Pharmacy Policy Bulletin: J-1056 Zokinvy (lonafarnib) – Commercial and Healthcare Reform	
Number: J-1056	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Miscellaneous Specialty Drugs Oral = Yes w/ Prior Authorization **Quantity Limits (1., 2., 3., or 4.):** **1.** Rx Mgmt Quantity Limits = Safety/Specialty **2.** Rx Mgmt Quantity Limits = Safety/Specialty + Dose Opt **3.** Rx Mgmt Quantity Limits = Safety/Specialty + Dose Opt + Watchful **4.** Quantity Limits = QPC = Yes **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-1056-007	**Original Date:** 01/27/2021
Effective Date: 02/14/2025	**Review Date:** 01/29/2025

Drugs Product(s):	• Zokinvy (lonafarnib)

FDA-Approved Indication(s):	• 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
	  ○ For treatment of processing-deficient Progeroid Laminopathies with either:
	  ▪ Heterozygous *LMNA* mutation with progerin-like protein accumulation
	  ▪ Homozygous or compound heterozygous *ZMPSTE24* mutations

Background:	• Zokinvy works by inhibiting the enzyme farnesyltransferase. Inhibiting the enzyme prevents farnesylation, which is the process that leads to the accumulation of progerin and progerin-like proteins in the inner nuclear membrane of cells. • Hutchinson-Gilford Progeria Syndrome (HGPS or Progeria) is caused by a mutation in the *LMNA* gene and is known as the “Benjamin Button” disease. • HGPS and Progeroid Laminopathies (PL) are ultra-rare, genetic conditions that cause premature aging and death through the acceleration of cardiovascular disease due to the buildup of defective progerin or progerin-like protein in cells. Many patients die before 15 years of age from cardiovascular issues such as heart failure, heart attack, or stroke. Other characteristics of the diseases include growth failure, loss of body fat and hair, and aged-looking skin. HGPS and PL affect

roughly 1 in 20 million people and 1 in 36 million people, respectively. It is estimated that there are 400 active cases of HGPS and 200 active cases of PL worldwide, and about 20 of those patients reside in the United States.

Table 1: Initiation Therapy; *Note: The quantity limit is coded as 2 capsules per day.*

Recommended Dosage and Administration for the Starting Dosage of 115 mg/m^2 Twice Daily (First 4 Months of Treatment)						
Body Surface Area (BSA) (m^2)	Total Daily Dosage Rounded to Nearest 25 mg	Morning Dosing Number of Capsule(s)		Evening Dosing Number of Capsule(s)		Total Number of Capsules Needed per Day
		Zokinvy 50 mg	Zokinvy 75 mg	Zokinvy 50 mg	Zokinvy 75 mg	
0.39 – 0.48	100	1		1		2
0.49 – 0.59	125		1	1		2
0.60 – 0.70	150		1		1	2
0.71 – 0.81	175	2			1	3
0.82 – 0.92	200	2		2		4
0.93 – 1	225	1	1	2		4

Table 2: Maintenance Therapy; *Note: The quantity limit is coded as 2 capsules per day.*

Recommended Dosage and Administration for 150 mg/m^2 Twice Daily (Maintenance Dose after First 4 Months of Treatment)						
BSA (m^2)	Total Daily Dosage Rounded to Nearest 25 mg	Morning Dosing Number of Capsule(s)		Evening Dosing Number of Capsule(s)		Total Number of Capsules Needed per Day
		Zokinvy 50 mg	Zokinvy 75 mg	Zokinvy 50 mg	Zokinvy 75 mg	
0.39 – 0.45	125		1	1		2
0.46 – 0.54	150		1		1	2
0.55 – 0.62	175	2			1	3
0.63 – 0.7	200	2		2		4
0.71 – 0.79	225	1	1	2		4
0.80 – 0.87	250	1	1	1	1	4
0.88 – 0.95	275		2	1	1	4
0.96 – 1	300		2		2	4

- Prescribing Considerations:
  - Zokinvy should be prescribed by or in consultation with a pediatric genetic disease specialist.
  - The starting dose is 115 mg/m^2 twice daily with morning and evening meals. After 4 months, the dose should be increased to 150 mg/m^2 twice daily. Round all total daily doses to the nearest 25 mg increment.
  - An appropriate dosage strength of Zokinvy is not available for patients with a BSA of less than 0.39 m^2. BSA should be monitored throughout treatment, and at the 4 month dose adjustment.
  - Zokinvy is contraindicated for use in patients taking strong or moderate CYP3A inhibitors or inducers, midazolam, lovastatin, simvastatin, and atorvastatin.
  - Zokinvy has warnings or precautions for risk of reduced efficacy or adverse

	reactions due to drug interactions, laboratory abnormalities, nephrotoxicity, retinal toxicity, impaired fertility, and embryo-fetal toxicity.

Approval Criteria

I. Initiation (First 4 Months of Treatment)

A. HGPS (Progeria)

When a benefit, initiation of Zokinvy may be approved when all of the following criteria are met **(1. through 5.)**:

1. The member is 12 months of age or older.
2. The member has a diagnosis of HGPS (Progeria) (no ICD-10 code).
3. The provider submits documentation showing the member has a mutation in the *LMNA* gene.
4. The prescriber submits member documentation of a BSA of 0.39 m^2 or above.
5. Based on the member's BSA, the requested dosing regimen aligns with the FDA-approved labeled dosing regimen **(refer to Table 1 in Background)**.
   - **a.** *Note: If approved, enter a PLA if the requested dosage regimen exceeds the coded quantity limit of 2 capsules per day.*

B. Processing-Deficient PL

When a benefit, initiation of Zokinvy may be approved when all of the following criteria are met **(1. through 4.)**:

1. The member is 12 months of age or older.
2. The member has a diagnosis of processing-deficient PL (no ICD-10 code) with one (1) of the following **(a. or b.)**:
   - **a.** The provider submits documentation showing both of the following **(i. and ii.)**:
     - **i.** The member has a heterozygous *LMNA* mutation.
     - **ii.** The member has progerin-like protein accumulation.
   - **b.** The provider submits documentation showing that the member has one (1) of the following **(i. or ii.)**:
     - **i.** Homozygous *ZMPSTE24* mutations
     - **ii.** Compound heterozygous *ZMPSTE24* mutations
3. The prescriber submits member documentation of a BSA of 0.39 m^2 or above.
4. Based on the member's BSA, the requested dosing regimen aligns with the FDA-approved labeled dosing regimen **(refer to Table 1 in Background)**.
   - **a.** *Note: If approved, enter a PLA if the requested dosage regimen exceeds the coded quantity limit of 2 capsules per day.*

II. Maintenance (After 4 Months of Treatment)

A. HGPS (Progeria)

When a benefit, maintenance of Zokinvy may be approved when all of the following criteria are met **(1. through 5.)**:

1. The member is 12 months of age or older.
2. The member has a diagnosis of HGPS (Progeria) (no ICD-10 code).
3. The provider submits documentation showing the member has a mutation in the *LMNA* gene.
4. The prescriber submits member documentation of a BSA of 0.39 m^2 or above.
5. Based on the member's BSA, the requested dosing regimen aligns with the FDA-approved labeled dosing regimen **(refer to Table 2 in Background)**.
   - **a.** *Note: If approved, enter a PLA if the requested dosage regimen exceeds the coded quantity limit of 2 capsules per day.*

B. Processing-Deficient PL

When a benefit, maintenance of Zokinvy may be approved when all of the following criteria are met **(1. through 4.)**:

1. The member is 12 months of age or older.
2. The member has a diagnosis of processing-deficient PL (no ICD-10 code) with one (1) of the following **(a. or b.)**:
   - **a.** The provider submits documentation showing both of the following **(i. and ii.)**:
     - **i.** The member has a heterozygous *LMNA* mutation.
     - **ii.** The member has progerin-like protein accumulation.
   - **b.** The provider submits documentation showing that the member has one (1) of the following **(i. or ii.)**:
     - **iii.** Homozygous *ZMPSTE24* mutations
     - **iv.** Compound heterozygous *ZMPSTE24* mutations
3. The prescriber submits member documentation of a BSA of 0.39 m^2 or above.
4. Based on the member's BSA, the requested dosing regimen aligns with the FDA-approved labeled dosing regimen **(refer to Table 2 in Background)**.
   - **a.** *Note: If approved, enter a PLA if the requested dosage regimen exceeds the coded quantity limit of 2 capsules per day.*

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Zokinvy is not indicated for other Progeroid Syndromes or processing-proficient PL. Based upon its mechanism of action, Zokinvy would not be expected to be effective in these populations.

II. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.

III. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

Initiation

- Commercial and HCR Plans: If approved, up to a 4 month authorization may be granted.
  - *For Delaware Commercial fully-insured and ACA members, a 12 month authorization must be granted pursuant to 18 Del. C. §§3376(a) and 3586(a) and market conduct examination docket #5467 (Exam Authority #53287-22-701).*

Maintenance

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None

References:

1. Zokinvy [package insert]. Palo Alto, CA: Eiger Biopharmaceuticals, Inc.; March 2024.
2. U.S. Food & Drug Administration. FDA News Release. FDA approves first treatment for Hutchinson-Gilford Progeria Syndrome and some Progeroid Laminopathies. Available at:

https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-hutchinson-gilford-progeria-syndrome-and-some-progeroid-laminopathies. Accessed December 14, 2021.
3. PR Newswire. Eiger Biopharmaceuticals announces FDA approval of Zokinvy (lonafarnib): The first treatment for Hutchinson-Gilford Progeria Syndrome and processing-deficient Progeroid Laminopathies. Available at: https://www.prnewswire.com/news-releases/eiger-biopharmaceuticals-announces-fda-approval-of-zokinvy-lonafarnib-the-first-treatment-for-hutchinson-gilford-progeria-syndrome-and-processing-deficient-progeroid-laminopathies-301178343.html. Accessed December 14, 2021.

Pharmacy policies do not constitute medical advice, nor are they intended to govern physicians' prescribing or the practice of medicine. They are intended to reflect the plan's coverage and reimbursement guidelines. Coverage may vary for individual members, based on the terms of the benefit contract.

The plan retains the right to review and update its pharmacy policy at its sole discretion. These guidelines are the proprietary information of the plan. Any sale, copying or dissemination of the pharmacy policies is prohibited; however, limited copying of pharmacy policies is permitted for individual use.