Clinical Policy Title:	Ionafarnib
Policy Number:	RxA.670
Drug(s) Applied:	Zokinvy™
Original Policy Date:	3/9/2021
Last Review Date:	2/5/2021
Line of Business Policy Applies to:	All Line of Business

Background

Zokinvy™ is a farnesyltransferase inhibitor 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
- For treatment of processing deficient Progeroid Laminopathies with either:
  - Heterozygous LMNA mutation with progerin-like protein accumulation
  - 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.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
Ionafarnib (Zokinvy™)	Hutchinson-Gilford Progeria Syndrome	Initial: 115 mg/ m^2/dose by mouth twice daily with morning and evening meals for 4 months, then increase to 150 mg/m^2/dose twice daily.	150 mg/m^2 twice daily
	Processing-deficient Progeroid Laminopathies with either: - Heterozygous LMNA mutation with progerin-like protein accumulation - Homozygous or compound heterozygous ZMPSTE24 mutations		

Dosage Forms

- Capsules: 50 mg and 75 mg

Clinical Policy

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

I. Initial Approval Criteria

A. Hutchinson-Gilford Progeria Syndrome (HGPS)

1. Confirmed diagnosis of HGPS;
2. Patient is 12 months of age or older;
3. BSA of at least 0.39 m^2;
~~3.~~4. Prescribed by or in consultation with a specialist in progeria, genetics, and/or metabolic disorders;
~~4. Patient does not have overt renal, hepatic, or pulmonary disease or immune dysfunction;~~
5. Requested dose is appropriate for patient's BSA and dose does not exceed 150 mg/m^2 twice daily.

Approval Duration:
Commercial: 12 months
Medicaid: 12 months

B. Processing-deficient Progeroid Laminopathies

1. Confirmed diagnosis of processing-deficient progeroid laminopathy with either heterozygous LMNA mutation with progerin-like protein accumulation or homozygous or compound heterozygous ZMPSTE24 mutations;
2. Patient is 12 months of age or older;
3. BSA of at least 0.39 m^2;
~~3.~~4. Prescribed by or in consultation with a specialist in progeria, genetics, and/or metabolic disorders;
~~4. Patient does not have overt renal, hepatic, or pulmonary disease or immune dysfunction;~~
5. Requested dose is appropriate for patient's BSA and dose does not exceed 150 mg/m^2 twice daily.

Approval Duration:
Commercial: 12 months
Medicaid: 12 months

II. Continued Therapy Approval

A. Hutchinson-Gilford Progeria Syndrome (HGPS) (must meet all)

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. Requested dose is appropriate for patient's BSA and dose does not exceed 150 mg/m2 twice daily.

Approval Duration:
Commercial: 12 months
Medicaid: 12 months

B. Processing-deficient Progeroid Laminopathies (must meet all)

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. Requested dose is appropriate for patient's BSA and dose does not exceed 150 mg/m2 twice daily.

Approval Duration:
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
HGPS: Hutchinson-Gilford Progeria Syndrome

APPENDIX B: Therapeutic Alternatives
N/A

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s): Zokinvy™ is contraindicated in patients taking: Strong or moderate CYP3A inhibitors or inducers, midazolam, lovastatin, simvastatin, and atorvastatin.

- Boxed Warning(s):
  - N/A

APPENDIX D: General Information

Hutchinson-Gilford Progeria Syndrome (HGPS) and Progeroid Laminopathies (PLs) are premature aging diseases. In HGPS, the premature aging is due to a point mutation in the lamin A/C gene (LMNA) that leads to the production and permanent farnesylation of a mutant lamin A protein called progerin. PLs, however, are due to various mutations either in the LMNA gene and/or the ZMPSTE24 gene. The mutant protein produced in these conditions is distinct from progerin; however, it is also permanently farnesylated, like progerin. The clinical manifestations of HGPS include a general failure to thrive and progressive growth retardation noticed in the first years of life. The condition is also characterized by dental abnormalities, dermatologic manifestations including a loss of adipose tissue and skin that appears abnormally aged (dry, wrinkled, and taut), and progressive musculoskeletal manifestations including osteoporosis, joint contractures, and skeletal dysplasia. Finally, the finding that is primarily responsible for the mortality of these patients is premature, widespread arteriosclerosis, which can lead to heart failure, myocardial infarction, stroke, or a transient ischemic attack. Patients with HGPS and PLs have a significantly reduced life span, with a range of approximately 8 to 21 years of age and the average age of death being 13 to 14 years.

References

1. Hennekam RC. Hutchinson-Gilford progeria syndrome: review of the phenotype. Am J Med Genet A 2006; 140:2603. Accessed February 5, 2021.
2. Zokinvy™ prescribing information. Palo Alto, CA: Eiger BioPharmaceuticals Inc; November 2020. Accessed February 5, 2021.
3. Zokinvy™, Lexi-Drug. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Accessed with subscription at: http://online.lexi.com. Accessed February 5, 2021.
4. Clinical Pharmacology [database online] powered by ClinicalKey. Tampa, FL: Elsevier, 2020. Accessed with subscription at: http://www.clinicalkey.com. Updated November 25, 2020. Accessed February 5, 2021.
5. Eiger sought regulatory approval of Zokinvy™ to ensure continued access to the only drug proven to reduce the risk of death in patients with Progeria," said Eldon Mayer, Chief Commercial Officer of Eiger. Available at: https://www.prnewswire.com/news-releases/eiger-biopharmaceuticals-announces-us-commercial-availability-of-zokinvy-lonafarnib-the-first-and-only-treatment-approved-for-progeria-and-processing-deficient-progeroid-laminopathies-301213799.html. Accessed February 5, 2021.
6. Zokinvy™, IPD Analytics Rx Insights_New Drug Approval Review_Zokinvy_12 2020_1. Accessed with subscription at: https://www.ipdanalytics.com/. Accessed February 5, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	2/5/2021	3/9/2021