Engagement Report

Topic details

Title of policy or policy statement:	Lonafarnib for Hutchinson-Gilford progeria syndrome (12 months of age and over)
Programme of Care:	Women and Children
Clinical Reference Group:	Paediatric Medicine
URN:	2402

1. Summary

This report summarises the feedback NHS England received from engagement during the development of this policy proposition, and how this feedback has been considered.

2. Background

Progeroid laminopathies are rare, fatal genetic conditions characterised by an appearance of accelerated aging in children. The majority of patients with progeroid laminopathies have the type, Hutchinson-Gilford progeria syndrome (HGPS). This condition is also known as ‘progeria’.

A specific pathogenic variant (gene change) in the LMNA gene, located on chromosome 1, is responsible for HGPS. This genetic variant is sporadic and occurs without family history. The LMNA gene produces the Lamin protein, which is part of the structural scaffolding that holds the nucleus of a cell together. It is believed that the defective Lamin A protein makes the nucleus unstable. That cellular instability leads to the process of premature aging.

Although individuals are born appearing healthy, children with progeria begin to display many characteristics of accelerated aging within the first two years of life. Progeria signs include growth failure, loss of body fat and hair, aged-looking skin, stiffness of joints, hip dislocations, atherosclerosis, cardiovascular disease and stroke. Children with progeria have significant physical disability and require help with all activities of daily living, but they are cognitively normal. Children with progeria usually die of atherosclerosis (heart disease) at an average age of 14.5 years.

There is no current clinical commissioning policy or arrangement for these patients. Current standard of care involves multi-disciplinary clinical monitoring by local teams with monitoring of growth and weight, bone density scans, dental reviews, cardiology reviews, hearing tests and psychological support due to visible differences.

Treatment is supportive and does not involve attempting to reduce the accumulation of progerin and its expression. Examples of supportive care include hearing aids; ocular

lubrication for exposure keratopathy; tooth extractions for dental crowding; physical and occupational therapy for skeletal abnormalities and joint contractures and annual cardiac screening. Mortality in these patients is usually attributed to cardiovascular complications, therefore supportive treatments aim to reduce cardiovascular sequelae, such as low-dose aspirin, statins to lower cholesterol, antihypertensives and anticoagulants. These medications may not be started at the time of diagnosis but are started when felt to be clinically needed.

Lonafarnib is a potent and specific inhibitor of farnesyltransferase, therefore blocking the farnesylation of progerin and reducing the accumulation of progerin and progerin-like proteins in the cells.

Lonafarnib is licensed for the treatment of patients 12 months of age and older with a genetically confirmed diagnosis of HGPS or a processing-deficient progeroid laminopathy associated with either a heterozygous LMNA mutation with progerin-like protein accumulation or a homozygous or compound heterozygous ZMPSTE24 mutation. This policy proposition is applicable to patients 12 months of age and older with a genetically confirmed diagnosis of HGPS with a heterozygous LMNA mutation with progerin-like protein accumulation in line with the findings from the evidence review.

This policy proposition recommends lonafarnib to be available as a treatment option for HGPS within the criteria outlined in the policy proposition.

3. Engagement

The policy proposition underwent a two-week stakeholder testing between the 21st May and 4th June 2025 with registered stakeholders from the following Clinical Reference Groups:

- Specialised paediatric rheumatology
- Paediatric haematology
- Specialised paediatric gastroenterology
- Specialised paediatric renal services
- Specialised paediatric respiratory
- Metabolic disorders
- Congenital heart services
- Specialised paediatric endocrinology
- Specialised dermatology
- Genomics Clinical Reference Group

Respondents were asked the following consultation questions:

- Do you support the proposal for Lonafarnib for Hutchinson-Gilford progeria syndrome (12 months of age and over) through routine commissioning based on the evidence review and within the criteria set out in this document?
- Do you believe that there is any additional information that we should have considered in the evidence review? If so, please give brief details.
- Do you believe that there are any potential positive and/or negative impacts on patient care as a result of making this treatment option available? If so, please give details.
- Do you have any further comments on the proposal?
- Do you support the Equality and Health Inequalities Impact Assessment (EHIA)?

- Does the Patient Impact Assessment (PIA) present a true reflection of the patient and carers lived experience of this condition?
- Do you have any potential conflict of interest relating to this document or service area?

The comments have then been shared with the Policy Working Group to enable full consideration of feedback and to support a decision on whether any changes to the proposition might be recommended.

A 13Q assessment has been completed following stakeholder testing.

The Programme of Care has decided that the proposition offers a clear and positive impact on patient treatment, by potentially making a new treatment available which widens the range of treatment options without disrupting current care or limiting patient choice, and therefore further public consultation was not required. This decision has been assured by the Patient Public Voice Advisory Group.

4. Engagement Results

The policy proposition received 4 stakeholder responses from 4 individuals.

This was deemed to be a significant stakeholder response, given the rarity of the condition. The majority of stakeholders agreed with the policy proposition and felt this offered patients a positive change.

5. How has feedback been considered?

Responses to engagement have been reviewed by the Policy Working Group and the Women and Children PoC. The following themes were raised during engagement:

Keys themes in feedback	NHS England Response
Support for proposal	
Three stakeholders supported the proposal. One stakeholder queried the exclusion criteria which had been included in the policy.	Noted. The exclusion criteria in the policy proposition have been taken from Section 4.3 of the Medicines and Healthcare products Regulatory Agency (MHRA) approved Summary of Product Characteristics (SmPC) which outlines contraindications to Lonafarnib use.
Evidence review	
Three stakeholders agreed that the relevant evidence had been identified. One stakeholder asked that clinical tests be included to see if further exclusion criteria were necessary.	Noted. Further clinical tests are not proposed as the exclusion criteria in the policy proposition have been taken from Section 4.3 of the MHRA approved SmPC which outlines contraindications to Lonafarnib use.
Impact on patient care from making treatment option available	
Three stakeholders agreed that the treatment option would have a positive impact on patient care. One stakeholder said they were unsure but did not provide any reasoning for this response.	Noted.
Potential impact on equality and health inequalities	

All stakeholders agreed with the equalities and health inequalities impact assessment.	Noted.
Patient impact assessment	
All stakeholders agreed with the patient impact assessment.	Noted.

3. Has anything been changed in the policy proposition as a result of the stakeholder testing and consultation?

No.

Are there any remaining concerns outstanding following the consultation that have not been resolved in the final policy proposition?

No.