



Original Effective Date: 05/01/2021
Current Effective Date: 10/12/2025
Last P&T Approval/Version: 07/30/2025
Next Review Due By: 07/2026
Policy Number: C21125-A

Zokinvy (lonafarnib)

PRODUCTS AFFECTED

Zokinvy (lonafarnib)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:

Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:

Hutchinson-Gilford Progeria Syndrome (HGPS or Progeria), Processing-deficient Progeroid Laminopathies (PL)

REQUIRED MEDICAL INFORMATION:

This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. HUTCHINSON-GILFORD PROGERIA SYNDROME (HGPS), PROGEROID LAMINOPATHY:

1. (a) Documented diagnosis of Hutchinson-Gilford progeria syndrome (HGPS) [DOCUMENTATION

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REQUIRED]

OR

(b) Documentation of Processing-deficient progeroid laminopathy with either Heterozygous LMNA mutation with progerin-like protein accumulation; OR Homozygous or compound heterozygous ZMPSTE24 mutations [DOCUMENTATION REQUIRED]

NOTE: Zokinvy is not indicated for other Progeroid Syndromes or processing-proficient Progeroid laminopathies. Based on the mechanism of action, Zokinvy would not be expected to be effective in these populations.

AND

2. Documentation member has at least ONE of the following clinical characteristics:
 - a) Failure to thrive in the first year of life
 - b) Characteristic facial appearance with micrognathia, prominent eyes, and circumoral cyanosis
 - c) Alopecia and prominent scalp veins
 - d) Sclerotic skin changes with outpouching and dimpling/mottling, especially on the abdomen
 - e) Decreased joint range of motion and joint contracture
- AND
3. Documentation member's current BSA is at least 0.39 m²

CONTINUATION OF THERAPY:

A. HUTCHINSON-GILFORD PROGERIA SYNDROME (HGPS), PROGEROID LAMINOPATHY:

1. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
- AND
2. Documentation of positive clinical response as demonstrated by low disease activity and/or improvements in the condition's signs and symptoms.

DURATION OF APPROVAL:

Initial authorization: 12 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:

Prescribed by, or in consultation with, a board-certified geneticist, or physician experienced in the treatment of progeria syndrome/metabolic disorders. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:

12 months of age and older

QUANTITY:

Initial dosing not to exceed 115 mg/m² twice daily (first 4 months of treatment)

Maintenance dosing not to exceed 150 mg/m² twice daily- one-month supply per dispense. See Appendix.

PLACE OF ADMINISTRATION:

The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:

Oral

DRUG CLASS:

Farnesyltransferase Inhibitors

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FDA-APPROVED USES:

Indicated in patients 12 months of age and older with a body surface area of 0.39 m² and above to reduce risk of mortality in Hutchinson-Gilford Progeria Syndrome (HGPS or Progeria) and for treatment of processing-deficient Progeroid Laminopathies (PL) with either: heterozygous LMNA mutation with progerin-like protein accumulation or Homozygous or compound heterozygous ZMPSTE24 mutations.

Limitations of Use: 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.

COMPENDIAL APPROVED OFF-LABELED USES:

None

APPENDIX

APPENDIX:

Table 1: Recommended Dosage and Administration for 115 mg/m² Body Surface Area-Based Dosing

| 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 - 0.48 | 100 | 1 | | 1 | |
| 0.49 - 0.59 | 125 | | 1 | 1 | |
| 0.6 - 0.7 | 150 | | 1 | | 1 |
| 0.71 - 0.81 | 175 | 2 | | | 1 |
| 0.82 - 0.92 | 200 | 2 | | 2 | |
| 0.93 - 1 | 225 | 1 | 1 | 2 | |

Table 2: Recommended Dosage and Administration for 150 mg/m² Body Surface Area-Based Dosing

| 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 |

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

Zokinvy is a farnesyltransferase inhibitor indicated in patients 12 months of age and older with a body surface

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area of 0.39 m² and above to reduce the risk of mortality in Hutchinson-Gilford Progeria syndrome (HGPS) and for the treatment of processing-deficient Progeroid Laminopathies (PLs) with either heterozygous LMNA mutation with progerin-like protein accumulation or homozygous or compound heterozygous ZMPSTE24 mutations. Zokinvy is NOT indicated for other Progeroid Syndromes or processing proficient Progeroid Laminopathies. Based on the mechanism of action, Zokinvy would not be expected to be effective in these populations.

Zokinvy is the first FDA approved therapy for the treatment of HGPS and processing deficient PLs. Limited clinical trial data evaluated the use of pravastatin and zoledronic acid but use of these agents is not endorsed or recommended by any guidelines or organizations.

The approval was based on data from an Observational Cohort Survival Study, which retrospectively compared survival data from two phase 2 studies (NCT00425607 and NCT00916747) in 62 patients with HGPS to those from a natural history cohort (N=81). Results from these trials showed that Zokinvy significantly reduced the incidence of mortality and increased the lifespan of HGPS patients. The most common adverse reactions (incidence greater than or equal to 25%) reported with Zokinvy include vomiting, diarrhea, infections, nausea, decreased appetite, fatigue, upper respiratory tract infection, abdominal pain, musculoskeletal pain, electrolyte abnormalities, decreased weight, headache, myelosuppression, increased AST/ALT, decreased blood bicarbonate, cough, and hypertension.

Zokinvy is contraindicated with concomitant use of strong or moderate CYP3A inhibitors or inducers, midazolam, lovastatin, simvastatin or atorvastatin. Additionally, coadministration with other drugs (CYP2C9 inhibitors, CYP3A substrates, loperamide, CYP2C19 substrates, P-gp substrates) may result in clinically significant interactions that may reduce the efficacy of Zokinvy and increase the risk of adverse reactions from Zokinvy or the co-administered drug.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Zokinvy (lonafarnib) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Zokinvy (lonafarnib) include: patients taking strong or moderate CYP3A inhibitors or inducers, Midazolam, Atorvastatin, Lovastatin, and Simvastatin.

OTHER SPECIAL CONSIDERATIONS:

None

CODING/BILLING INFORMATION

CODING DISCLAIMER. Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.

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| HCPCS CODE | DESCRIPTION |
|------------|-------------|
| NA | |

AVAILABLE DOSAGE FORMS:

Zokinvy CAPS 50MG

Zokinvy CAPS 75MG

REFERENCES

1. Zokinvy (lonafarnib) capsules, for oral use [prescribing information]. Palo Alto, CA: Eiger BioPharmaceuticals; March 2024.
2. Progeria Research Foundation. PRF by the numbers. Published September 30, 2020. Accessed February 4, 2020. <https://www.progeriaresearch.org/wp-content/uploads/2020/10/PRF-By-the-Numbers-FINAL-October2020.pdf>.
3. National Institutes of Health. In NIH trial, Phase II Trial of Lonafarnib (a Farnesyltransferase Inhibitor) for Progeria (Study 1, NCT00425607). www.clinicaltrials.gov. Published May 2017. Updated June 2019.
4. National Institutes of Health. In NIH trial, Study of Zoledronic Acid, Pravastatin, and Lonafarnib for Patients With Progeria (Study 2, NCT00916747). www.clinicaltrials.gov. Published June 2009. Updated January 2020.

| SUMMARY OF REVIEW/REVISIONS | DATE |
|--|----------------------------|
| REVISION- Notable revisions: Required Medical Information Continuation of Therapy | Q3 2025 |
| REVISION- Notable revisions: Required Medical Information Duration of Approval References | Q3 2024 |
| REVISION- Notable revisions: Diagnosis Required Medical Information Continuation of Therapy Prescriber Requirements Age Restrictions Drug Class FDA-Approved Uses Available Dosage Forms | Q3 2023 |
| REVISION- Notable revisions: Required Medical Information Continuation of Therapy Quantity Appendix | Q3 2022 |
| Q2 2022 Established tracking in new format | Historical changes on file |

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