PLASMINOGEN DEFICIENCY FOUNDATION

Frequently Asked Questions Toolkit

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Plasminogen Deficiency Foundation
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Overview

Congenital plasminogen deficiency, hypoplasminogenemia or PLGD-1, is an ultra-rare disorder. People with PLGD-1 do not produce enough of the clotting factor plasminogen. In the U.S., a rare disorder is any condition that affects fewer than 200,000 people. While there is not an accepted national definition of an ultra-rare disorder, the estimated incidence of PLGD-1 is 1.6 cases per million population. This is far less than 200,000 people. Even though PLGD-1 is ultra-rare, you are not alone! The Plasminogen Deficiency Foundation is a community of patients, families, and care providers. We are ready to support you in the next steps on your journey.

Goals of this Handout

1. To answer common questions about living with PLGD-1.
2. To provide general guidelines for care in certain situations.

Living with PLGD-1, Frequently Asked Questions: Important Terms

Term	Definition
Peak Level	A peak level is your level of plasminogen activity between 5 and 30 minutes after you have a dose of your plasminogen treatment.
Trough Level	A trough level is your plasminogen activity taken right before your next scheduled dose.
Replacement Therapy	Replacement therapy is the medicine used to treat PLGD-1. It's called replacement therapy because it replaces the plasminogen that your body should be making on its own. The only replacement therapy that is available in the U.S. is a medicine called Ryplazim.
Maintenance Therapy	Maintenance means you are receiving replacement therapy on a regular schedule and your PLGD-1 symptoms are well-controlled.
Dose	A dose of replacement therapy is based upon your weight in kilograms times the amount of plasminogen recommended for each treatment (6.6 milligrams per kilogram). Each vial of plasminogen contains a certain amount of the factor. When calculating a dose, the entire contents of each vial should be used; never waste product to achieve an exact dose. It is acceptable to use plus or minus approximately 10% of each calculated dose.

Living with PLGD-1, Frequently Asked Questions: Levels & Lesions

Questions	Answers
How often should I check my plasminogen activity level or have a trough level?	**If you are in maintenance, have no lesions or symptoms, and are well:** – Check your trough level every 6 months. This will ensure that your treatment is appropriate. Your trough level data can be entered into a database. This database helps to predict the best dose of replacement therapy for you. Adding your data to this system helps others, too. The information in the database is based upon many people's data. Ask your physician about this system as they can enter your data for you. – **Growing children** need to have their trough level checked as their weight changes. The trough level should be checked and the dose changed based upon desired trough level, calculated dose and vial size. They may need dose changes as they grow. Since young children can grow very quickly, trough level checks and dose calculations should be checked more often. **You may need to check your trough levels or change your dose in these situations:** • **If you are an adult or teen and you lose or gain more than 10 kilograms (about 22 pounds)** • **If you develop any lesions or symptoms** • **If you need or want to change your dosing schedule. It takes time (about 5 half-lives of the replacement therapy; each dose has a half-life of about 2.2 days) to reach a new baseline or new trough level of plasminogen activity after a dose change.** **You will need to check your trough levels and change your dose more often if you:** – Are not in maintenance and are starting treatment for the first time. – Are not clinically stable (if your lesions are getting worse or you have new lesions)

Living with PLGD-1, Frequently Asked Questions: Levels & Lesions *(continued)*

Questions	Answers
Do I need medical tests to check for lesions?	Your hematologist should go over your current health and your medical history (this is called a review of systems). They should also perform a physical exam. **If your hematologist does not find anything concerning during the exam or review of systems:** – **You may not need more studies such as imaging or testing.** For example, your hematologist can listen carefully to your chest with their stethoscope to check for lung lesions. If you have no current symptoms or history of symptoms like a cough, wheezing or lung issues, this exam may take the place of a chest x-ray. It is important to limit your exposure to radiation and invasive procedures that could possibly create lesions. – You need to know how to recognize early signs and symptoms of problems caused by PLGD-1. Some signs and symptoms could be caused by PLGD-1 or by another, more common disorder. **WATCH OUT FOR THESE SYMPTOMS:** • **Chronic cough or wheezing. This is often thought to be asthma but could be from lesions in your airways.** • **Hoarse voice or cough: You may develop these as part of an upper respiratory infection but they may continue after an illness.** • **Chronic ear infections, failed hearing tests, or blocked ear tubes: These may be a sign of lesions in the ears.** • **Stomach upset, chronic reflux, or ulcers: These may be a sign of lesions in the gastrointestinal tract (such as in your esophagus, stomach, or small or large intestine).** **If you have symptoms or any of your review of systems are abnormal:** – **Your symptoms or abnormal areas should be checked (this includes things like chronic cough, repeated ear infections, blocked ear tubes, hoarse voice, or stomach symptoms).** Testing is based on symptoms. If you have symptoms that need to be checked out, your doctors should choose the least invasive method possible. – If you have lesions in certain organs, you may need radiology studies (this includes scans like CT, MRI, or ultrasound). These studies can help find the lesion location and size before starting therapy. This screening may not always be possible depending on where your lesions are.

Living with PLGD-1, Frequently Asked Questions: Surgery

Questions	Answers
How will my treatment change if I need surgery?	Your body uses more plasminogen during surgery and the healing process. You may need to change your dosing schedule when you have surgery. Your hematologist will create a plan for your plasminogen treatments around and after surgery. The plan may depend on whether you are in maintenance or not, and whether it is a major or a minor surgery. **MAJOR surgery includes:** • **Surgery on your brain or other parts of your central nervous system** • **Heart surgery** • **Orthopedic surgery (surgery on your bones)** • **Any surgery to your abdomen, like getting your appendix or gall bladder removed.** **MINOR surgery includes:** • **Getting tubes in your ears** • **Dental surgery** • **Eye surgery such as getting cataracts removed.** • **Biopsies (when a small amount of tissue is removed and tested) for example skin and colon but not areas that are more difficult to reach like your liver or brain.** • **Scopes such as upper endoscopy (looking at your esophagus and stomach with a flexible tube with a camera at the end) or colonoscopy (looking at your colon and large intestine with a flexible tube with a camera at the end).** **If you are in maintenance and your symptoms are well controlled, and are preparing to have surgery:** – **For MAJOR surgery your plan may include:** o A dose of Ryplazim right before surgery (Ryplazim is replacement therapy used by people with PLGD-1 who have symptoms). Using Ryplazim before surgery will ensure you have a good peak level during your procedure. o Your doctor may want your trough level to be higher while you are healing. If so, you may need replacement therapy more often during this period. o Your doctor may want you to check your plasminogen activity levels more often after your surgery to make sure your levels are high enough. o Once you've healed, you will slowly return to your normal maintenance schedule.

Living with PLGD-1, Frequently Asked Questions: Surgery (*continued*)

Questions	Answers
Continued: **How will my treatment change if I need surgery?**	**If you are in maintenance and your symptoms are well controlled, and are preparing to have surgery:** – **For MINOR surgery the plan may include:** o A few extra doses (right before or after), and then go back to your normal maintenance schedule. o For some minor surgeries, you may not need to do anything different. For example, let's say you are in maintenance, and you need a colonoscopy. You are not having any symptoms of PLGD-1 in your colon or large intestine. For something like this, it is likely okay to schedule the procedure soon after a regularly scheduled dose so you are near your peak level. o But, if you need a colonoscopy and have lesions in your colon or large intestine that will need to be biopsied, you might need a dose of replacement therapy right before the scope to prevent lesions from forming. You might also need a dose while you are healing. This should be coordinated with your hematologist. **If you are NOT in maintenance, or are having active symptoms, and are having surgery, your plan may include:** o A dose before surgery o More frequent dosing around the procedure, and during the time when you are healing. How often you receive a dose should be based on several things: ▪ How severe your symptoms are, ▪ Whether your surgery was major or minor, ▪ How long it will take for you to heal. o You may need to start regular replacement therapy. This will depend on your symptoms and your health. – Right now, we do not have enough data to say for certain what your trough level should be for any procedure. As we collect more data from people who take Ryplazim, this will help us develop guidelines for surgery. Until then, your hematologist should always be part of your surgery planning.

Living with PLGD-1, Frequently Asked Questions: Menstruation

Questions	Answers
What happens when I start my period? Do I need to adjust my dose?	**If you are currently in maintenance, and are clinically stable (your symptoms of PLGD-1 are well controlled):** – Keep a record of your period each month. Keep track of the following information: o How long your period lasts o How heavy your period is (how many pads or tampons you are using) o If you pass any lesions which look different than clots o Whether you are having any other symptoms like pain or cramping – Keeping track of this information can be hard at first. Your periods may not happen at regular times. You may sometimes have a month with no period at all. – See your gynecologist if you have any of these problems with your period. You should have a pelvic exam to look for lesions and make sure your tissue is healthy: o If your period is not happening at regular times (you are having a period more often than every 21 days, or less often than every 35 days). o If your period is very heavy (soaking 1 pad or tampon more than every 2 hours) o Any gushing/flooding or passage of clots greater than the size of a dime o You are having pain or cramps that you cannot control with over the counter pain medicine – Together, your gynecologist and hematologist will decide if you need to increase how often you take replacement therapy. You might also need medicine to stop your period for a time. This decision is based on the severity of your symptoms. **If you are NOT currently in maintenance:** – Keep a record of your period each month. Keep track of the following information: o How long your period lasts o How heavy your period is (how many pads or tampons you are using) o If you pass any lesions which look different than clots o Whether you are having any other symptoms like pain or cramping – Keeping track of this information can be hard at first. Your periods may not happen at regular times. You may sometimes have a month with no period at all.

Living with PLGD-1, Frequently Asked Questions: Menstruation
(continued)

Questions	Answers
Continued: **What happens when I start my period? Do I need to adjust my dose?**	– You should see your gynecologist once a year based on your age or as directed by your hematologist based on your symptoms. Your pelvic exam should look at your internal and external tissue to make sure it looks normal. It's important for every patient with PLGD-1 who has periods to keep careful records about their period and symptoms!
Do I need to start taking Ryplazim if I am not already?	**If you are NOT currently in maintenance:** – If your tissue looks normal, talk to your hematologist about whether you need to start plasminogen replacement therapy. o Some people with PLGD-1 will have normal periods and no visible lesions even if they are not on replacement therapy. o Some people may have lesions that may not be seen on a usual external and internal exam. These lesions may cause symptoms such as menstrual pain or excessive blood flow. These lesions may also make it difficult or impossible to become pregnant. Therefore, it is important to continue to track and report your symptoms. – If your pelvic exam is not normal, or you begin having symptoms or problems with your cycle (heavier bleeding, more pain with your period, pain with sexual intercourse), you will need to start replacement therapy. It's important for every patient with PLGD-1 who has periods to keep careful records about their periods and symptoms!

Living with PLGD-1, Frequently Asked Questions: Pregnancy

Questions	Answers
What happens to my treatment if I am pregnant? How should my treatment change during pregnancy and delivery?	Being pregnant can affect your plasminogen levels. You may need more replacement therapy while you're pregnant to support a safe pregnancy and delivery. **If you are currently in maintenance, and are clinically stable (your symptoms of PLGD-1 are well controlled):** – Your hematologist may choose a higher trough goal during your pregnancy. Remember, your trough level is your plasminogen activity right before your next scheduled dose of replacement therapy. You may need to receive your replacement therapy more often to raise your trough level. – Your hematologist will check your plasminogen activity levels during your pregnancy. You might need more frequent checks during your last trimester (the last 13 weeks of pregnancy). – Your hematologist and obstetrician (the doctor you see during pregnancy and who cares for you during your delivery) will make a schedule for your delivery and replacement therapy. **If you are NOT currently in maintenance:** – Some women can go through pregnancy and delivery without needing replacement therapy. Your hematologist will need to review your medical history. They will talk to you about whether you need replacement therapy to get pregnant or carry a baby to term. – You may need replacement therapy when you're pregnant even if you have not needed it before. This is an important discussion to have with your doctors.
Should patients with PLGD-1 wear a medical alert bracelet or carry any other kind of medical identification?	Yes! The PLGD Foundation created a wallet card that you and your hematologist can add your information to. You should always carry this card with you. You could also get this information engraved onto a medical ID bracelet. You should think about having a Medical Travel Letter with you when you travel. This letter will be helpful if you need medical care when you are away from your normal care team. You can find copies of the Wallet Card and Travel Letter in Appendix A.

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APPENDIX A: PLGD-1 Medical Card for Wallet + Travel Letter