Clinical Policy: Lonafarnib (Zokinvy)

Reference Number: CP.PHAR.499
Effective Date: FDA Approval Date
Last Review Date: 08.20
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Lonafarnib (Zokinvy®) is farnesyltransferase inhibitor.

FDA Approved Indication(s) [Pending]

Zokinvy is indicated for the treatment of Hutchinson-Gilford progeria syndrome (HGPS).

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Zokinvy is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria*

**Criteria will mirror the clinical information from the prescribing information once FDA-approved*

A. Progeria (must meet all)**:**

1. Diagnosis of progerin-producing HGPS confirmed by both of the following (a and b):
   a. Presence of clinical features (e.g., growth deficiency, characteristic facial features, and atherosclerosis) (*see Appendix D*);*
   b. Presence of heterozygous variant in LMNA gene confirmed by genetic testing;*
2. Prescribed by or in consultation with a pediatrician, orthopedist, or cardiologist;*
3. Age ≥ 1 year;*
4. Dose does not exceed 300 mg/m^2 per day.*

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy*

**Criteria will mirror the clinical information from the prescribing information once FDA-approved*

A. Progeria (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy (*see Appendix D*);*
3. If request is for a dose increase, new dose does not exceed 300 mg/m^2 per day.*

Approval duration: 12 months

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
HGPS: Hutchinson-Gilford progeria syndrome

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings [Pending]

- Contraindication(s): pending
- Boxed warning(s): pending

Appendix D: General information

- The diagnosis of HGPS is established in a proband with characteristic clinical features, along with identification of a heterozygous pathogenic variant in LMNA that results in production of the abnormal lamin A protein, progerin. HGPS is characterized by the following clinical features that typically develop in childhood and resemble some features of accelerated aging:
  - Growth deficiency: Profound failure to thrive usually occurs during the first year. Poor weight gain and loss of subcutaneous fat results in weight less than the third percentile for age, and weight that is distinctly low for height. Stature also decreases to below the third percentile for age.
  - Characteristic facial features: a head that appears disproportionately large for face, narrow nasal ridge with a narrow nasal tip, thin vermilion of the upper and lower lips, small mouth, retrognathia, and micrognathia.
  - Cardiovascular/cerebrovascular: Individuals with HGPS develop severe atherosclerosis, usually without obvious abnormalities in lipid profiles. Systolic dysfunction is usually present in the setting of advanced disease, with or without identified coronary vascular insufficiency. Clinical symptoms of angina, dyspnea on exertion, or overt heart failure appear as late findings in the course of disease.

- Endocrine: Affected individuals do not become sexually mature. Females reach Tanner Stage 1 (78%) or 2 (22%) during pubertal years, and approximately 60% of females experience menarche
- Musculoskeletal: Individuals with HGPS are particularly susceptible to hip dislocation because of the progressive coxa valga malformation, which can be accompanied by avascular necrosis of the hip (osteonecrosis).

- Individuals with classic genotype HGPS are heterozygous for pathogenic variant c.1824C>T (~90% of individuals with HGPS). Individuals with nonclassic genotype HGPS have the characteristic clinical features of HGPS and are heterozygous for another LMNA pathogenic variant in exon 11 or intron 11 that results in production of progerin (~10% of individuals with HGPS).
- Examples of positive response to therapy include but are not limited to: no new or worsening heart failure, no stroke incidence, or reduction in seizures.
  - ProLon1 clinical trial: 26 participants were treated for a minimum of 2 years. Frequency of clinical strokes, headaches, and seizures was reduced from pretrial rates. Three patients with a history of frequent TIAs and average clinical stroke frequency of 1.75/year during the year before treatment experienced no new events during treatment. Children with HGPS die of premature atherosclerosis, the lower mortality rate may have been attributable to cardiovascular and possibly cerebrovascular benefit. This premise is supported by Prolon1 showing evidence of decreased carotid-femoral pulse wave velocity, carotid artery wall echodensity, stroke incidence, headache, and seizures.
- Genetic testing can be obtained through The Progeria Research Foundation Diagnostic Testing Program, provided at no cost to families.

V. Dosage and Administration [Pending]

Indication	Dosing Regimen	Maximum Dose
HGPS	115 to 150 mg/m^2 PO BID*	300 mg/m^2/day*

VI. Product Availability [Pending]

Pending

VII. References

1. ClinicalTrials.gov. Bethesda (MD): National Library of Medicine (US). Identifier NCT03895528, Lonafarnib for Patients With Hutchinson-Gilford Progeria Syndrome or Progeroid Laminopathy. Available at https://clinicaltrials.gov/ct2/show/record/NCT03895528. Accessed June 29, 2020.
2. Gordon L, Shappell H, Massaro J, et al. Association of Lonafarnib Treatment vs No Treatment With Mortality Rate in Patients With Hutchinson-Gilford Progeria Syndrome. JAMA. 2018;319(16):1687-1695.
3. Gordon L, Brown T, Collins F, et al. Hutchinson-Gilford Progeria Syndrome. Dec 2003 [Updated Jan 2019]. GeneReviews [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2020.
4. Gordon L, Kleinman M, Miller D, et al. Clinical trial of a farnesyltransferase inhibitor in children with Hutchinson–Gilford progeria syndrome. PNAS. 2012:109(41):16666-16671.

5. Ullrich NJ, Kieran MW, Miller DT, et al. Neurologic features of Hutchinson-Gilford progeria syndrome after lonafarnib treatment. Neurology. 2013;81(5):427-430.

Coding Implications [Pending]
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
Pending	Pending

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	06.27.20	08.20

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.