Augmentation Therapy

THE SPECIFIC THERAPY FOR ALPHA-1 LUNG DISEASE

WHAT IS AUGMENTATION THERAPY?

Augmentation therapy is an FDA-approved therapy used to treat Alpha-1 related lung disease, specifically emphysema. Alphas on this life-saving therapy get weekly infusions of alpha-1 antitrypsin (AAT). These infusions boost AAT levels in the lungs and bloodstream.

Augmentation therapy is the only FDA-approved specific therapy for Alpha-1 related lung disease. But you'll use other approaches to treat your lung disease, like:

- Inhaled medicines
- Treating exacerbations (flare-ups) with antibiotics and/or oral corticosteroids
- Vaccines for whooping cough, pneumonia, and the flu
- Exercise
- Pulmonary Rehabilitation ("Rehab")
- Oxygen therapy
- Reducing or removing environmental risk factors at home and work.

CROSS REFERENCE: For more information about ways to avoid the risk of disease, see ***Staying Healthy,*** another AlphaNet ***Skinny Little Reference Guide,*** or find short articles at **https://www.alphanet.org/living-with-alpha-1/**.

WHAT ARE THE GOALS OF THERAPY?

The primary goal of augmentation therapy is to increase the AAT level in your lungs. AAT also protects your lungs from the damaging effects of neutrophil elastase. Your body's white blood cells release this enzyme in response to inflammation or infection.

Boosting your AAT levels slows or stops lung damage. It can help prevent exacerbations or make them less severe. It can even treat Alpha-1 related skin disease. But it doesn't restore lost lung function, and it's not a cure.

KEY LEARNING: Therapy cannot restore lost lung function, nor is it considered a cure. The hope is that by replacing the deficient AAT protein, the progression of lung destruction will be slowed or stopped.

YOUR OPTIONS FOR AUGMENTATION THERAPY

In 1987, the FDA approved Prolastin. Since then, it has approved the four other currently available augmentation therapy products in the U.S. All four are safe and effective for boosting AAT levels in the blood and lungs.

- Prolastin®-C Liquid
- Aralast NP®
- Zemaira®
- Glassia®

You may have more options in the future. That's because researchers are always working on developing new therapies. And, other products are available in other parts of the world.

Understanding infusions

Augmentation therapy infusions require specific preparations. You usually get them in a doctor's office, an infusion center, or at home. But some Alphas choose to self-infuse. You can self-infuse, if your health care and health insurance providers allow it. You just need to learn how to do it safely.

Infusions in the home rarely cause severe allergic reactions. However, many home nurses and care providers keep an EpiPen around, just in case. EpiPens contain epinephrine, strong medicine that stops allergic reactions. You can give yourself a shot while you're on your way to the emergency room.

In summary, most Alphas find that the benefit of slowing emphysema progression outweighs the burden of infusions and side effects.

CONSIDERING AUGMENTATION THERAPY: IS IT RIGHT FOR YOU?

Are you considering augmentation therapy? Experts agree that Alphas with emphysema should get it. However, they disagree about whether it's the right approach for people with very mild or very severe lung disease.

Some research studies have shown that people who fall in the middle range of severity get the most benefit from augmentation therapy. Why? With mild lung disease, you might not notice any improvement. If you have severe lung disease, your lung function declines very slowly. Again, it's not easy to see any improvement.

Some members of the healthcare community use these findings to suggest that only people with moderate lung disease should receive augmentation therapy. But augmentation therapy "puts the brakes" on lung damage. Why wouldn't you begin therapy as soon as you know you have lung disease due to Alpha-1?

We don't know which Alphas will get lung disease. So, we could argue that all Alphas should get augmentation therapy to keep their lungs as healthy as possible. And if it were safe, easy, inexpensive, proven to be effective and available in unlimited supply, most Alphas would probably get it. But that's not the case.

Here's a list of things to do before you start augmentation therapy:

1. Get an IgA deficiency test.

Immunoglobulin A (IgA) is a protein that fights infection. If you have inherited an IgA deficiency, you may have severe allergic-type reactions to plasma products.

2. Get Hepatitis A and B vaccines.

These vaccines reduce your risk of liver injury. You'll get a series of three shots over a six-month period.

3. Learn about augmentation side effects.

The vast majority of people who get this therapy have no side effects. The most common side effect is feeling drained or having flu-like symptoms. These effects last up to 24 hours after having an infusion. Slowing the rate of infusion can reduce or remove the symptoms.

Other possible side effects include:

- Hives
- Itching
- Tightness in the chest
- Shortness of breath (dyspnea)
- Wheezing

NOTE: Taking an antihistamine like Benadryl before an infusion can sometimes improve or prevent these side effects.

In clinical trials, all four of the augmentation therapy products currently available showed similar rates of side effects.

Switching to a different brand of augmentation therapy may get rid of persistent side effects. However, if you have severe systemic reactions to a certain brand, your doctor should monitor you closely while you try a new brand.

4. Find the dose that's right for you.

The FDA-approved dose for all four available augmentation products is 60 mg/kg of body weight given once a week by intravenous (IV) infusion. So, if you weighed 165 lbs (or 75 kg), your recommended dose would be 4,500 mg per week.

Some doctors think they should monitor your alpha-1 antitrypsin (AAT) levels and adjust your dose based on these levels. We don't recommend this dosing approach at the present time.

That's because AAT levels found **in your lungs** after long-term augmentation therapy tend to be much more stable and consistent than the levels found **in your blood**. Adjusting your dose based on blood levels may not have the desired effect on your lungs.

The FDA's recommended doses promote a consistent protective level of AAT within your lungs. They won't stop the progression of lung disease entirely. But so far, no study has found a dose that can do that. So, we suggest sticking with the FDA-approved dose of 60 mg/kg of body weight once a week.

If you have trouble getting to your infusion center or your doctor's office, your doctor may adjust your dosing schedule to every two weeks. They may also suggest an extra dose if travel plans affect your infusion schedule. But evidence shows that weekly dosing is the most effective.

An interesting note.

Individuals on augmentation therapy who have their phenotype re-tested will return a result of PiMZ if they were PiZZ prior to therapy. This is because Pi-typing looks at the types of AAT protein in the blood, and augmentation therapy delivers normal, PiMM protein to individuals who are PiZZ. Pi-typing will reveal both the Alpha's own AAT phenotype, as well as the augmentation-delivered normal phenotype. Genotyping, rather than Pi-typing, would be required to determine an individual's underlying AAT genetics while on augmentation therapy. For more in-depth information on Alpha-1 testing, please visit the Big Fat Reference Guide (BFRG).

AUGMENTATION THERAPY ACCESS DEVICE OPTIONS

Most Alphas who get augmentation therapy use a simple IV catheter or needle placed in their hand or arm at the time of each infusion. These simple devices have many benefits:

- They're comfortable.
- They're easy to place and stay in place during your infusion.
- They have very few complications.
- Most people can use them without any problems.

Other options for your augmentation therapy access device

Your doctor might recommend an "indwelling IV access device" for your infusions. These devices are inserted directly into your vein, and they can stay in place for months or years. They include:

- Implanted Vascular Access Devices (IVADs), also called ports
- Tunneled central catheters
- Peripherally Inserted Central Catheters (PICC)

How to choose your augmentation therapy access device

Ports and catheters make IV access easier. But having these devices in place does pose some risk. Before you make your decision, discuss the risks and benefits of each device with your doctor. Then, choose the one that makes the most sense for your situation.

What to consider when choosing an IVAD or central catheter

These questions may help you make your decision:

- Can you see the veins on your hands and forearms?
- Are these veins accessible and in good condition?
- Have you had trouble with IV insertions in the past?
- Have you had good experiences with certain nurses and bad experiences with others?
- What is your infusion schedule?
- Do you plan on doing your own infusions? Or will a spouse or partner do them for you?
- Do you understand the risks and benefits of the device you've chosen? If so, do the benefits outweigh the risks?
- Do you understand the insertion procedure for each device?
- Have you talked with others who have had an implanted device?
- Will you need any special care with a certain device?
- Do you understand how to maintain the device?

NOTE: Choose an augmentation therapy access device that meets your needs, not someone else's.

PORT INFECTIONS: PREVENTION & TREATMENT

The signs and symptoms of port or central catheter infections often look like a reaction to augmentation therapy. It's important to learn how to tell the difference between the two.

Port and central catheter infections

External infections are located at the spot where the catheter enters your skin, under the skin, or along the tunneled area of the catheter.

Internal infections occur within the port's reservoir or along the walls of the central catheter in the vein.

Bacteria may get into the device through lapses in sterile technique, poor skin prep, or contaminated equipment. The device may also attract bacteria from other infections in your body, which then grow in your catheter.

If you access and flush your device when you have an infection, it can send a shower of bacteria into your bloodstream.

Important signs of infection include:

- Redness, swelling, tenderness, or drainage at the insertion site
- Body aches
- Weakness
- Shaking, chills, and/or fever over 101° F
- Pain in your belly
- Nausea and vomiting
- Increased difficulty breathing

Many people assume these symptoms mean they're reacting to the augmentation therapy medicine. Some people do have side effects. But you should rule out infection before assuming that you're having such a reaction.

BURNING ISSUE: Though some patients do have side effects from their therapy, a patient with an indwelling port or a central catheter must first consider an infection, and this should be ruled out before assuming that a medication reaction has occurred.

Troubleshooting central catheter problems

1. If you have problems during or shortly after your infusion, tell your nurse and doctor right away.
2. Check your temperature, especially if shaking or chilled.
3. Call your doctor promptly if you have a fever over 101° F.
4. If your symptoms are severe, seek immediate medical attention.

Your doctor will order tests to check for an infection. They'll take blood from a vein in your arm and from your device.

If you are due for an infusion while undergoing a workup for infection, you may still receive your infusion, if your doctor says it's OK. However, you should get your infusion through an IV catheter in your hand or arm.

Your doctor will watch for symptoms. If you have them even when using a different infusion device, you may be having a reaction to the medicine.

If you have an infection, your doctor may prescribe IV antibiotics. In some instances, your device will need to be removed. If your blood cultures are negative, your doctor will continue to monitor you to see if you are reacting to your medication.

Make prevention your priority

If you have a port or other central device, preventing infection should be your first priority. After all, they provide a direct connection from the outside world into your body's large blood vessels.

Follow these guidelines to prevent infection:

- Wash your hands before touching your device.
- Maintain sterile technique while performing all device-related procedures.
- Limit the people who handle your port or central line.
- Make sure anyone who cares for your device wears a mask.

The more careful you are, the less chance you have of getting an infection.

INSURANCE AND AUGMENTATION THERAPY

Augmentation therapy is expensive, so having insurance coverage for your infusions is very important. When your insurance changes or there is an open season, coverage for your augmentation therapy should be a major consideration.

Here are some questions to ask your HR department or the insurance company:

- Does your insurance have a high deductible? You can sometimes buy a "cheaper" plan that ends up costing you a lot more in deductibles, cost-sharing or copays than the premiums themselves.
- Is augmentation therapy covered under major medical or the drug plan? Is there a separate deductible for each?
- Will I be able to get my infusions at home? Is there a cost difference for home infusions versus going to an infusion center or a doctor's office?

There are some assistance programs available for Alphas on augmentation therapy. Ask your AlphaNet Coordinator for information on the programs. They cannot tell you if you qualify, but they can point you to programs that you should investigate.

Traditional Medicare normally covers infusions under Part B in a hospital setting and in some situations at home. If you do not have a supplement, you will have a significant cost share.

Infusions can sometimes be covered under Part D or Part C (Advantage Plans), but be diligent about checking formularies and deductibles and copays. Advantage plans should only be chosen if you are certain augmentation therapy is a covered item if the Advantage Plan includes a drug plan. Not all do.

If you are doing well on one augmentation therapy, try to remain on it if possible. Some Alphas have more side effects on a particular brand, but many do not have side effects on any brand. Staying with an augmentation therapy brand that is working well should be a consideration when picking insurance coverage.

There is more information on insurance in the Big Fat Reference Guide, which can be found at www.alphanet.org.

TABLE OF SPECIFIC THERAPIES FOR ALPHA-1 LUNG DISEASE (U.S.)

	PROLASTIN®-C LIQUID	ARALAST NP®	ZEMAIRA®	GLASSIA®
Current version entered market	2018	2007	2003	2010
Marketed by	Grifols	Takeda	CSL Behring	Takeda
Recommended dose	60mg/kg IV weekly	60mg/kg IV weekly	60mg/kg IV weekly	60mg/kg IV weekly
Storage (Do not use after expiration date printed on label)	Refrigerate at 2–8°C (36–46°F) [May be stored at room temperatures up to 25°C (77°F) but must be used within one month] Do not freeze	Temperature not to exceed 25°C (77°F) Do not freeze	Temperature not to exceed 25°C (77°F) Do not freeze	Refrigerate at 2–8°C (36–46°F) [May be stored at room temperatures up to 25°C (77°F) but must be used within one month] Do not freeze
Dilutent (sterile water) or volume of product for liquid formulations	20ml for 1,000mg vial Liquid formulation	50ml for 1,000mg vial Freeze-dried powder	20ml for 1,000mg vial Freeze-dried powder	50ml for 1,000mg vial Liquid formulation
Infusion rate (average)	0.08 ml/kg per min	0.2 ml/kg per min	0.08 ml/kg per min	0.2 ml/kg per min
Infusion time (approximate)	15 minutes	Not listed	15 minutes	15 minutes
Contraindications	IgA deficiency with antibodies against IgA; history of severe reaction to augmentation therapy	IgA deficiency with antibodies against IgA; history of severe reaction to augmentation therapy	IgA deficiency with antibodies against IgA; history of severe reaction to augmentation therapy	IgA deficiency with antibodies against IgA; history of severe reaction to augmentation therapy
Common side effects	Diarrhea and fatigue	Headache, somnolence, chills, fever, vasodilation, pruritus, (itching) rash, abnormal vision, chest pain, increased cough, and dyspnea	Headache, sinusitis, respiratory infection, bronchitis, asthenia, cough, fever, injection site hemorrhage, rhinitis, sore throat, and vasodilation	Headache, respiratory infections, cough, sinus infection, chest discomfort, dizziness, increased liver enzymes, shortness of breath, nausea, and fatigue
Viral inactivation processes	Solvent detergent and Nanofiltration	Solvent detergent and Nanofiltration	Heat treatment and Nanofiltration	Solvent detergent and Nanofiltration
Number for reporting adverse events	800-520-2807	800-828-2088	800-504-5434	800-828-2088

NOTES

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