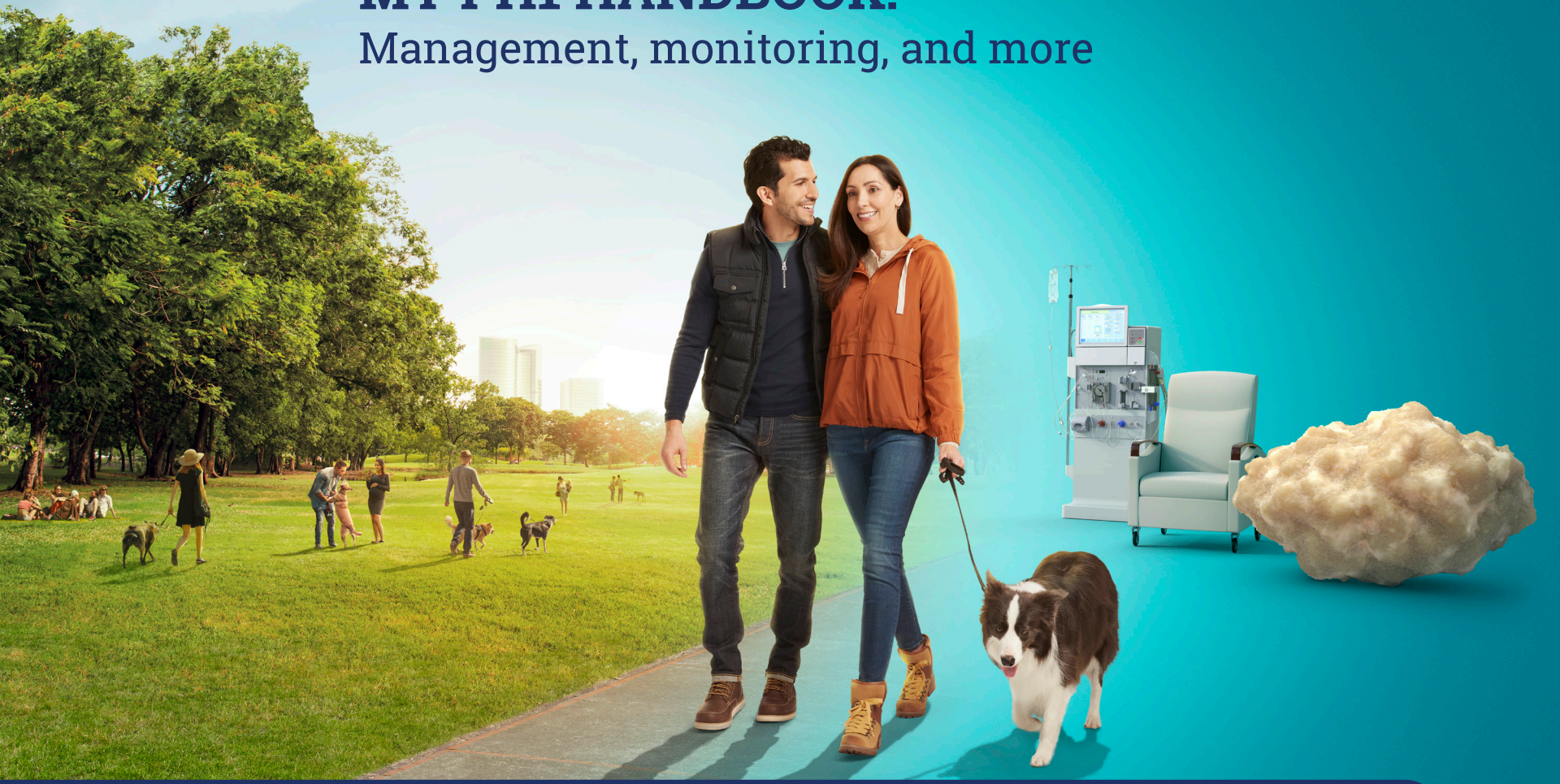
MY PH1 HANDBOOK:
Management, monitoring, and more



Welcome to a guide that includes information and tips for taking on primary hyperoxaluria type 1 (PH1) in your daily life

TAKE ON PH1™

NAME: _____

TABLE OF CONTENTS

Know your opponent: What is PH1?

Primary hyperoxaluria type 1 (PH1) is a rare, inherited disease that causes the **overproduction of oxalate.**

PRIMARY	HYPER OXAL URIA	TYPE 1
inherited	too much oxalate urine	a certain kind

A disease you are born with

that causes too much oxalate in the urine

and has different types. Type 1 is the most common and serious.

What is oxalate?

Oxalate is a waste product normally present in small amounts in the body. It cannot be further broken down or used by the body for anything, and it is primarily removed by the kidneys. **In PH1, the liver makes too much oxalate,** and the kidneys eventually can't keep up with removing it.

Too much oxalate can be a cause for concern

Oxalate overproduction can damage the kidneys and can affect your body's ability to filter waste from the blood. With or without symptoms, this damage is progressive, meaning it can be getting worse over time and cause permanent damage.

Because of the progressive nature of the disease, it's important that PH1 is diagnosed as early as possible, so that you can take proactive steps with your healthcare provider to manage your PH1.

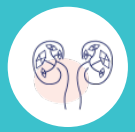
How does PH1 affect the body?

Kidney stones that form due to oxalate overproduction in the liver are the most common symptom of PH1.

Symptoms of kidney stones may include:

- Pain in the side of the body
- Painful and/or bloody urination
- Urinary tract infection

Other symptoms of PH1 may include:



- Crystal deposits in the kidneys, known as nephrocalcinosis

- Crystal deposits in other organs (systemic oxalosis), including the eyes, bones, skin, heart, and central nervous system

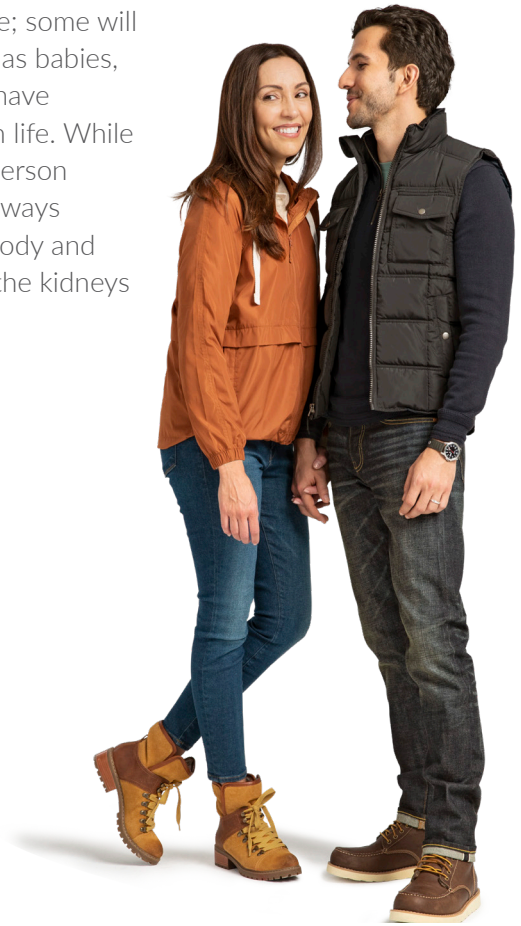
- Kidney failure

- Failure to thrive in babies

These are not all the possible symptoms of PH1.

Does everyone with PH1 have the same symptoms?

Patients with PH1 may experience different symptoms at different times in life; some will experience symptoms as babies, while others may not have symptoms until later in life. While symptoms vary from person to person, oxalate is always overproduced in the body and can cause damage to the kidneys and other organs.



PH1 is passed down through families

It is important that **family members, especially siblings of a person with PH1, consider having a conversation with a healthcare provider about getting tested for the disease with a genetic test.** If a healthcare provider decides genetic testing is right for an individual, one option is Alnylam Act®.

Alnylam Act®: One option for genetic testing and counseling

The Alnylam Act® program is available if you meet certain criteria.

The test is done using a blood, saliva, or buccal sample. Eligible siblings and family members may also be tested through Alnylam Act®.

The Alnylam Act® program was created to provide access to no-charge genetic testing and counseling to patients as a way to help people make more informed decisions about their health.

- While Alnylam provides financial support for this program, tests and services are performed by independent third parties
- Healthcare professionals must confirm that patients meet certain criteria to use the program
- Alnylam receives de-identified patient data from this program, but at no time does Alnylam receive patient-identifiable information. Alnylam may use healthcare professional contact information for research purposes
- Both genetic testing and genetic counseling are available in the US and Canada
- Healthcare professionals or patients who use this program have no obligation to recommend, purchase, order, prescribe, promote, administer, use, or support any Alnylam product
- No patients, healthcare professionals, or payers, including government payers, are billed for this program

For more information and program rules, download the Alnylam Act® Genetic Testing and Counseling Brochure for PH1. *AlnylamActPH1.com*

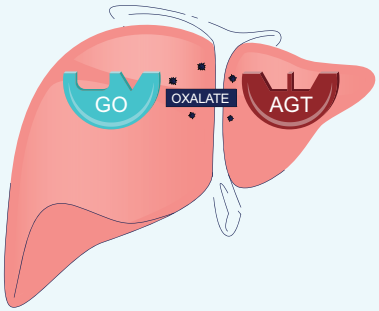
HAVE FAMILY MEMBERS BEEN GENETICALLY TESTED FOR PH1? ☐ Yes ☐ No

ADDITIONAL INFORMATION: *www.invitae.com/en/alnylam-act-hyperoxaluria-type-1*

PH1 causes the liver to make too much oxalate.

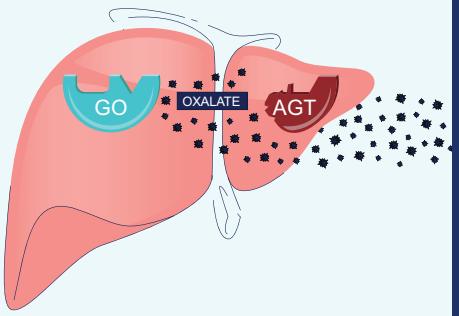
NORMAL PROCESS

GO and AGT enzymes in the liver work together to regulate levels of oxalate



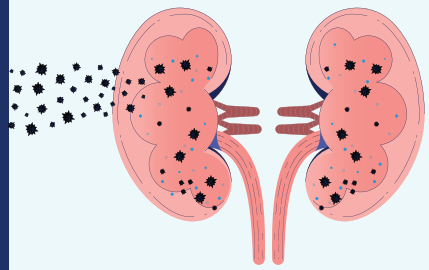
PH1 PROCESS

When AGT is broken, GO can cause problems leading to the overproduction of oxalate



PH1 PROCESS

With PH1, the body makes more oxalate than usual and the kidneys can't keep up with the amount being produced. This causes continuous damage and can get worse over time

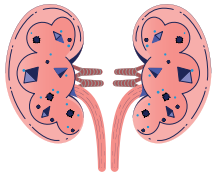


GO enzyme: glycolate oxidase enzyme
AGT enzyme: alanine:glyoxylate aminotransferase enzyme

PH1 is considered a disease of oxalate overproduction, so oxalate levels are one of the things your healthcare provider likely tracks.

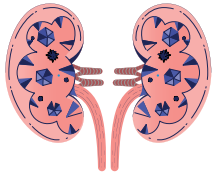
The kidneys fight to get rid of oxalate, but it can still build up.

In PH1, there can be too much oxalate, and the kidneys can't get rid of it all, causing the symptoms of the disease.



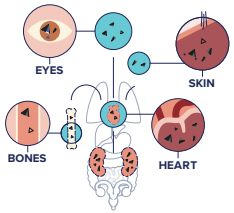
Oxalate forms into crystals in the kidneys

Once in the kidneys, oxalate combines with calcium in urine. When oxalate and calcium combine, crystals are formed. Over time, more and more crystals are made that get trapped in the kidneys.



Oxalate crystals cause damage to the kidneys

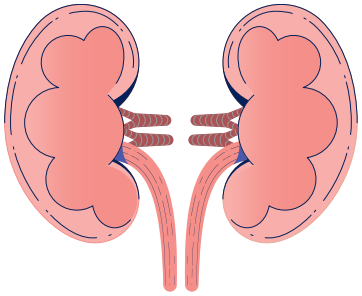
Crystals can clump together to create hard masses (kidney stones), or they can be deposited in the kidneys themselves (nephrocalcinosis).



PH1 tends to worsen over time

The buildup of crystals in the kidneys can lead to chronic kidney disease (CKD) or even kidney failure.

As kidney function worsens, the kidneys are no longer able to remove oxalate properly, and it starts to spread and cause damage elsewhere—a process called "systemic oxalosis."



Symptoms of Kidney Failure:

- Producing less urine
- Nausea or vomiting
- Pale skin color
- Swelling of the hands and feet
- Fatigue and weakness

These are not all the symptoms of kidney failure. Patients experiencing these symptoms should see a doctor immediately.

People with PH1 should strive to keep up with the management plan they have developed with their healthcare provider.

Making a game plan to manage your condition.

Your doctor will work with you to develop a management plan tailored to your symptoms.

The goal: help slow progression

As part of your management plan, your healthcare provider may measure different things, including your **oxalate levels** (how much oxalate is in your urine and/or blood) and your **kidney function** (how well your kidneys are able to filter waste products).

Your healthcare provider may recommend that you use **multiple PH1 management options at the same time.** Your doctor's recommendations may shift or change over time, depending on how your disease is progressing.

PH1 management options your healthcare provider may recommend

- Lifestyle changes
- Hyperhydration (drinking a lot of water)
- Prescription medications (RNAi therapies)
  - These work by reducing the amount of oxalate that your body is producing

- Supplements (such as alkali citrate or vitamin B6)
  - These work by reducing the formation of oxalate crystals
- Dialysis (to help remove oxalate from your body when your kidneys are no longer able to do it on their own)

- Surgery (including transplantation)

Your doctor can help you understand which management options are best for you.

Patients with PH1 should always talk to their doctor before making changes to their disease management plan.

> *We feel like it's been really important to her health to be consistent with her diet, to be consistent with her medications, and to be consistent with her hydration.*

DAN W.
DAD OF A CHILD WITH PH1

It takes a team to take on PH1.

PH1 requires lifelong management and monitoring. Since PH1 is a personal experience and affects everyone differently, your doctors and healthcare team will help you approach the different aspects that managing PH1 can involve and work with you to create a personalized plan. Because your care plan is based on how your disease is progressing, it is important that you attend all appointments with the various members of your healthcare team. You can use this page to help keep track of their names and their contact info.

The extended healthcare team in your corner

These are some of the specialists you may meet in your journey with PH1.

NEPHROLOGIST A physician who specializes in diagnosing and treating kidney conditions.	**UROLOGIST** A surgeon who specializes in disorders of the urinary tract and often addresses kidney stones in patients with PH1.
GENETIC COUNSELOR A specialist who can answer questions you might have about genetic testing and interpret your results.	**PRIMARY CARE DOCTOR** A doctor who acts as the main healthcare point of contact for all of a patient's basic medical needs.
DIALYSIS NURSE A nurse who oversees the process of dialysis, a life-saving procedure for patients with end-stage kidney disease.	**RADIOLOGY TEAM** Medical doctors that specialize in diagnosing and treating injuries and diseases using medical imaging and tests.
TRANSPLANT TEAM A large team that is specially trained in meeting the needs of kidney transplant patients and caring for them throughout the process.	**NUTRITIONIST** An expert who coaches you through diet and lifestyle choices to manage various conditions and improve overall health.

It takes a team to take on PH1.

You will have your own healthcare team on your PH1 journey. It can be helpful to keep their names and contact information in one place so you can easily access them.

As you are working with your healthcare team, friends and family may also be able to provide invaluable emotional and practical support.

The extended healthcare team in your corner

Write down the names and information of the members of your care team.

NEPHROLOGIST

NAME: _____

CONTACT INFO: _____

UROLOGIST

NAME: _____

CONTACT INFO: _____

GENETIC COUNSELOR

NAME: _____

CONTACT INFO: _____

PRIMARY CARE DOCTOR

NAME: _____

CONTACT INFO: _____

DIALYSIS NURSE

NAME: _____

CONTACT INFO: _____

RADIOLOGY TEAM

NAME: _____

CONTACT INFO: _____

TRANSPLANT TEAM

NAME: _____

CONTACT INFO: _____

NUTRITIONIST

NAME: _____

CONTACT INFO: _____

Taking control of your PH1 management plan.

It can be challenging to manage PH1—from potentially taking multiple medications to drinking substantial amounts of water to attending frequent dialysis sessions. However, there are techniques you can try to help you feel more in control when managing PH1 seems overwhelming. **Just remember to always discuss your management plan with your healthcare provider before making any changes to your routine.**

> *My advice would be to just keep moving forward, to accept the support that so many people want to give you.*

PAT C.
MOM OF AN ADULT WITH PH1

Tips for drinking enough water

If hydration is part of your management plan, it's essential to be aware of situations that can make you dehydrated, such as sickness (as with diarrhea, vomiting, or fever), intense physical activity, and not drinking enough water.

You should always talk to your doctor before making changes to your disease management plan.

Getting others involved in helping you manage your PH1 can help you feel supported and motivated to take on your disease.

Taking control of your PH1 management plan.

Check off all of the things you are currently doing or would like to do:

PREPARATION

- ☐ Make sure you always have plenty of water available by keeping bottles filled up around the house, in your car, and in all your bags
  Where else do you often go where you can store water bottles?
- ☐ Bring water with you when going to a new place
  Can you create a list of things you need to bring before you go out?

REMINDERS

- ☐ Set alarms on your phone to remind yourself to drink water
  Can you make it fun or set the alarm to a sound you like?
- ☐ Set deadlines for yourself to drink a certain amount by a particular time
  How can you reward yourself when you meet your goals?

GET CREATIVE

BRAINSTORM WITH YOUR HEALTHCARE TEAM*

- ☐ Eat foods with high water content, especially fruits and vegetables
  What are some other ways you can drink more water?
- ☐ Though drinking water is the preferred way to stay hyperhydrated, you can ask your healthcare team about including other fluids like milk and orange juice
  List some of your favorite beverages and check their water content

*Dietary changes should always be discussed with your doctor.

Your journey with PH1.

Although consistent management may help some people, other people with PH1 may experience continued disease progression; dialysis and/or transplant surgery may eventually be necessary.

- Continuous buildup of oxalate can lead to rapid and unpredictable disease progression and decline in kidney function
  - In some cases, a single incident of dehydration has led to kidney function decline, including in people with previously stable disease
  - Your doctor can help you understand which management options are best for you

Dialysis

- If the kidneys become damaged, dialysis may be needed to remove oxalate and other waste products from the blood
- Monitoring oxalate levels in your blood may help determine the frequency and length of your dialysis sessions; however, oxalate may continue to build up throughout your body over time. Your doctor may individualize your dialysis regimen based on your oxalate levels
- It is important to stick to a management plan as discussed with your doctor

Transplant

- Oxalate overproduction can cause permanent damage, and transplant surgery may eventually be necessary
- Although PH1 primarily damages the kidneys, it originates in the liver, and patients may need a liver and kidney transplant to stop the overproduction of oxalate and replace the damaged kidney. A transplant is a surgical procedure in which a damaged or nonfunctioning organ is replaced with a healthy one
- A liver transplant from a donor without PH1 is a cure, but transplants are major surgeries that require long-term follow-up and life-long medications. Talk to your healthcare provider to understand if transplant surgery is a treatment option for you

It's more than caring for your kidneys—it's caring for yourself, too.

Navigating your overall health is important as you continue to take on PH1.

Nutrition

You should talk to your healthcare team to discuss the most appropriate nutrition plan. People with PH1 can usually have a standard diet while managing PH1. Strictly avoiding foods high in oxalate is not typically necessary in PH1.

> *We're doing all we can to preserve her kidneys and do things that help to keep them going and not damaged. So, drinking water, eating the right diet, taking her medicine routinely and not forgetting.*

LAURA W.
MOM OF A CHILD WITH PH1

Mental health

For people with PH1, being unable to recognize when you're experiencing symptoms of kidney disease can make you feel as if you are not in control. It's been shown that in people with kidney disease, the outlook on their disease can cause symptoms of anxiety and depression. **Consider speaking to a mental health professional if you feel like you need extra support.**

If you are already working with a mental health professional, you can use the space below to write down their name and contact information.

MENTAL HEALTH PROFESSIONAL:

CONTACT INFO:

Keeping your body and mind healthy and strong can help you take on PH1.

Expand your circle of support.

Healthcare providers, independent advocacy groups, and other people living with PH1 can be great resources for additional tips and guidance. Below are some resources that are just a search away.

TakeOnPH1.com
An educational website, brought to you by Alnylam, that includes real patient stories, videos, tips, and downloadable resources for anyone looking to learn more about PH1 and living with PH1.

The Oxalosis & Hyperoxaluria Foundation (OHF)
www.ohf.org
The OHF is an independent advocacy group dedicated to finding treatments and a cure for all forms of hyperoxaluria, and it supports thousands of healthcare professionals, patients, and their families.

American Kidney Fund (AKF)
www.kidneyfund.org
AKF works on behalf of the 37 million Americans living with kidney disease and millions more at risk, providing resources that support people in their fight against kidney disease, including rare diseases such as PH1.

National Kidney Foundation (NKF)
www.kidney.org
The NKF works to prevent kidney and urinary tract diseases in the United States, focusing its mission on organ donation advocacy and patient and caregiver support.

National Organization for Rare Disorders (NORD)
www.rarediseases.org
NORD works to improve the health and well-being of people living with rare diseases, offering its growing Rare Disease Database and patient assistance programs to help with access and caregiver support.

Global Genes
www.globalgenes.org
Global Genes works to eliminate the burdens and challenges of rare diseases for patients and families globally.

National Center for Advancing Translational Sciences
https://rarediseases.info.nih.gov/diseases/2835/primary-hyperoxaluria-type-1

National Institute of Diabetes and Digestive and Kidney Diseases
https://www.niddk.nih.gov/

TAKE ON PH1™

With the right information, support, and mindset, you can feel motivated to **get ahead of your PH1**.

Alnylam® PHARMACEUTICALS