# SmartPA Criteria Proposal

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|---|---|
| **Drug/Drug Class:** | Zokinvy Clinical Edit |
| **First Implementation Date:** | November 18, 2021 |
| **Revised Date:** | TBD |
| **Prepared for:** | MO HealthNet |
| **Prepared by:** | MO HealthNet/Conduent |
| **Criteria Status:** | ☐Existing Criteria<br>☐Revision of Existing Criteria<br>☒New Criteria |

## Executive Summary

**Purpose:** Ensure appropriate utilization and control of Zokinvy™ (lonafarnib)

**Why Issue Selected:** Zokinvy (lonafarnib), FDA approved in November 2020, represents the first disease-modifying treatment for Hutchinson-Gilford Progeria Syndrome (HGPS) and Progeroid Laminopathies (PLs). HGPS and PLs are rare, genetic, and inevitably fatal conditions diagnosed between 9 and 24 months of age. According to the Progeria Research Foundation, as of September 30, 2020, there are 128 individuals worldwide living with HGPS and 51 with PLs, 18 and 13 of which live within the United States. HGPS is caused by pathogenic variants in the *LMNA* gene which leads to the synthesis of a truncated protein, progerin, which accumulates within the nuclear envelope and leads to cellular instability and premature aging. PLs are caused by pathogenic variants in either the *LMNA* gene and/or the *ZMPSTE24* gene, and do not result in the production of progerin but are associated with disease characteristics and traits that overlap with Progeria. The characteristic appearance of premature aging is often associated with alopecia, head/facial abnormalities, cardiovascular disease, stroke, joint stiffness, and lipodystrophy. Atherosclerosis, the primary cause of premature death, occurs by age 13 on average. Zokinvy inhibits farnesyltransferase to prevent farnesylation and subsequent accumulation of progerin and progerin-like proteins in the inner nuclear membrane. Based on an analysis from GoodRx®, Zokinvy is ranked as the second most expensive medication in the United States with an annual estimated cost of $1,032,480. Due to the high cost and specific approved indications, MO HealthNet will impose clinical criteria to ensure appropriate utilization of Zokinvy.

**Program-Specific Information:**

| Drug | Cost per capsule | Cost per bottle of 30 capsules |
|---|---|---|
| ZOKINVY 50 MG CAPSULE | $714.13 MAC | $21,423.90 MAC |
| ZOKINVY 75 MG CAPSULE | $1,071.19 MAC | $32,135.70 MAC |

**Type of Criteria:**

☐ **Increased risk of ADE**
☒ **Appropriate Indications**
☐ **Preferred Drug List**
☒ **Clinical Edit**

**Data Sources:**

☐ **Only Administrative Databases**
☒ **Databases + Prescriber-Supplied**

## Setting & Population

- Drug class for review: Zokinvy™ (lonafarnib)
- Age range: All appropriate MO HealthNet participants

## Approval Criteria

- Prescribed by or in consultation with a geneticist or other specialist in the treated disease state **AND**
- Documented diagnosis of HGPS or processing-deficient PLs with either heterozygous *LMNA* pathogenic or likely pathogenic variant with progerin-like protein accumulation or homozygous or compound heterozygous *ZMPSTE24* pathogenic or likely pathogenic variants **AND**
- Participant has a BSA ≥ 0.39 $m^2$ **AND**
- Participant is not currently pregnant

## Denial Criteria

- Therapy will be denied if all approval criteria are not met
- Concurrent therapy with midazolam, lovastatin, simvastatin, or atorvastatin in the past 45 days

## Required Documentation

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|---|---|---|---|
| Laboratory Results: | X | Progress Notes: | |
| MedWatch Form: | | Other: | X |

## Disposition of Edit

Denial: Exception code "0682" (Clinical Edit)
Rule Type: CE

## Default Approval Period

1 year

## References


- ZOKINVY™ (lonafarnib) [package insert]. Palo Alto, CA: Eiger BioPharmaceuticals, Inc.; November 2020.
- NIH: U.S. National Library of Medicine. Phase II Trial of Lonafarnib (a Farnesyltransferase Inhibitor) for Progeria. https://clinicaltrials.gov/ct2/show/NCT00425607?term=NCT00425607&draw=2&rank=1. 10 December 2020.
- National Organization for Rare Disorders (NORD): Hutchinson-Gilford Progeria. https://rarediseases.org/rare-diseases/hutchinson-gilford-progeria/. 10 December 2020.
- Gordon, L.B, 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 April 24; 319(16):1687-1695. 10 December 2020.
- Dorado, B., Ploen G.G., Barettino, A., et al. Generation and characterization of a novel knockin minipig model of Hutchinson-Gilford progeria syndrome. Cell Discovery. https://www.nature.com/articles/s41421-019-0084-z#citeas. 10 December 2020.

- U.S. Food & Drug Administration (FDA): News Release: FDA Approved First Treatment for Hutchinson-Gilford Progeria Syndrome and Some Progeroid Laminopathies. https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-hutchinson-gilford-progeria-syndrome-and-some-progeroid-laminopathies. 10 December 2020.
- IPD Analytics: New Drug Review: Zokinvy (lonafarnib). Accessed 10 December 2020.
- Progeria Research Foundation. PRF by the numbers. Published September 30, 2020. Accessed 10 December 2020. https://progeriaresearch.org/wp-content/uploads/2020/10/PRF-By-the-Numbers_-FINAL-October2020.pdf
- Clements, C.S., Bikkul, M.U., Ofosu, W., et. al. Presence and distribution of progerin in HGPS cells is ameliorated by drugs that impact on the mevalonate and mTOR pathways. Biogerontology. 20, 337-358 (2019). https://doi.org/10.1007/s10522-019-09807-4
- Chase, Lauren. The 10 Most Expensive Drugs in the U.S., Period. Goodrx. https://www.goodrx.com/blog/most-expensive-drugs-period/