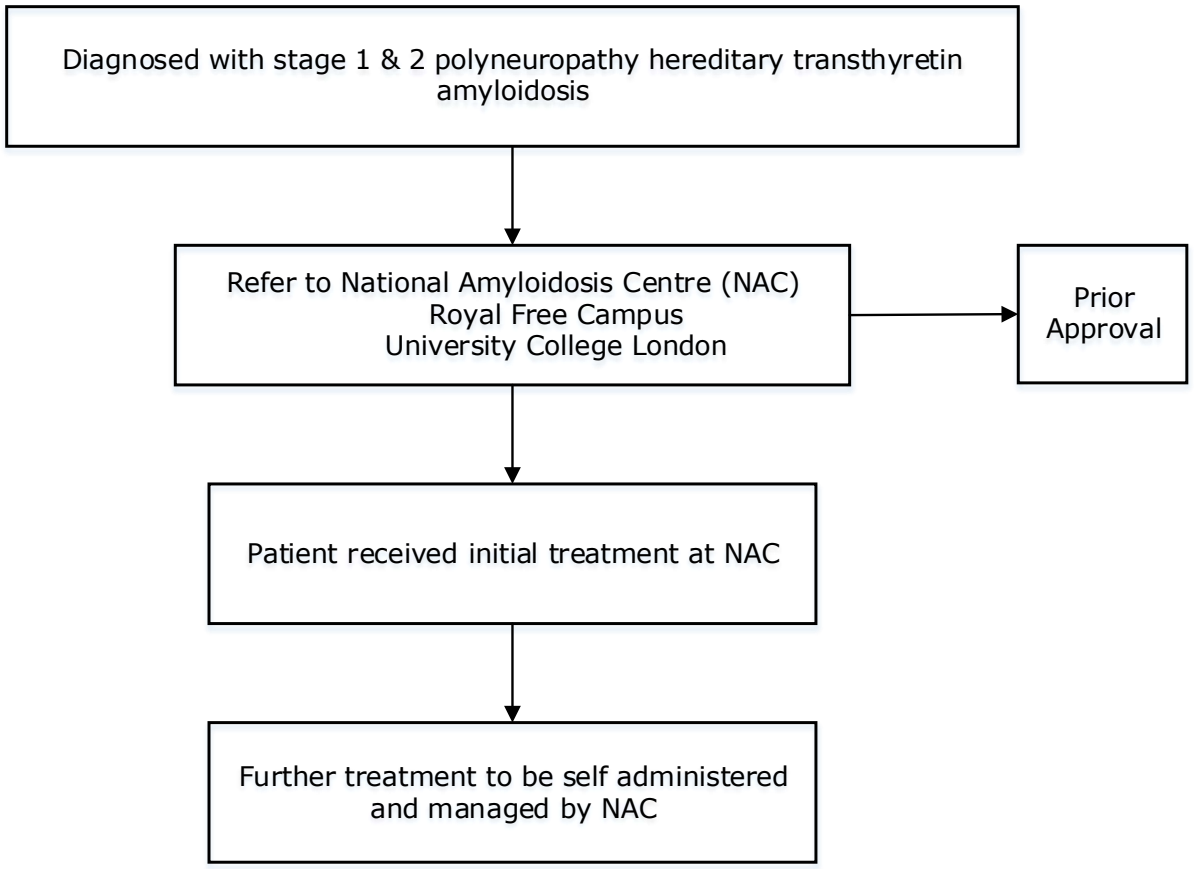
The Equality Impact Assessment (EQIA) process has been developed to help promote fair and equal treatment in the delivery of health services. It aims to enable Welsh Health Specialised Services Committee to identify and eliminate detrimental treatment caused by the adverse impact of health service policies 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 Patient Pathway

Pathway for Adults with stage 1 and stage 2 polyneuropathy



# Annex ii Checklist

**Inotersen for stage 1 and stage 2 polyneuropathy in adults with hereditary transthyretin amyloidosis**

**Patisiran for stage 1 and stage 2 polyneuropathy in adults with hereditary transthyretin amyloidosis**

The following checklist should be completed for every patient to whom the policy applies:

- Where the patient meet the criteria **and** the procedure is included in the contract **and** the referral is received by an agreed centre, the form should be completed and retained by the receiving centre for audit purposes.
- The patient meets the criteria **and** is received at an agreed centre, but the procedure is not included in the contract. The checklist must be completed and submitted to WHSSC for prior approval to treatment.
- The patient meets the criteria but wishes to be referred to a non-contracted provider. An Individual Patient Funding Request (IPFR) Form must be completed and submitted to WHSSC for consideration.
- 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.

# Annex iv Abbreviations and Glossary

## Abbreviations

**hATTR** Hereditary transthyretin

**IPFR** Individual Patient Funding Request

**NAC** National Amyyloidosis Centre

**UCL** University College London

**WHSSC** Welsh Health Specialised Services

## Glossary

### Hereditary Transthyretin Amyloidosis

Hereditary transthyretin amyloidosis is a condition caused by inherited gene mutations that cause the liver to produce abnormal proteins.

### Inotersen

Is a medication given as an injection which slows the progression of neuropathy symptoms but does not reverse or cure the condition. This can allow patients to maintain a higher quality of life for longer.

### 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.

### National Amyloidosis Centre

The centre is University College London, it is the only highly specialised service for people with amyloidosis and related disorders in the UK.

### Neuropathy

Disease or dysfunction of one or more peripheral nerves, typically causing numbness or weakness.

### Patisiran

Patisiran (Onpattro, Alnylam) is a ribonucleic acid interference agent that suppresses transthyretin (TTR) production by the liver (including abnormal TTR). It is administered once every 3 weeks by intravenous infusion

### 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.

## Annex v 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<br>☐ NICE Technology Appraisals and Highly Specialised Technology Appraisals<br>☐ 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:<br>(**Please provide a copy of the latest clinical report**) |
| Additional information to support the referral:<br>(e.g. relevant clinical letters/reports ) |
| Recommendation as per NICE or AWMSG<br>(please enter the published recommendation) |
| 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
Pontypridd
CF37 5YL

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

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