Lonafarnib Managed Access Program (MAP)
Information, Questions and Answers for
Patients, Caregivers and Doctors

Eiger BioPharmaceuticals, the manufacturer of the drug lonafarnib, is sponsoring a Managed Access Program (MAP) for eligible patients in countries where the medication has not yet been approved for commercial distribution. The purpose of this MAP is to allow eligible patients with Hutchinson-Gilford Progeria Syndrome (HGPS or Progeria) or a processing deficient Progeroid Laminopathy (PDPL) to gain access to treatment with lonafarnib. The Managed Access Program will be available to eligible patients with HGPS or a PDPL in the categories described below:

1) those who have never taken lonafarnib before;

2) those who have taken lonafarnib before but are not currently taking lonafarnib and no longer have access to the medication;

3) those who have been taking lonafarnib as part of a clinical trial and would like to continue lonafarnib treatment upon completion of their participation in the clinical trial. If you/your child is currently participating in the trial at Boston Children's Hospital and you/your child is in the portion of the study that includes the drug everolimus, you will have the opportunity to receive lonafarnib through the MAP after the trial is finished. If you/your child is in the extension study of the Boston Children's Hospital trial, and currently taking ONLY lonafarnib, you/your child will transition to the MAP. The transition will be carefully planned so that drug supply remains consistent.

In November 2020, lonafarnib was approved by the United States Food and Drug Administration (FDA) under the brand name of Zokinvy 50mg and 75mg capsules. The formal indications of use are as follows:

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

- To reduce the risk of mortality in HGPS
- For the treatment of processing deficient progeroid laminopathies with either:
  - Heterozygous LMNA mutation with progerin-like protein accumulation
  - Homozygous or compound heterozygous ZMPESTE24 mutations

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.

Despite FDA's approval of lonafarnib, some countries currently consider it to be an investigational treatment for Hutchinson-Gilford Progeria Syndrome and processing deficient Progeroid Laminopathies. This means that outside of the United States you cannot go to a local

pharmacy with a prescription and get the product. For those eligible HGPS and PDPL patients residing in a country that allows the lonafarnib MAP to be offered, it will be the sole means of gaining access to the medication, unless you/your child is still participating in a Boston Children's Hospital study that includes lonafarnib. The lonafarnib MAP will remain operational until commercial supply of lonafarnib for HGPS and PDPLs is available in your country. If that should change, affected MAP participants will be notified.

The subsequent pages include a list of Questions and Answers and Appendices A and B.

Questions and Answers

1. What is a Managed Access Program (MAP)?

- A managed access program enables an eligible patient with a life-threatening condition to gain access to a medicine that has not yet been approved by their country's regulatory authority for commercial sale. The program can only be offered by the maker of the medication.

2. What do I need to do to be considered for the Lonafarnib Managed Access Program?

- All patients wishing to participate in the lonafarnib MAP must have a local doctor that is willing to fulfill the requirements of the program.
- Because lonafarnib is an investigational drug product, it is very important that each patient's doctor understands how to use lonafarnib in the treatment of patients with HGPS or a processing deficient Progeroid Laminopathy. Important information will be provided to the treating doctor upon their enrollment in the lonafarnib MAP.
- Eiger BioPharmaceuticals uses a highly experienced company named Clinigen to help your local doctor transition you/your child into the MAP. Clinigen will also oversee the program on an ongoing basis.
- The doctor is responsible for registering themselves and you/your child with Clinigen. Registration must be completed by the local doctor. This is accomplished by contacting Clinigen. Families/patients cannot register themselves.
- The treating doctor ensures that Clinigen has all the appropriate information necessary so that lonafarnib can be dispensed appropriately.
- After successful enrollment by the doctor and ensuring the patient fulfills the program's criteria, the treating doctor orders the child's lonafarnib from Clinigen.
- The lonafarnib is delivered to the local doctor's hospital/clinic pharmacy. Lonafarnib can be ordered by the treating doctor 6-weeks before the patient's supply of lonafarnib is depleted. In the event the doctor has not ordered lonafarnib at least one month before drug supply is expected to be finished, a reminder e-mail will be sent to the doctor prompting a re-order. Each shipment of lonafarnib contains a 4-month supply. If this should change, all MAP participants will be notified.
- The doctor will then dispense the drug to you/your child.
- Not all countries allow MAPs to be offered to their residents. Appendix A includes a list of countries and their lonafarnib MAP status. If the country you/your child reside within is not listed, MAP may still be possible. In this situation, please contact The Progeria Research Foundation at 978-535-2594 or emailing info@progeriaresearch.org. Conversely, the treating doctor can contact Clinigen's Medicine Access Team at +44 (0) 1932 824123 or by emailing medicineaccess@clinigengroup.com.

3. What is required for eligibility in the Managed Access Program?

To be eligible for the MAP, you/your child must be at least 12 months of age and meet all of the following criteria:

1. A genetic test confirming a diagnosis of either HGPS (Progeria) or a processing deficient progeroid laminopathy.
2. Blood tests must ensure that you/your child's liver and kidneys can process lonafarnib properly.
3. No uncontrolled infection or other serious medical illness that might make it unsafe for you/your child to participate in the MAP.
4. A negative pregnancy test if you/your child is female and of child-bearing age.
5. Some medications and some foods cannot be taken while you/your child is taking lonafarnib. Your doctor will discuss these with you. You should not use lonafarnib with strong or moderate CYP3A inhibitors or inducers. Lonafarnib should not be used with midazolam. Lonafarnib should not be used with the statins atorvastatin, lovastatin or simvastatin. These medications can alter the metabolism of lonafarnib. Speak with your doctor about the medications that meet any of these criteria.
    a. Tell the treating doctor about all medications and herbal remedies you are taking. Certain medications and herbal remedies may be classified as CYP3A inhibitors or inducers. This means they may alter the metabolism of lonafarnib. People taking lonafarnib should discontinue the use of herbal remedies, medicines, and foods (grapefruit juice and Seville oranges) that inhibit or induce CYP3A. Please see FDA approved complete prescribing information at www.zokinvy.com.
    b. Patients taking lonafarnib must not be taking midazolam. If a surgical procedure is needed where midazolam will be used, temporarily discontinue lonafarnib for 10-14 days before and 2 days after administration of midazolam during the surgical procedure. Please see FDA approved complete prescribing information at www.zokinvy.com.
    c. Patients taking lonafarnib must not be taking atorvastatin, lovastatin or simvastatin.

Appendix B includes the full MAP eligibility and non-eligibility criteria. The treating doctor will want to see both sets of criteria.

4. How long can a patient be treated with lonafarnib as part of the Managed Access Program?

- Eiger's intention is to provide access to lonafarnib through Clinigen until the medication is available generically or you decide to discontinue treatment or until lonafarnib is approved by your country's regulatory agency and the drug is commercially available in your country. Once approved and available, you will be able to obtain lonafarnib by getting a prescription

from your/your child's treating doctor. Certain unknown circumstances may lead to changes in the MAP. Eiger maintains the ability to change the managed access program at any time. If the program is changed, the doctors that have enrolled will be made aware of the change/s and will facilitate communication with the patient or their legal guardian.

5. **How frequently will I need to visit my doctor to pick-up lonafarnib during the program?**

- You or your caregiver should plan on picking-up lonafarnib from the treating doctor approximately every 4-months unless otherwise communicated to you.

6. **Once successfully registered for the MAP, how do I continue to get refills of lonafarnib?**

- The treating doctor will place an order for lonafarnib through an online system offered by Clinigen. Lonafarnib will be shipped to your doctor's designated hospital and can usually be picked-up by you/your caregiver at that location.

7. **Who will help with information concerning side effects associated with lonafarnib or if there are questions, I have while taking lonafarnib?**

- Your treating doctor will manage your side effects. If your doctor has any questions, they can contact Eiger's Medical Affairs department by sending an e-mail to ProgeriaMA@eigerbio.com. Your doctor is asked to provide their contact information in the e-mail. This will enable Eiger to call if the question/s cannot be answered by e-mail.

8. **In the event of a Serious Adverse Event or an Adverse Event, who should be contacted?**

- The patient and doctor maintain the responsibility of reporting both Serious Adverse Events and Adverse Events associated with lonafarnib's use in accordance with local health authority requirements.
- IQVIA is the company providing all safety reporting services for the MAP. As such, Serious Adverse Events (SAEs) and Adverse Events should be reported using the IQVIA SAE report form available on the Cliniport system. Doctors may also call IQVIA directly using the global phone number included within the Cliniport system.
- Serious Adverse Events and Adverse Events **SHOULD ONLY** be reported to IQVIA.
- Serious Adverse Events and Adverse Events **SHOULD NOT** be reported to Clinigen.

9. **Who do I speak with if I have additional questions regarding the lonafarnib Managed Access Program?**

- Patients or caregivers should always start by asking questions to their doctors. In the event your/your child's doctor cannot answer the question, the doctor can contact Clinigen's Medicine Access Team at +44 (0) 1932 824123 or by emailing medicineaccess@clinigengroup.com. The doctor may also e-mail Eiger at

ProgeriaMA@eigerbio.com. Patients or caregivers should **not** contact Clinigen. Instead, patients and caregivers should only contact The Progeria Research Foundation at 978-535-2594 or by sending an e-mail to info@progeriaresearch.org.

Appendix A

Country Managed Access Program Status

If your country of interest is not on any of these lists, please contact The Progeria Research Foundation at 978-535-2594 or by sending an e-mail to info@progeriaresearch.org.

Countries with Lonafarnib MAP Available March 2021	
Algeria	Kazakhstan
Argentina	Luxembourg
Australia	Malaysia
Bangladesh	Mexico
Brazil	Namibia
Belgium	Oman
Canada	Pakistan
China	Philippines
Colombia	Poland
Denmark	Portugal
Dominican Republic	Russia
Egypt	Saudi Arabia
France*	Serbia
Germany	South Africa
India	South Korea
Indonesia	Spain
Iraq	Sweden
Ireland	Taiwan
Israel	Thailand
Italy*	Turkey
Japan	Ukraine

*Separate government programs may exist in these countries. In the event these government programs are unavailable, the MAP may be considered.

Countries Where Lonafarnib MAP Will NOT Be Available**	
Honduras	Sri Lanka
Iran	Suriname
Libya	Tajikistan
Nepal	Tanzania
Palestine-Gaza	Togo

**This may not be a comprehensive list. If you/your child is from one of these countries and wants access to lonafarnib for HGPS or PLs, please contact The Progeria Research Foundation.

Appendix B

Eligibility and Non-Eligibility Criteria

This section contains medical language and is intended primarily for you to be able to communicate with your/your child's local doctor.

Eligibility Criteria

Patients must meet all of the following eligibility criteria to enroll in the program.

1. Patient is 12 months of age or older.
2. Patient must have a genetic test confirming a diagnosis of either Hutchinson-Gilford Progeria Syndrome or a processing deficient progeroid laminopathy (processing deficient heterozygous LMNA mutation with progerin-like protein accumulation or homozygous or compound heterozygous ZMPSTE24 mutations).
3. Patients must have adequate hepatic function as defined by SGPT (ALT) and SGOT (AST) ≤5 times upper limit of normal range for age.
4. Signed informed consent/assent of parent(s) or guardian(s) must be obtained prior to any program procedures.
5. Female patients of childbearing age or sexually active must have pregnancy test before starting lonafarnib.

Non-Eligibility Criteria

Patients meeting **any** of the following criteria will be ineligible for the program:

1. Patients must have no uncontrolled infection.
2. Patients must have no active clinically relevant medical condition that in the opinion of the treating physician would preclude them from safely participating in the program.
3. Patients must not have known or suspected hypersensitivity to any of the excipients included in the formulation.
4. Patients must not be pregnant or breast-feeding or plan to become pregnant while on therapy.