

**INFORMED CONSENT TO PARTICIPATE IN A RESEARCH STUDY  
PARTICIPANTS AND PARENTS**

**Study:** CP-AI-007

**Title:** A Phase 3, Double-Blind, Multicenter, Multinational, Randomized, Placebo-Controlled Trial Evaluating Aztreonam Lysinate for Inhalation in Cystic Fibrosis Patients with Pulmonary *P. aeruginosa* (AIR-CF1)

**Sponsor:** [REDACTED]

**Investigator (study doctor):**

**Institution Name:**

**Institution Address:**

**24-hour emergency telephone number:** \_\_\_\_\_

*Parent(s) and legally authorized representative(s) / guardian(s) signing on behalf of the child should refer to “your child” when reading “you.”*

**1. Introduction**

You are being asked to take part in a research study conducted by Dr. \_\_\_\_\_. This study is sponsored by [REDACTED]. The purpose of this consent form is to provide you with the information you will need to decide whether or not to be in the study. Please read the form carefully. You may ask questions about the purpose of the research, what you will be asked to do, the possible risks and benefits, your rights as a volunteer and anything else about the research or this form that is unclear. When all your questions have been answered, you can decide whether you want to be in the study. If you agree to take part, you will be required to sign this document to show that you have reviewed the contents, have had your questions answered, and are choosing to be in the study.

**2. Purpose of this Research Study**

You are being asked to participate in this study because you have cystic fibrosis (CF). The purpose of this research study is to test an experimental drug called Aztreonam Lysinate for Inhalation (AI, study drug).

People with CF often have lung infections which occur repeatedly or worsen over time. The lung infections are caused by bacteria (germs). Treatment with antibiotics (a type of

medicine) is used to stop or slow down the growth of bacteria. The antibiotics may be given by mouth, into a vein (IV), or inhaled as a mist.

The purpose of this study is to find out if AI is safe and effective in CF patients with lung infections. AI is an investigational drug. The US Food and Drug Administration (FDA), Health Canada, the Therapeutic Goods Administration (TGA) in Australia, and Medsafe in New Zealand are allowing it to be used in people for clinical research purposes only.

You will be assigned to receive either 75 mg of AI (active study drug) or placebo (sugar powder containing no drug) 3 times a day for 28 days. Treatment with AI or placebo will be blinded, meaning neither you nor your doctor(s) will know if you are taking AI or placebo. The information about whether you are receiving AI or placebo will be made available to your study doctor in case of an emergency. If you participate, you will be randomly assigned (like flipping a coin) to receive either AI or placebo. You will have the same chance of getting AI as you have of getting the placebo.

AI or placebo will be taken using the eFlow<sup>®</sup> Electronic Nebulizer. The eFlow is permitted for use by the US FDA and Health Canada. The eFlow is an investigational device in Australia and New Zealand. The Australian TGA and Medsafe are allowing it to be used in people for clinical research purposes only. The eFlow is a reusable device that mixes air with the study drug solution (AI or placebo) so that it becomes a mist that is inhaled (breathed in). The device works using a porous membrane (thin metal layer with many holes) that vibrates and allows you to inhale AI or placebo into your lungs. This helps lessen the amount of drug left in your mouth and throat.

### **3. Where this Study is Being Done and Number of People Participating**

This study is taking place in approximately 70 centers throughout the United States, Canada, Australia and New Zealand. Approximately 140 people that are 6 years of age or older are expected to take part.

### **4. Length of Your Participation**

Your participation in the study will last approximately 56 days. You will have 5 study visits.

### **5. Study Procedures**

The following describes what will occur at each visit:

Visit 1, Screening: This visit will take about 1 to 2 hours. The screening visit lets the study doctor(s) know if you are able to participate in the study. The study will be explained to you. If you think you want to be in the study, you will be asked to sign this consent form. The procedures that will be done at this visit include:

- 1) Ask you questions about your medical history and about medications you are taking.

- 2) Measure your height and weight.
- 3) Perform a physical exam, including vital signs (temperature, heart rate, breathing rate, and blood pressure).
- 4) Perform oximetry (a small clip will be placed on your finger to measure the amount of oxygen in your blood).
- 5) Collect a small amount of blood (2 to 3 teaspoons) to check your blood count and liver and kidney function. Females of childbearing years will also have a pregnancy test performed.
- 6) Collect sputum (at least 1 gram – smaller than a teaspoon) to test for current lung infections. If you cannot cough up sputum, a throat culture will be obtained.
- 7) Perform spirometry (PFTs). You will blow into a machine to check your lung function.
- 8) Perform a chest X-ray, only if you have not had one within the last 90 days or if you have had a significant illness since your last chest X-ray.
- 9) Schedule your next visit. If you decide to participate and the study doctor feels that you are a match for the study, you will be asked to come back to the clinic in about 14 days for Visit 2.

Visit 2: This visit will take up to 4 hours. You will take your first dose of study drug at the clinic during this visit. You will have procedures done before and after you take a dose of study drug. The procedures that will be done at this visit before you take your dose of study drug include:

- 1) Measure your weight.
- 2) Complete the Quality of Life Cystic Fibrosis Questionnaire (CFQ-R). This form asks questions about how you are feeling. You will be shown how to complete this form. The CFQ-R helps us better understand how CF affects your daily activities. Parents with children 13 years of age or younger will also be asked to complete a questionnaire. The same parent/guardian will need to complete these questionnaires throughout the study.
- 3) Ask you about any changes in health or medicines you are taking.
- 4) Perform a physical exam, including vital signs (temperature, heart rate, breathing rate, and blood pressure).
- 5) Collect sputum (at least 1 gram – smaller than a teaspoon) to test for current lung infections. If you cannot cough up sputum, a throat culture will be obtained.
- 6) Collect a small amount of blood (1 teaspoon) to see how much study drug is in your body.
- 7) You will be trained on how to use the eFlow<sup>®</sup> Electronic Nebulizer

- 8) Perform spirometry (PFTs). You will blow into a machine to check your lung function. You will receive an inhaled medicine (bronchodilator) to open up your airways before the spirometry.

After you take your study drug, the procedures that will be done include:

- 1) Collect a small amount of sputum and blood (1 teaspoon) to see how much study drug is in your body. You will not have a throat swab if you cannot produce sputum.
- 2) Perform a physical exam, including vital signs.
- 3) Perform spirometry (PFTs).

At the end of this visit you will be given a 28-day supply of study drug and the eFlow device. You will also be given instructions on using the study drug and storing, using, and cleaning the eFlow device. You will be reminded to bring one dose of study drug and the eFlow device to Visit 3 and to take your last dose of study drug at least 4 hours before your scheduled visit.

Visit 3: This visit will take up to 4 hours. You will take a dose of study drug at the clinic during this visit. You will have procedures done before and after you take a dose of study drug. The procedures that will be done at this visit before you take your dose of study drug include:

- 1) Measure your weight.
- 2) Complete the Quality of Life Cystic Fibrosis Questionnaire (CFQ-R). The same parent/guardian will need to complete these questionnaires throughout the study.
- 3) Ask you about any changes in health or medicines you are taking.
- 4) Perform a physical exam, including vital signs (temperature, heart rate, breathing rate, and blood pressure).
- 5) Collect sputum (at least 1 gram – smaller than a teaspoon) to test for current lung infections. If you cannot cough up sputum, a throat culture will be obtained.
- 6) Perform spirometry (PFTs). You will blow into a machine to check your lung function. You will receive an inhaled medicine (bronchodilator) to open up your airways before the spirometry.

After you take your study drug, the procedures that will be done include:

- 1) Collect a small amount of sputum and blood (1 teaspoon) to see how much study drug is in your body. You will not have a throat swab if you cannot produce sputum.
- 2) Perform a physical exam, including vital signs.
- 3) Perform spirometry (PFTs).

At the end of this visit you will be reminded to take your last dose of study drug as least 4 hours before your next scheduled visit. You will also be reminded to bring all used and unused study drug and the eFlow device to Visit 4.

Visit 4: This visit will take up to 4 hours. You must return all used and unused study drug and the eFlow device to the clinic at this visit. You will take your last dose of study drug at the clinic during this visit. You will have procedures done before and after you take a dose of study drug. The procedures that will be done at this visit before you take your dose of study drug include:

- 1) Measure your weight.
- 2) Complete the Quality of Life Cystic Fibrosis Questionnaire (CFQ-R). The same parent/guardian will need to complete these questionnaires throughout the study.
- 3) Ask you about any changes in health or medicines you are taking.
- 4) Perform a physical exam, including vital signs (temperature, heart rate, breathing rate, and blood pressure).
- 5) Collect sputum (at least 1 gram – smaller than a teaspoon) to test for current lung infections. If you cannot cough up sputum, a throat culture will be obtained.
- 6) Collect a small amount of blood (2 to 3 teaspoons) to check your blood count and liver and kidney function. You will have additional blood (1 teaspoon) drawn to see how much study drug is in your body.
- 7) Perform spirometry (PFTs). You will blow into a machine to check your lung function. You will receive an inhaled medicine (bronchodilator) to open up your airways before the spirometry.

After you take your study drug, the procedures that will be done include:

- 1) Collect a small amount of sputum and blood (1 teaspoon) to see how much study drug is in your body. You will not have a throat swab if you cannot produce sputum.
- 2) Perform a physical exam, including vital signs.
- 3) Perform spirometry (PFTs)

At the end of this visit you will be reminded to bring your short-acting bronchodilator to your next scheduled visit.

Visit 5: This visit will take about 1 to 2 hours. The procedures that will be done at this visit include:

- 1) Measure your weight.
- 2) Complete the Quality of Life Cystic Fibrosis Questionnaire (CFQ-R). The same parent/guardian will need to complete these questionnaires throughout the study.

- 3) Ask you about any changes in health or medicines you are taking.
- 4) Perform a physical exam, including vital signs (temperature, heart rate, breathing rate, and blood pressure).
- 5) Collect sputum (at least 1 gram – smaller than a teaspoon) to test for current lung infections. If you cannot cough up sputum, a throat culture will be obtained.
- 6) Collect a small amount of blood (2 to 3 teaspoons) to check your blood count and liver and kidney function (only if the study doctor feels it is necessary).
- 7) Perform spirometry (PFTs). You will blow into a machine to check your lung function. You will receive an inhaled medicine (bronchodilator) to open up your airways before the spirometry.

If you stop taking part in this study for any reason, you will be asked to return to the clinic for an Early Termination Visit. The same procedures will be performed as at Visit 5 (see previous section).

## **6. Sputum Storage**

A little bit of the bacteria from the sputum you give at study visits will be stored for possible future microbiology testing to see whether your bacterial infection(s) has developed the ability to block the action of the study drug (drug resistance testing) and for other exploratory analyses. No genetic testing will be performed on your DNA.

## **7. Procedures that are Not Standard Care**

The AI study drug is an experimental treatment. The use of a placebo (sugar powder containing no active drug), the blinding to what study treatment you will receive (you and your doctor will not know what treatment you receive), and the randomization (to receive either AI or placebo) are procedures done only for research studies. Sputum and blood collection for drug levels are only being done for the purposes of the study and may not be part of your routine care. The questionnaire involved in this study is also not a routine part of your care. Each questionnaire will take about 10 to 20 minutes to complete.

## **8. Participant Responsibilities**

If you decide to be in this study, there are certain rules you must follow before, during, and after the study period. Some are listed below, but there could be others that the study doctor(s) will discuss with you:

- You must not become pregnant during this study.
- It is very important that you tell your doctors all the information you know about your health and medications you may be taking throughout the study period. If

you do not tell the study doctor everything you know you may be putting your health at risk.

- You must return all of the used and unused AI/placebo study drug to the clinic. At Visit 4, you will return all study drug materials and the eFlow device. When you are at home, you should remember to track any doses of study drug you miss and tell the study doctor at your next visit.
- You must follow all procedures given to you while you are participating in the study. If you do not, you may be discontinued. If you are unsure about what you are supposed to do, ask the study doctor.

## **9. Possible Risks, Stresses or Discomfort from Taking Part in this Study**

### Risks of AI/Placebo

It is possible for any drug to cause unwanted side effects. You need to know about side effects that could occur in this study before you agree to participate.

In a previous study, AI or placebo was given to approximately 105 CF patients aged 13 years and older with the same lung infection as you have. No serious side effects related to AI study drug were reported during the study. During the course of an ongoing open-label study with AI, there has been one report of a serious side effect that the study doctor considered possibly related to the study drug. The patient experienced joint pain and swelling which ended after taking medication. After reviewing all the symptoms, the study doctor decided to stop the patient's AI treatment.

As with any inhaled drug, taking AI or placebo may cause irritation of the airways. Side effects associated with AI include increased cough, shortness of breath, wheezing, chest tightness, unpleasant taste, and decrease in lung function. Bronchoconstriction (narrowing of the airways) is a potential complication with any inhaled medication.

Other possible side effects may include diarrhea, bloating, stomach pain, nausea, and vomiting.

Allergic reactions can also occur with any drug. Common symptoms may include rash, itching, or skin problems.

### Risks/Discomforts of Study Procedures

**Blood draws:** The blood draws in this study may cause discomfort. You may feel a sting when the needle is put in your arm to take blood. It is possible that there may be some swelling, bleeding, bruising where the needle enters the skin. Some people have also felt light-headed when their blood was being taken. About 2 to 4 teaspoons will be collected during each blood draw.

**Spirometry:** You may have some coughing or shortness of breath after spirometry, but there is no pain expected with these tests.

**Chest X-ray:** A chest X-ray (or chest radiography) provides your doctor with an image of your heart, lungs, and surrounding organs. Getting an X-ray is like having a picture taken. The procedure should not cause any pain. Because the X-ray procedure involves the use of radiation, there is a very low risk from radiation exposure. However, there are procedures in place to make sure that the least amount of radiation is used. Pregnant women and children are most susceptible to the risks of radiation exposure.

### Unknown Risks

As with any new drug candidate, there may be unknown risks which could be serious or life-threatening. All of the tests and measurements performed during this study are designed to watch you closely for any signs of side effects. AI is still being tested for the treatment of CF. Therefore, it is possible that there may be other side effects that we do not know about yet. If any new information about the study drug is known during the study, the study doctor will immediately tell you or your legal guardian so you can decide if you still want to be in the study.

### Pregnancy and Birth Defects

The effects of AI on an unborn child are not known at this time. Therefore, if you are sexually active, you must use adequate birth control while participating in this study. Acceptable methods include birth control pills, Depo-Provera, diaphragm, intrauterine device (IUD), cervical cap, abstinence, or condom with sponge/foam. All women who can become pregnant must have a negative pregnancy test prior to starting study drug. If you become pregnant during this study, you must stop taking the study drug and call the study doctor immediately.

## **10. Costs**

There is no cost to you for study-related clinic visits or study-related procedures that are part of this study. All clinic visits, laboratory testing, study drug (AI/placebo), and the eFlow device for study drug administration you will receive are free.

## **11. Payment**

You will receive a small payment for participating in this study to cover food and travel to and from the clinic (\$X per visit).

## **12. Study Sponsor**

This study is sponsored by [REDACTED] who will pay the study doctor or his/her institution for the work he/she does if you are included in this study. The Cystic Fibrosis Foundation has also provided some funding to [REDACTED] for this study.

**13. Anticipated Benefits to You and to Others**

No specific health benefits can be guaranteed as a result of taking part in this study. You may have some improvement in your health from the study medication you receive in this study. However, it is possible that the medication will not produce any benefits or that the benefits may only be temporary.

The main goal of this study is to learn more about how AI can help patients with CF. The results of this study could also help in the future to treat other patients with CF.

**14. Alternatives to Being in this Study**

An alternative to taking part in this study is to continue with your current treatment(s) for CF. CF treatments may include use of other antibiotics to treat infection. You may choose not to participate in this study and keep taking your current treatment, or you may choose not to receive any treatment at this time. If any new therapy becomes available for CF, your doctor will tell you.

**15. New Information**

The study doctor will tell you or your legal guardian about any new and significant information that becomes available during the study that may affect your willingness to continue the trial. You should discuss this with the study doctor.

**16. About Participating in this Study**

**Taking part in this study is voluntary.** You may stop being in this study at any time. Your decision not to take part in this study or to stop being in the study will not affect your medical care or any benefits to which you are entitled. If you decide to stop taking part in this study, you should tell the study doctor immediately. You will be asked to return for a final study visit during which the study doctor will perform safety tests, you will fill out a questionnaire, and you will return all used and unused study drug supplies and the device.

The study doctor or your regular doctor may stop your participation in the study at any time. This could happen because it is no longer safe for you to continue in the study or if you are not following rules or instructions given to you by the study staff. The study sponsor who is running the study may also decide to take you out of the study or end the study at any time.

**17. Compensation for Injury**

If you get hurt or sick as a result of being in this study, the study sponsor will pay for any medical care you might need that is not paid for by your insurance. This assistance will be provided as long as you followed all study-related instructions given to you by your study doctor or study staff, and you told the study doctor of your injury or illness as soon

as it happened. This treatment will include any necessary emergency treatment and proper follow-up care.

Injuries caused by the negligence of any person, or the intentional misconduct of any person outside of [REDACTED] will not be covered by [REDACTED]. No other compensation for such injury is available.

The sponsor will not pay for things like lost wages, disability (payment while you are not able to work because of an injury), or discomfort due to injury or illness. You should notify your study doctor of your injury or illness immediately. The doctor's phone number is located on the front page of this form.

By signing this consent form you will not waive any of your legal rights nor release the parties involved in this study from liability for negligence.

### 18. Confidentiality of Study Records and Medical Records

Information collected for this study is confidential. Data collected from you and other participants in this study will be shared with other research doctors, but no patient names will be used. There will be no names or other patient identification in any study documents.

Your records may be reviewed by representatives from the following groups: the US FDA, Health Canada, the Australian TGA, New Zealand Medsafe, an Institutional Review Board (IRB) or Ethics Committee (EC), [REDACTED]

[REDACTED] If your study record is reviewed by any of these groups, they may also need to review your medical record.

Data collected and recorded on study forms are the property of [REDACTED]. In the event of any publication regarding this study, your name will not be disclosed.

### 19. Names of Contacts for Questions about this Study

You may ask the study doctor and his/her staff any questions you may have about this study at any time. If you have any questions or would like additional information about AI, please contact: \_\_\_\_\_ at \_\_\_\_\_.

If you think you have experienced an injury due to being in this study or if you do not feel well, you should contact: \_\_\_\_\_ at \_\_\_\_\_.

If you have any questions about what it means to be part of a research study or about your rights as a research participant, you can call the Institutional Review Board (IRB)/Ethics Committee (EC) – the committee that approved this research project: \_\_\_\_\_ at \_\_\_\_\_.

**SIGNATURE OF RESEARCH PARTICIPANT**

Your signature below indicates that you have read this document, understand its meaning, have had a chance to ask questions, have had those questions answered to your satisfaction, and agree to be in this study. You have been given a signed and dated copy of this form for your own records.

\_\_\_\_\_  
Name of participant  
(Please Print)

\_\_\_\_\_  
Signature of participant

\_\_\_\_\_  
Date

\_\_\_\_\_  
Name(s) of legally authorized representative(s)  
(Please Print)

\_\_\_\_\_  
Signature(s) of legally authorized representative(s)    Date

**SIGNATURE OF INVESTIGATOR OR PERSON EXPLAINING CONSENT**

I have explained the research to the participant and/or the participant's parent(s)/legal representative(s) and have answered all of their questions. I believe that they understand all of the information described in this document and freely give consent/permission to participate.

\_\_\_\_\_  
Name of person who explained the study  
(Please Print)

\_\_\_\_\_  
Title

\_\_\_\_\_  
Signature of person who explained the study

\_\_\_\_\_  
Date