Alone we are Rare, Together we are Mighty

# Itching for a Cure

## Progressive Familial Intrahepatic Cholestasis
## Global Outreach Initiative

Translated materials can be requested in these languages from our website, https://www.pfic.org/hospital-outreach-form/

| | | |
|---|---|---|
| Arabic | Hungarian | Portuguese (Brazil) |
| Dutch | Italian | Portuguese |
| English | Japanese | (Europe) Slovenian |
| French (Europe) | Kurdish | Spanish |
| French (Canada) | Malayalam | Swedish |
| German | Mandarin | Turkish |
| Hindi | Polish | Urdu |

*The mission* of the PFIC Network is to improve the lives of patients and families worldwide affected by PFIC. We support research programs, provide educational materials, match families for peer support and participate in advocacy opportunities.

Created by Emily Ventura
PFIC Network, Inc.
a 501c3 charitable organization, USA
EIN 83-1084501.
www.pfic.org.

Created February 19, 2021
Updated August 7, 2021
Updated September 22, 2022

# Patient & Provider

## Outreach Program

Hello PFIC Providers, Nurses and Ancillary Services.

You are receiving this letter because your hospital may diagnose and treat patients with Progressive Familial Intrahepatic Cholestasis (PFIC).

We are the PFIC Advocacy and Resource Network (PFIC Network for short), a 501c3 charitable organization based in the United States and connected to patients and their families worldwide. Our mission is to enrich the lives of PFIC patients and families by supporting research programs, providing educational materials, matching families for peer support and by participating in advocacy opportunities. Our organization was founded by parents of pediatric PFIC patients. We have all experienced the ups and downs of this disease and are committed to being change agents for our small medical community. Together, we work alongside a team of very passionate and dedicated PFIC parents and patients from all over the world who are working hard to make our rare patient community feel connected, and not so rare.

We need your help. When our children were diagnosed, it took years before we connected with other parents or anyone who understood what it was like to live with and care for someone with this rare disease. Those years without connection were isolating and filled with sadness and hopelessness. We know that you have likely seen the same feelings among your patients, and many times you are left with few resources to provide. Now, with the development of our Network and patient community, paired with your help in sharing our information (brochures, web address, and contact information), will help to end the isolation many families feel early on in their PFIC diagnosis.

The day we found a community of families, our lives and outlooks changed, knowing we are not alone. Today, there are over 500 people to connect with who understand this PFIC life. These families are a wealth of knowledge and insight, and a tremendous source of peer support—many of these families from various parts of the world have stepped up to serve as mentors to others! Our team of patient and caregiver advocates have been working hard to develop resources for PFIC families to help make a difference in their quality of life.

PFIC Awareness Day is October 5, every year. This tradition started in 2019 and has been a popular effort. This year our PFIC Awareness Day hashtag and slogan is **#itchingforacure**. The slogan was developed and voted on by our patient community. As we come together as a community to support those who itch, we will plant seeds that will leave an impact for years to come. This welcome letter is a seed we hope to plant to grow support in the patient community. Please join us in our effort and share our toolkit with your PFIC patients and families.

Warm Regards,
Emily Ventura
Executive Director of the PFIC Network, Inc.

# In your Hospital Awareness Toolkit

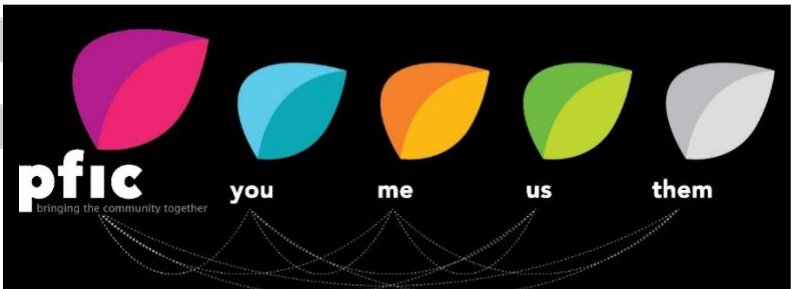
## This toolkit contains:

- Welcome to the community letter, for patients
- Care Package request form for patients & families
- PFIC Network Brochure (digital file available on our website)
- PFIC Educational Brochure (digital file available on our website)
- Information about the PFIC Patient Registry

## Programs for Your Patients

- PFIC Financial Assistance Program
- Care Package Program
- Community Engagement Program
- PFIC PALS: Kids Club
- Bereavement Program
- Mental Health Support for PFIC patients & families

**Translated materials available upon request.**
**For more information about our programs and to apply: visit www.pfic.org**



Dear PFIC family,

If you are reading this letter, you or your loved one has received a diagnosis of Progressive Familial Intrahepatic Cholestasis (PFIC). You may be feeling sad, confused, alone, angry, or worried. We know because we felt those things too, when we received a PFIC diagnosis for our children.

Today we share this letter with you to tell you: **you are not alone**.

There is a community of support—patients and caregivers—from all parts of the world, who get it. They get the struggle, the uncertainty, the itch, the disease, and even in many cases…the triumphs (even though those feel impossible to imagine right now). This community gets it because they live it and are ready and willing to support you.

There may not be a whole lot of answers right now. But please know, your hospital team is by your side, and will work hard to find you the best treatment options that they can and help guide you in the direction to make the best, most educated, decisions they can to improve your quality of life.

Our patient and caregiver community, the PFIC Network, Inc. is here to help. Check us out at www.pfic.org. The website was created specifically for PFIC families, by PFIC families. Take a look at "Resources for Families" under the "Connect & Support" tab to find ways to connect with others who will understand your journey. You will also find information about PFIC on the website, created with the help of PFIC specialists from all over the world, who want to help you learn and understand the diagnosis.

Contact us, connect with us, read about us, join us; whatever you need to do to help get through this process. We are here for you.

**Though we may be rare, we are mighty**. And together, we will fight this.

With Hope,

Emily, Melanie & Tara
Co-Founders
PFIC Network, Inc.


# Patient Information Resource

#PFICawareness #itchingforacure

**Progressive Familial Intrahepatic Cholestasis Advocacy and Resource Network, Inc.**

pfic
Advocacy & Resource Network, Inc.

# Progressive Familial Intrahepatic Cholestasis (PFIC) is a general term that represents a group of rare genetic disorders that cause a progressive liver disease and can lead to cirrhosis and end-stage liver disease. So what happens next?

Much like artists set up brushes and canvases as they begin creating beautiful works of art, this was created as a first step in familiarizing what a PFIC diagnosis means for you.

Think of this as a road map in understanding the PFIC diagnosis and terminology. This is a starting point between you and a strong support network.

## What Does PFIC Mean?

Progressive: getting worse over time
Familial: related to change in genes
Intrahepatic: disease inside the liver
Cholestasis: poor bile flow

It is important to follow up and stay in contact with your provider and specialist. Close monitoring by a Liver Specialist is an important part of achieving the best quality of life for the PFIC patient.

## What to Expect

### Diagnostic Testing

- Blood Tests: Liver enzymes, GGT and bile acid tests can be useful in identifying PFIC
- Genetic Testing: can be done with a blood sample and involves extracting code from DNA
- Liver Biopsy: a small piece of liver tissue is extracted and then examined under a microscope

## Possible Manifestations

### Symptoms of Cholestasis

- Itching
- Jaundice (yellow of skin or eyes)
- Swollen abdomen
- Yellow or brown urine
- Acholic stools (stools that are pale, grey or white)
- Bleeding or easy bruising
- Poor growth
- Vitamin deficiencies

### Symptoms Related to Vitamin Deficiencies:

- Vitamin A: can lead to problems with vision
- Vitamin D: can lead to poor bone formation and an increased risk of broken bones
- Vitamin E: can lead to problems with balance, strength and coordination
- Vitamin K: can lead to bleeding problems, which can be very dangerous especially if bleeding occurs in the brain

### Features of More Advanced Liver Disease

PFIC can progress to liver failure. If left untreated or unmanaged, liver failure may happen sooner. It is important to understand the difference between signs of cholestasis and signs of advanced liver disease.

- Bruising related to low platelet counts
- Ascites (fluid in the abdomen)
- Esophageal varices (enlarged veins that may bleed)
- Enlarged spleen
- Portal hypertension (high blood pressure in the veins leading to the liver)

### Possible Blood Test Findings with Cholestatic Liver Disease

- Elevated liver enzymes (AST, ALT, Alk Phos)
- Elevated bile acids
- Elevated bilirubin
- Decreased vitamin levels A,D and E
- Increased PT/INR (due to decreased vitamin K)

## Treatment

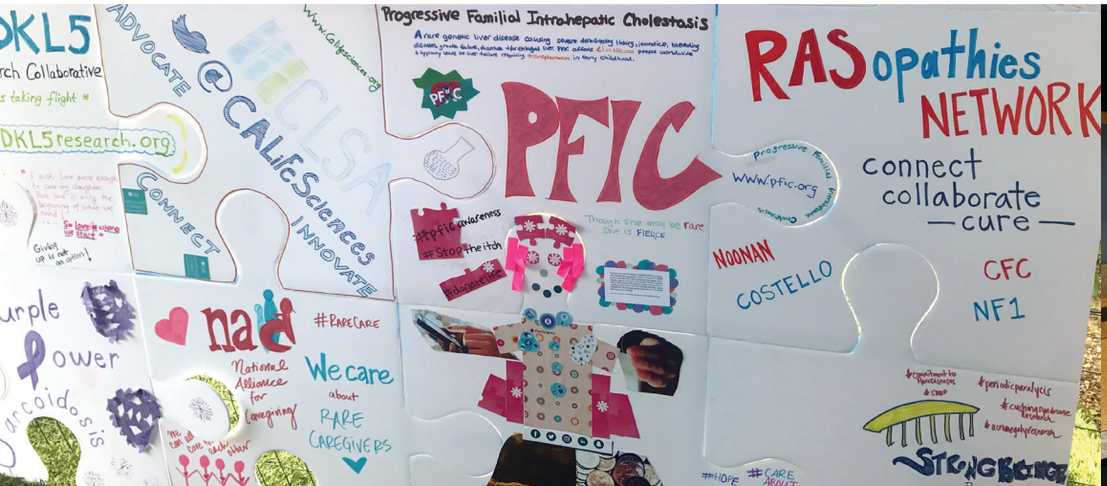
- Close monitoring of blood tests, liver ultrasound and frequent appointments with your hepatologists
- Using medications is the first line of defense, but if insufficient surgery may be necessary
- Surgical options aim to keep bile acids from entering the liver. They may include:
  - » Partial External Biliary Diversion
  - » Partial Internal Biliary Diversion
  - » Ileal Exclusion
- Liver Transplant may be necessary if medical and surgical options do not work

## Understanding PFIC

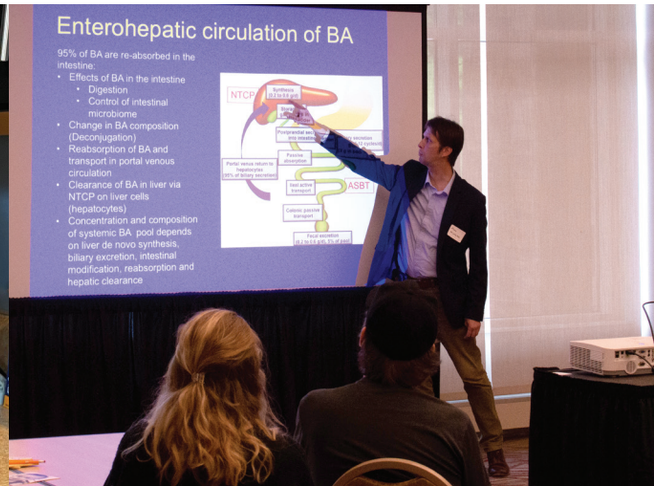
*General symptoms and considerations for PFIC apply to all of the subtypes on this table. This table is intended to highlight some of the potential differences in each diagnosis. Please note, the course of PFIC can be variable and unique, not all patients will experience the disease as it is outlined.*

| Common Name | Protein Deficiency | Mutated Gene | Pruritus (itch) | Other Potential Manifestations | GGT Cholestasis | Potential Clinical Outcomes, Treatment and Complications of Treatment |
|---|---|---|---|---|---|---|
| **PFIC 1** | FIC1 | *ATP8B1* | Intense | • Extrahepatic Symptoms<br>• Diarrhea<br>• May have pancreatitis<br>• May have cough, wheezing<br>• May have hearing loss | Normal GGT Cholestasis | • Moderate rate of progression<br>• Can lead to cirrhosis and end stage liver disease typically in the second or third decade of life<br>• Post-transplant hepatic steatosis (fatty change) and diarrhea<br>• Extrahepatic symptoms can worsen and new ones can develop after liver transplant<br>• BRIC presentations have been recorded* |
| **PFIC 2** | BSEP | *ABCB11* | Intense | • Potential for developing heptocellular carcinoma and cholangiocarcinoma (liver cancer)<br>• Gallstones | Normal GGT Cholestasis | • Moderate to rapid progression<br>• Success of surgical biliary diversion may depend on the specific genetic defects<br>• Liver transplant in PFIC 2 patients may lead to antibody induced BSEP deficiency in some<br>• Potential for retransplant<br>• BRIC presentations have been recorded* |
| **PFIC 3** | MDR3 | *ABCB4* | Mild to moderate | • Reduced bone density<br>• Potential for developing hepato-cellular carcinoma and cholan-giocarcinoma (liver cancer)<br>• Gallstones | Elevated GGT Cholestasis | • Highly variable rate of progression<br>• Medical management: those retaining MDR3 expression respond better to ursodiol<br>• Biliary diversion may not be as effective as in other forms of disease<br>• Liver transplant is curative<br>• BRIC presentations have been recorded* |

*(BRIC) Benign Recurrent Intrahepatic Cholestasis is a transient presentation of a known or unknown subtype of PFIC.












PFIC Subtypes

**I've been diagnosed with PFIC, but they can't tell me what type?** Genetic studies are underway to try to identify genetic factors contributing to PFIC when mutations are not found in any of the below listed genes. Identifications of these genes is very complicated and require state-of-the-art genetic investigations. Doctors and scientists are working on finding more answers for these patients.

**New genes have been identified.** Some of these new genes do not appear on this version of the table, namely *LSR* and *PLECTIN*.





PFIC Subtypes

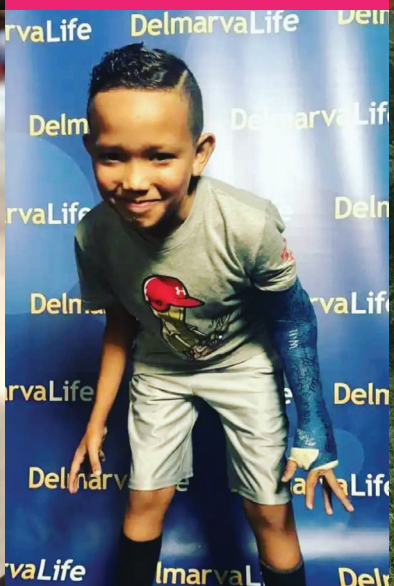
| Common Name | Protein Deficiency | Mutated Gene | Pruritus (itch) | Other Potential Manifestations | GGT Cholestasis | Potential clinical Outcomes, Treatment and Complications of Treatment |
|---|---|---|---|---|---|---|
| *The following subtypes are exceedingly rare in the reported literature (although being recognized more).* | | | | *This information is based on only a handful of patients in each group and should be viewed with that in mind.* | | |
| **PFIC 4** | TJP2 | *TJP2* | Unclear/variable | • Hearing loss<br>• Neurological Symptoms<br>• Respiratory Symptoms | Normal GGT Cholestasis | • Moderate to rapid progression<br>• Some reports of hepatocellular carcinoma |
| **PFIC 5** | FXR | *NR1H4* | Unclear/variable | • Vitamin K independent coagulopathy<br>• Can mimic BSEP deficiency | Normal GGT Cholestasis | • Very rapid progression<br>• Post-transplant hepatic steatosis<br>• Very rare (Only eight cases reported as of December, 2020). |
| **PFIC Associated with MYO5B defects** | MYO5B | *MYO5B* | Mild to moderate | • Potential for congenital diarrhea | Normal GGT Cholestasis | • Slow progression<br>• MicroVillus Inclusion Disease (MVID) can be experienced<br>• Lifelong TPN with associated MVID<br>• Combined bowel liver transplants may prevent post transplant cholestasis |
| | USP53 | *USP53* | Mild to moderate | • Hearing loss<br>• Heart failure reported in one patient | Normal GGT Cholestasis | • Slow progression<br>• Age of onset is variable<br>• Continued follow-up is needed for all patients<br>• First published in seven patients, in September, 2020 |
| | MRP9 | *ABCC12* | Intense | • Intrahepatic bile duct paucity | Normal GGT Cholestasis | • Slow progression<br>• Uncertainty whether PFIC occurs with (one) heterozygous mutation in ABCC12<br>• Only one case published as of March, 2021 |

**PFIC Definition of Terms**

**ALT and AST:** Markers of liver injury.
**Antibody Induced BSEP Deficiency (AIBD):** cholestasis that can develop after transplant in some PFIC 2 patients related to the development of BSEP antibodies.
**Autosome:** Any chromosome that is not a sex chromosome.
**Benign Recurrent Intrahepatic Cholestasis (BRIC):** Is a transient presentation of a known or unknown subtype of PFIC.
**Bile:** Bile is a yellow fluid that contains a number of compounds including bile acids, phospholipids, cholesterol and waste products from the body.
**Bile Acid/Bile Salt:** Bile acids are chemicals made by the liver from cholesterol. In a healthy individual bile acids are transported from the liver to the intestines where they help to absorb fats, fat soluble vitamins and other fat-soluble nutrients. They are then circulated back to the liver such that they can be reused.
**Cholestasis:** Means poor bile flow and build-up of substances in the liver that would normally be carried out of the liver into bile and then the intestines.
**Cholestatic Pruritus:** Is the sensation of itch due to liver disease.
**Chromosome:** Chromosomes are large molecules that mainly consist of DNA.
**Dominant:** Dominant disorders are a single defective copy of a gene that can lead to disease. The impact of that defective copy is dominant over the other copy which is healthy.
**Familial:** Originally described in families and related to changes in genes.
**Gamma GT (GGT):** A type of liver enzyme which may help to distinguish between the types of PFIC.
**Genes:** Genes are short parts of a chromosome that contain the genetic code for heritable characteristics. Some characteristics such as height are influenced by many genes, and some just by one single gene. Humans have two copies for most genes including those associated with PFIC.
**Hepatic Steatosis:** Fatty change in the liver.
**Hepatocytes:** Liver cells, responsible for making bile.
**Hepatologist:** A doctor who specializes in liver disease.
**Icterus:** Yellowing of the skin, mouth, tongue, etc.
**Intrahepatic:** Involves disease inside the liver.
**Jaundice:** Yellowing of skin.
**Liver:** The Liver is the largest solid organ in the body. It plays an essential role in many different body functions, such as removing toxic substances from the blood, or producing proteins and bio-chemicals (bile) that are necessary for digestion and growth.
**Microvillus Inclusion Disease:** A disease caused by structural changes in the small bowel usually, but not always, causing severe diarrhea.
**Mutations:** A change in the genetic code.
**Offspring:** A person's child or children.
**Progressive:** Tending to get worse over time.
**Recessive:** Two abnormal copies of a gene to have disease.
**Scleral Incterus:** Yellowing of the eyes.

**pfic.org**

#PFICawareness
#itchingforacure




The PFIC Network is a 501c3 charitable organization based in the United States, EIN 83-1084501. We are connected to patients and families around the world.

We kindly thank our donors, sponsors and partners for their generous support. For more information on our organization, our programs, our community and how to get involved, please visit **pfic.org**.


## Our Mission

PFIC Network's mission is to improve the lives of patients and families worldwide affected by Progressive Familial Intrahepatic Cholestasis (PFIC).

**What is PFIC?**

Progressive Familial Intrahepatic Cholestasis (PFIC) is a group of rare genetic disorders that is estimated to affect one in 50,000 to 100,000 people worldwide. PFIC causes progressive liver disease, which typically leads to liver failure. The disease typically manifests itself in the first year of life and may present with jaundice, irritability, growth failure, diarrhea, bleeding disorders, and/or enlarged liver. The hallmark feature of this disorder is severe debilitating pruritus (itching).

# PFIC Advocacy & Resource Network, Inc.

#PFICawareness


**pfic.org**

**#pficawareness #Itchingforacure**

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# Connecting the Dots Between Patients and Healthcare

### Programs to Provide Support, Education and Resources

Develop and equip as many patients as possible around the world with educational and support resources that are needed to better manage life with PFIC.

- **» Education**
  - Website (pfic.org)
  - PFIC Educational Brochure
  - Educational Webinars
  - Healthcare Provider Outreach Program
- **» Resources for Patients & Caregivers**
  - Mental Health Support Group
  - Financial Assistance Program
  - Bereavement Support
  - Translation and Interpretation Services
- **» Peer Support**
  - Mentorship Program for both patients and parents
  - PFIC Care Package Program
  - Kids Club

### Programs to Support Community Connection and Advocacy

Bringing the community together to make our voice heard. Identifying regional resource gaps and working together to create solutions.

- **» Community Engagement Programs**
  - Community Advisory Council
  - PFIC International Alliance
  - International Research and Registry Review Committee
- **» PFIC Advocacy Program**
  - Conference Participation
  - Engage with local, state and national policy makers and regulators to promote advancement of PFIC research and treatment options.
- **» PFIC Awareness Day: October 5, every year!**

### Activities to Support Research

Identify and address current gaps in knowledge and care through global outreach activities and collaborative research. Address patient priorities in research.

- **» PFIC Patient Registry**
- **» Research Grant Program**
- **» Family & Scientific Conference**

# Our Leadership Team

**Emily Ventura**
Executive Director, Co-Founder
Kentucky, USA | emily@pfic.org

**Walter Perez**
Board President
Alberta, Canada | walter@pfic.org

**Tara Kearns**
Board Vice President, Co-Founder
Maryland, USA | tara@pfic.org

**Hayley Watts**
Board Treasurer
Kentucky, USA | hayley@pfic.org

**Erin Hovey**
Board Secretary
Pennsylvania, USA

**Charmaine Gravener**
Board Director
New Jersey, USA

## Medical Advisory Board

**Dr. Richard Thompson, M.D.**
Kings College, London

**Dr. Ben Shneider, M.D.**
Texas Children's Hospital, USA

**Dr. James Squires M.D., M.S.**
Children's Hospital of Philadelphia, USA

**Dr. Laura Bull, Ph.D.**
University of California, San Fransisco, USA

**Dr. Ronald Sokol, M.D., FAASLD**
Children's Hospital Colorado, USA

**Dr. Henkjan Verkade, M.D., Ph.D.**
University of Groningen, Netherlands

**Dr. Pramod Mistry, MBBS, Ph.D., M.A., M.D.**
Yale Medicine, USA

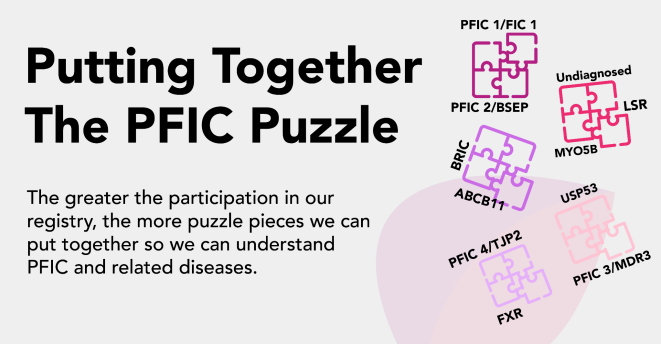
pfic Advocacy & Resource Network, Inc.

## What is the PFIC Network Patient Registry?

The PFIC Network Patient Registry is a secure data collection where patients or their caretakers provide information about their experience with the disease. The information provided is essential for furthering research efforts for better care of PFIC patients and families. All those diagnosed with PFIC are encouraged to participate. Parents can join the registry to enroll their child.

The patient registry collects information about:

- Diagnosis
- Itch
- Quality of life
- Medications
- Surgeries
- Sleep Quality
- General Health
- Patient demographics




## Why is it important?

The patient registry addresses the difficulty of locating PFIC patients and PFIC data to conduct research on our rare disease. Our aim with the patient registry is to add the patient's voice to every facet of PFIC research and to facilitate development of better treatments and a cure.

The purpose of the registry is to:

- Track PFIC disease status and symptoms
- Assist in clinical trial recruitment
- Allow patient participation at each level of research

The PFIC Network can work with registry information to identify knowledge and resource gaps so that we can work on creating solutions for the global patient community. The registry is vital in our search for a cure, because PFIC is rare and poorly understood. As more PFIC patients participate in the registry, researchers can conduct larger clinical trials for PFIC disease and symptom treatments, and eventually discover a cure.


## Learn More and Connect

Learn more and connect. We will help patients and caregivers get registered. Email melissa@pfic.org.

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# CARE PACKAGE PROGRAM

Free care packages are sent by PFIC Network to patients or caregivers who may be struggling with a new diagnosis, extended hospital stay or itching.

We welcome requests from providers on behalf of their PFIC patients who could use a pick-me-up.

*There is an option to remain anonymous to the recipient.*

## Please visit our website to make a request!

https://www.pfic.org/care-package-program/

# Global Ambassador Network

## Countries with a Charitable Organization

USA

Italy

## Countries with PFIC Leadership

Australia

Canada

Germany

Poland

Pakistan

## Countries with Ambassador Representation

India
Iraq
Netherlands
Colombia
Turkey
United Kingdom