Lonafarnib managed access programme (MAP) information, questions and answers for patients, caregivers and doctors

June 2019

Eiger BioPharmaceuticals, the manufacturer of the drug Lonafarnib, is sponsoring a Managed Access Programme (MAP). The purpose of this MAP is to allow eligible patients with Hutchinson-Gilford Progeria Syndrome (HGPS or Progeria) or a Progeroid Laminopathy (PL) to gain access to treatment with Lonafarnib. The MAP will provide Lonafarnib to eligible HGPS and PL patients in 3 categories:

1) Those who have never taken Lonafarnib before;

2) Those who have taken Lonafarnib before but are not taking Lonafarnib at this time;

3) Those who have been taking Lonafarnib as part of a clinical trial and would like to continue Lonafarnib treatment on 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.

Lonafarnib is currently considered an investigational treatment for HGPS and PLs. As of the writing of this communication, Lonafarnib has not been approved by any of the world's regulatory authorities for commercialisation. In other words, you cannot go to a local pharmacy with a prescription from your/your child's doctor and get the product.

For those eligible HGPS and PL patients residing in a country that allows the Lonafarnib MAP to be offered, it will be the sole means of gaining access to the drug, 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 PLs is available in your country. If that should change, all MAP participants will be notified.

The subsequent pages include a list of questions and answers, as well as appendices A and B.

Questions and answers

1. What is a managed access programme (MAP)?

- A MAP 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.

2. What do I need to do to be considered for the Lonafarnib MAP?

- All patients wishing to participate in the Lonafarnib MAP must have a local doctor that is willing to fulfil the requirements of the programme.
- 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 PLs. Important information will be provided to the treating doctor upon them enrolling in the Lonafarnib MAP.
- Eiger BioPharmaceuticals is using a highly experienced company named Clinigen to help your local doctor transition you/your child into the MAP. Clinigen will also oversee the programme 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 enrolment by the doctor and ensuring the patient fulfils the programme's criteria, the treating doctor orders the patient's Lonafarnib from Clinigen.
- The Lonafarnib is delivered to the local doctor's office or a 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 in is not listed, MAP may still be possible. In this situation, please contact the Progeria Research Foundation at 00 1 978 535 2594 or emailing info@progeriaresearch.org. Conversely, the treating doctor can contact Clinigen's Medicine Access Team at +44 (0) 193 282 4123 or by e-mailing medicineaccess@clinigengroup.com.

3. What is required for eligibility in the MAP?

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

1. A diagnosis of HGPS (Progeria) or a PL.
2. Blood tests to make sure 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. Caution is advised with the use of Lonafarnib and any sensitive CYP3A substrates and strong or moderate CYP3A inhibitors or inducers. 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 the 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 (like grapefruit juice and Seville oranges) that inhibit or induce CYP3A.

Appendix B includes the full MAP inclusion and exclusion 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 MAP?

- Eiger will continue to provide access to Lonafarnib through Clinigen until you decide to discontinue treatment or until Lonafarnib is approved and available commercially in your country. Once it is available commercially, you will be able to obtain Lonafarnib with a prescription from your/your child's treating doctor.

5. How often will I need to visit my doctor to collect Lonafarnib during the programme?

- You or your caregiver should plan on collecting Lonafarnib from the treating doctor at least every 4 months.

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 and you/your caregiver can usually collect it from their office.

7. How does my physician register for MAP?

- Your treating doctor will register for MAP by calling Clinigen at +44 (0) 193 282 4123 or by e-mailing medicineaccess@clinigengroup.com. Your treating doctor is the only person who can register you for the MAP. Patients or caregivers should **not** contact Clinigen regarding registration for MAP.

8. **Who will help with information concerning side effects associated with Lonafarnib or if I have questions 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.

9. **In the event of a serious adverse event, who should be contacted?**

- The patient and doctor maintain the responsibility of reporting serious adverse events (SAEs) associated with the use of Lonafarnib in accordance with local health authority requirements.
- Novella is the company providing all safety reporting services for the MAP. As such, SAEs should be reported using the Novella SAE report form available on the Cliniport system. Doctors may also call Novella directly using the directory of global phone numbers included in the Cliniport system.
- Any type of adverse event **SHOULD NOT** be reported to Clinigen.

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

- Patients or caregivers should always start by asking their doctors questions. In the event your/your child's doctor cannot answer the questions, the doctor can contact Clinigen's Medicine Access Team at +44 (0) 193 282 4123 or by e-mailing 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 00 1 978 535 2594 or by sending an e-mail to info@progeriaresearch.org.

Appendix A

Country MAP status

If your country of interest is not on any of these lists, please contact the Progeria Research Foundation at 00 1 978 535 2594 or by sending an e-mail to info@progeriaresearch.org.

Countries with an available Lonafarnib MAP June 2019				
Yes	United States		Yes	Kazakhstan
Yes	Algeria		Yes	Mexico
Yes	Argentina		Yes	Namibia
Yes	Australia		Yes	Oman
Yes	Bangladesh		Yes	Pakistan
Yes	Brazil		Yes	Portugal
Yes	Canada		Yes	Russia
Yes	China		Yes	Serbia
Yes	Colombia		Yes	South Africa
Yes	Denmark		Yes	South Korea
Yes	Dominican Republic		Yes	Spain
Yes	France		Yes	Sweden
Yes	India		Yes	Ukraine
Yes	Indonesia		Yes	United Kingdom
Yes	Israel			

Countries where a Lonafarnib MAP will become available*		
Belgium		Philippines
Egypt		Poland
Germany		Saudi Arabia
Iraq		Taiwan
Italy		Turkey
Japan		

*The exact dates for MAP availability in these countries are unknown. If you/your child is from one of these countries and you/your child is interested in participating in the Lonafarnib MAP, please contact the Progeria Research Foundation.

Countries where Lonafarnib MAPs will NOT be available**		
Honduras		Tajikistan
Libya		Tanzania
Nepal		Togo
Palestine-Gaza		
Sri Lanka		
Suriname		

**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

Inclusion and exclusion criteria

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

Inclusion criteria

Patients must meet all the following inclusion criteria to be eligible for enrolment in the programme.

1. Clinical diagnosis of HGPS or PLs by a qualified medical doctor (based on common phenotype as described in Gordon et al, 2015 and Meredith et al, 2008). Confirmation with genetic testing is preferred but not required
2. Patient is at least 12 months of age
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 programme procedures

Exclusion criteria

Patients meeting **any** of the following criteria will be excluded from the programme:

1. Patients must not be taking medications or foods that are known to be moderate or strong inducers or inhibitors of CYP3A4 or sensitive CYP3A substrates (list provided with informed consent).
2. Patients must not be taking Digoxin, a P-gp substrate with a narrow therapeutic window.
3. Patients must have no uncontrolled infection.
4. Patients must have no overt hepatic dysfunction.
5. Patients must have no active clinically relevant medical condition that in the opinion of the treating doctor would preclude them from safely participating in the programme.
6. Patients must not have known or suspected hypersensitivity to any of the excipients included in the formulation.
7. Patients must not be pregnant or breast-feeding or plan to become pregnant while on therapy.