NHS ENGLAND SPECIALISED SERVICES

CLINICAL PANEL REPORT

Date: 19th March 2025

Intervention: Lonafarnib

Indication: Hutchinson-Gilford progeria syndrome (12 months of age and over)

URN: 2402

Gateway: 2, Round 1

Programme: Women and Children

CRG: Paediatric Medicine

Information provided to the Panel

Policy Proposition

Change of Policy Title report

Evidence Review completed by Solutions for Public Health

Clinical Priorities Advisory Group (CPAG) Summary Report

Evidence to Decision (EtD) Summary

Equalities and Health Inequalities (EHIA) Assessment

Patient Impact Assessment

Blueteq® Form

Policy Working Group (PWG) Appendix

This Policy Proposition recommends the licensed use of Lonafarnib in Hutchinson-Gilford progeria syndrome (12 months of age and over). Progeroid laminopathies are rare, fatal genetic conditions characterised by an appearance of accelerated aging in children. The majority of patients with progeroid laminopathies have Hutchinson-Gilford progeria syndrome (HGPS). The genetic variant is sporadic and occurs without family history. Current standard of care involves multi-disciplinary clinical monitoring by local teams and treatment is supportive care. 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.

An evidence review was completed which included six papers – two non-comparative phase II single arm trials, two matched cohort studies, a retrospective analysis of a phase I trial, and a cohort study. No evidence for cost-effectiveness was identified. Limitations of the studies were highlighted including the potential for overlap of patients within and across three studies, population heterogeneity, and very small sample sizes due to the rarity of the condition.

Outcomes that were considered critical and important to decision making were presented to Panel members. The evidence was graded of low to very low certainty. Two matched cohort studies reported that survival rates statistically significantly increased in patients receiving lonafarnib compared to those receiving no treatment. Improvements were reported in weight gain, and the reduction of seizure rates and strokes.

Adverse events were noted although no patients had to stop treatment as a result.

The proposition and the supporting documentation were presented to Clinical Panel members. Some points for amendment were identified.

Panel members were informed that a Prescribing Planning Meeting is convened when cases arise, with the lead clinician/team responsible for prescribing and monitoring being agreed.

It was questioned whether this should be put forward to the Generation Study. When a policy has been agreed for commissioning and is published, then it can be referred.

EHIA – no amendments requested.
PIA – no amendments requested.

Recommendation

Clinical Panel recommends that this proposition progresses as a routine commissioning policy proposition.

Why the panel made these recommendations

Panel members agreed that the evidence base, although of low to very low certainty, supported the proposition. The condition is extremely rare so studies will not be of higher certainty. Statistical significance in survival rates and improvements across other outcomes were clearly reported.

Documentation amendments required

Policy Proposition:

- Summary section at the beginning of the proposition – reference should be made to the full marketing authorisation and that the proposition is based on the evidence review.
- About Lonafarnib section, page 3 - clearly state that the medicine has a marketing agreement and link to the Summary of Product Characteristics (SmPC).
- Inclusion criteria – 2nd bullet point needs to state this is based on the evidence review
- Data collection and reporting requirements should be reviewed and strengthened than is currently stated.

Blueteq® Form:

- The form refers to the patient. It just needs to reflect the cohort of whom are being treated.
- The last criterion needs to be amended to state treatments is in line with the policy and SmPC.

Declarations of Interest of Panel Members: None received

Panel Chair: James Palmer, Medical Director, Specialised Services

Policy proposition		
Panel Comment	**Amendment**	**Page number (if applicable)**
Summary section at the beginning of the proposition – reference should be made to the full marketing authorisation and that the proposition is based on the evidence review	The summary section has been amended to include reference to the full marketing authorisation.	P2
About Lonafarnib section, page 3 - clearly state that the medicine has a marketing agreement and link to the Summary of Product Characteristics (SmPC).	About Lonafarnib section has been updated to state the marketing authorisation and include a link to the SmPC.	P3
Inclusion criteria – 2nd bullet point needs to state this is based on the evidence review	It has been clarified with the PWG that the inclusion criteria directly reflect the patient cohort covered by the evidence review.	P4
Data collection and reporting requirements should be reviewed and strengthened than is currently stated.	The data collection and reporting requirements have been strengthened. Discussions have been had with the National Congenital Anomaly and Rare Disease Registration Service (NCARDRS) to establish data collection nationally. Additional outcomes are able to be collected regarding patient outcomes which will be reported to NHS England on an annual basis.	P8
Blueteq® Form	**Amendment**	**Page number (if applicable)**
The form refers to the patient. It just needs to reflect the cohort of whom are being treated.	Reference has been made to the 'patient or parent/carer'.	P2
The last criterion needs to be amended to state treatments is in line with the policy and SmPC.	Amended to state treatments are in line with the policy and SmPC.	P2