Clinical Policy: Lonafarnib (Zokinvy)

Reference Number: CP.PHAR.499
Effective Date: 11.20.20
Last Review Date: 02.26
Line of Business: Commercial, HIM, Medicaid

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)

Zokinvy is indicated in patients 12 months of age and older with a body surface area of 0.39 m^2 and above:

- To reduce risk of mortality in Hutchinson-Gilford progeria syndrome (HGPS)
- For treatment of processing-deficient progeroid laminopathies with either:
  - Heterozygous *LMNA* mutation with progerin-like protein accumulation
  - Homozygous or compound heterozygous *ZMPSTE24* mutations

Limitation(s) of use: Zokinvy is not indicated for other progeroid syndromes or processing-proficient progeroid laminopathies. Based upon its mechanism of action, Zokinvy would not be expected to be effective in these populations.

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

A. Progeria and Progeroid Laminopathy (must meet all)**:**

1. Diagnosis of one of the following (a or b):
   a. HGPS with documentation of genetic mutation in the *LMNA* gene;
   b. Processing-deficient progeroid laminopathy with documentation of one of the following (i or ii):
      i. Heterozygous *LMNA* mutation with progerin-like protein accumulation;
      ii. Homozygous or compound heterozygous *ZMPSTE24* mutations;
2. Prescribed by or in consultation with a geneticist, metabolic disorder specialist, or progeria specialist;
3. Age ≥ 1 year;
4. Body surface area (BSA) ≥ 0.39 m^2;
5. Member does not have a history of cardiac arrhythmias;
6. Documentation of current electrocardiogram (ECG) QTc interval < 500 msec;
7. Dose does not exceed any of the following (a or b):

a. New starts or treated for less than 4 months: 230 mg/m^2 per day, rounded to the nearest 25 mg dose (*see table in Section V*) for a total of 4 months;
b. Maintenance after 4 months: 300 mg/m^2 per day, rounded to the nearest 25 mg dose (see table in Section V).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Progeria and Progeroid Laminopathy (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 300 mg/m^2 per day, rounded to the nearest 25 mg dose (*see table in Section V*).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 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.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents;
B. Other progeroid syndromes;
C. Processing-proficient progeroid laminopathies.

IV. Appendices/General Information

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

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): concomitant use of Zokinvy with:
  - Strong or moderate CYP3A inhibitors
  - Strong or moderate CYP3A inducers
  - Midazolam
  - Lovastatin, simvastatin, or atorvastatin
- Boxed warning(s): none reported

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 non-classic 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).
- Genetic testing can be obtained through The Progeria Research Foundation Diagnostic Testing Program, provided at no cost to families. Current link can be found here: https://www.progeriaresearch.org/the-prf-diagnostic-testing-program/.

V. Dosage and Administration

<table>
<tr><th>Indication</th><th>Dosing Regimen</th><th>Maximum Dose</th></tr>
<tr><td>Progeria and progeroid laminopathy</td><td>Initial BSA-based dosage for the starting dosage of 115 mg/m^2 twice daily for 4 months:
<table>
<tr><th rowspan="2">BSA (m^2)</th><th rowspan="2">Total Daily Dosage Rounded to Nearest 25 mg</th><th colspan="2">Morning Dosing Number of Capsule(s)</th><th colspan="2">Evening Dosing Number of Capsule(s)</th></tr>
<tr><th>Zokinvy 50 mg</th><th>Zokinvy 75 mg</th><th>Zokinvy 50 mg</th><th>Zokinvy 75 mg</th></tr>
<tr><td>0.39 - 0.48</td><td>100</td><td>1</td><td></td><td>1</td><td></td></tr>
<tr><td>0.49 - 0.59</td><td>125</td><td></td><td>1</td><td>1</td><td></td></tr>
<tr><td>0.6 - 0.7</td><td>150</td><td></td><td>1</td><td></td><td>1</td></tr>
<tr><td>0.71 - 0.81</td><td>175</td><td>2</td><td></td><td></td><td>1</td></tr>
<tr><td>0.82 - 0.92</td><td>200</td><td>2</td><td></td><td>2</td><td></td></tr>
<tr><td>0.93 – 1</td><td>225</td><td>1</td><td>1</td><td>2</td><td></td></tr>
</table></td><td>300 mg/m^2/day</td></tr>
</table>

Indication	Dosing Regimen	Maximum Dose
	Maintenance BSA-based dosage of 150 mg/m^2 twice daily:	

BSA (m^2)	Total Daily Dosage Rounded to Nearest 25 mg	Morning Dosing Number of Capsule(s)		Evening Dosing Number of Capsule(s)	
		Zokinvy 50 mg	Zokinvy 75 mg	Zokinvy 50 mg	Zokinvy 75 mg
0.39 - 0.45	125		1	1	
0.46 - 0.54	150		1		1
0.55 - 0.62	175	2			1
0.63 - 0.7	200	2		2	
0.71 - 0.79	225	1	1	2	
0.8 - 0.87	250	1	1	1	1
0.88 - 0.95	275		2	1	1
0.96 – 1	300		2		2

VI. Product Availability

Capsules: 50 mg, 75 mg

VII. References

1. Zokinvy Prescribing Information. Palo Alto, CA: Eiger BioPharmaceuticals, Inc.; March 2024. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/213969s002s003lbl.pdf. Accessed: November 7, 2025.
2. Gordon LB, Shappel 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. doi:10.1001/jama.2018.3264.
3. Harhouri K, Frankel D, Bartoli C, et al. An overview of treatment strategies for Hutchinson-Gilford Progeria syndrome. Nucleus 2018; 9(1):246-257. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5973194/pdf/kncl-09-01-1460045.pdf. Accessed: November 7, 2025.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2022 annual review: no significant changes; added to Section III that other progeroid syndromes or processing-proficient progeroid laminopathies will not be coverable per PI; references reviewed and updated.	09.27.21	02.22

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Template changes applied to other diagnoses/indications and continued therapy section.	10.03.22	
1Q 2023 annual review: no significant changes; updated Appendix D to include Progeria Research Foundation Diagnostic Testing Program link; references reviewed and updated.	11.11.22	02.23
1Q 2024 annual review: no significant changes; references reviewed and updated.	11.13.23	02.24
1Q 2025 annual review: no significant changes; references reviewed and updated.	10.21.24	02.25
1Q 2026 annual review: added safety criteria regarding hx of arrhythmias and QTc threshold per labeling updates; extended initial approval duration from 4 months for new starts to 12 months; references reviewed and updated.	11.07.25	02.26

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.