Amicus Therapeutics has developed this educational resource in collaboration with the rare disease community and thought leaders.

INFORMATION FOR PEOPLE LIVING WITH POMPE DISEASE
What is Pompe disease?
(Please note some words that may be unfamiliar are highlighted and are defined in the glossary at the end of this brochure)

Pompe disease is a rare neuromuscular disorder. It is a serious genetic disorder that is inherited from both parents in what is called an autosomal recessive pattern. Other names are sometimes used for Pompe disease, including acid maltase deficiency and glycogen storage disease type II. It is a type of condition known as a glycogen storage disease, and is also part of a larger group of conditions called lysosomal disorders. There are 2 main types of Pompe disease: infantile-onset and late-onset. The infantile-onset type of Pompe disease begins during the first year of life and has a classic form and a nonclassic (less severe) form. Late-onset Pompe disease appears later in childhood or during adulthood. Usually, the earlier the signs and symptoms of Pompe disease appear, the more quickly they get worse and the more severe they may eventually become. Sometimes it’s difficult for doctors to diagnose Pompe disease, since many of its symptoms can be mistaken for those of other neuromuscular disorders.

How does Pompe disease affect families?

People have two copies of most of the genes in their cells. One of these copies is inherited from their father and one from their mother. If BOTH copies of a person’s GAA gene have a variant associated with Pompe disease, he or she will have Pompe disease. But if ONLY ONE copy has a variant and the other copy is normal, he or she will be a carrier of Pompe disease. Carriers of Pompe disease can pass the disease down to their children, but usually do not have any of its signs or symptoms themselves. Whether or not a person gets Pompe disease depends on their parents’ genes and how they are passed down. For example, if both parents are carriers (see graphic below), each of their children will have:

- A 1-in-4 (25%) chance of inheriting 2 normal genes and being unaffected
- A 1-in-2 (50%) chance of inheriting 1 copy of the variant and 1 normal gene, and being a carrier
- A 1-in-4 (25%) chance of inheriting 2 copies of the variant and having Pompe disease

Other scenarios also can occur, depending on the parents’ genes. For example, if one parent has Pompe disease and the other parent is unaffected, none of their children will develop Pompe disease, but all of them will be carriers.

What should I know about Pompe disease?

Depending on where you live, Pompe disease is estimated to affect as many as 1 in every 20,000–40,000 births.

Pompe disease is caused by certain variants in a specific gene (called the GAA gene).

People who have gene variants that cause Pompe disease have difficulty making a specific lysosomal enzyme.

The purpose of lysosomal enzymes is to help process or break down specific substances within the lysosomes of cells.

In Pompe disease, the affected enzyme is acid α-glucosidase, also known as GAA.

Normally, the GAA enzyme breaks down a complex carbohydrate called glycogen and converts it into a simple sugar.

But people who have Pompe disease have very little GAA, or almost none at all. The GAA they do have also may not work properly. This causes glycogen to build up in the cells of muscles, as well as other tissues and organs.

This buildup of glycogen in the lysosomes of cells increases over time, gradually causing more and more damage to tissues and organs (especially muscles) and leading to the signs and symptoms of Pompe disease.
What causes Pompe disease?

DNA is inherited through genes that are passed down from the person’s mother and father.

Sometimes, gene variants (also called mutations) occur in the DNA code that makes up a particular gene that can change the way the gene functions.

A blood test is done to measure the level of GAA enzyme activity.

GAA activity is absent or reduced AND/OR there is glycogen buildup

The person does NOT have Pompe disease

DNA testing is done to look for common gene variants associated with Pompe disease

The test does not detect a variant that causes Pompe disease

A blood test is done

The test does not detect a variant that causes Pompe disease

The person does NOT have Pompe disease

GAA activity is normal AND/OR there is no glycogen buildup

The person has Pompe disease

A blood test is done to measure the level of GAA enzyme activity

The test detects a variant that causes Pompe disease

The test does not detect a variant that causes Pompe disease

The test detects a variant that causes Pompe disease

The test detects a variant known to cause Pompe disease

The test does not detect a variant that causes Pompe disease

A doctor suspects Pompe disease—here’s an example of what can happen

How is Pompe disease treated?

Currently, enzyme replacement therapy (ERT) is the only FDA-approved treatment for Pompe disease.

ERT works by replacing the nonfunctioning or missing GAA with functioning GAA.

An infant’s cross-reactive immunological material (CRIM) status can help determine his or her response to treatment. CRIM-positive infants make some GAA, while CRIM-negative infants make no GAA.

People with Pompe disease also may receive supportive treatments to help manage the signs and symptoms of the disorder. For example, physical therapy can help improve muscle strength, and the use of a walker or wheelchair may help improve mobility. Mechanical ventilators or feeding tubes may be necessary in some cases.

Other potential therapies for Pompe disease are being researched. These include new forms of ERT, as well as another type of treatment called gene therapy. Although some of these investigational therapies have shown promise, their safety and efficacy in Pompe disease have not been proven, and they are not currently approved to treat the disease.

More information about clinical research in Pompe disease can be found by visiting clinicaltrials.gov or clinicaltrialsregister.eu or by talking with a health-care professional.

A VISUAL GUIDE TO UNDERSTANDING POMPE DISEASE

What are the signs and symptoms of Pompe disease?

How mild or severe the signs and symptoms of Pompe disease are—and how quickly they get worse—may vary from person to person in both the infantile-onset and late-onset types of the disease. This may be determined by how much GAA enzyme a person has and how well it is functioning, as well as other possible factors. Not every person who has Pompe disease will experience every sign and symptom listed below.

The test detects a variant

The test detects a variant that causes Pompe disease

The test detects a variant that causes Pompe disease

A VISUAL GUIDE TO UNDERSTANDING POMPE DISEASE

INFANTILE-ONSET POMPE DISEASE

• Difficulty breathing; loss of ability to breathe independently
• Respiratory infections

DIGESTIVE SYSTEM
• Feeding difficulties
• Reduced gag reflex
• Difficulty swallowing
• Failure to thrive
• Loss of bladder or bowel control

LIVER
• Enlarged liver

SKELETAL MUSCLE
• Rapidly worsening muscle weakness
• Diminished muscle tone
• Floppy limbs
• Difficulty holding up head
• Motor delay (abnormally slow development of motor skills)
• Inability to sit up, roll over, or stand without assistance

BONES/JOINTS
• Osteoporosis (weakened, fragile bones)
• Fractures
• Scoliosis (abnormally curved spine)
• Diminished muscle tone
• Reduced ability to cough

NERVES
• Nerve pain (most common in hands and feet)

DIGESTIVE SYSTEM
• Poor appetite/early satiety (feeling full after eating only small amounts of food)
• Chronic diarrhea or chronic constipation
• Loss of bladder or bowel control

MOUTH
• Problems with speech
• Difficulty chewing and swallowing

Heart
• Enlarged heart

LIVER
• Enlarged liver

SKELETAL MUSCLE
• Weakness
• Exercise intolerance/fatigue
• Problems with walking (may result in wheelchair dependency)
• Winging of the shoulder blades
• Absent or reduced glycogen buildup
• Protruding shoulder blades

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How are Pompe disease prevented?

Every newborn infant in the United States is universally screened for Pompe disease at birth. The screening test looks for GAA activity.

Not everyone with Pompe disease will experience every sign and symptom listed below.

For example, some people may not have any of the symptoms listed above. Others may present with only some of the signs and symptoms. How mild or severe the signs and symptoms of Pompe disease are—and how quickly they get worse—may vary from person to person in both the infantile-onset and late-onset types of the disease. This may be determined by how much GAA enzyme a person has and how well it is functioning, as well as other possible factors.

How is Pompe disease diagnosed?

A doctor suspects Pompe disease—here’s an example of what can happen

A sequencing test is done

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The test detects a variant that causes Pompe disease

The test detects a variant known to cause Pompe disease

The test does not detect a variant that causes Pompe disease

The test does not detect a variant

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The person does NOT have Pompe disease

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The person has Pompe disease

A blood test is done to measure the level of GAA enzyme activity

Some people with Pompe disease have gene variants that cause their bodies to make very little or no GAA.

Others have different variants that cause their bodies to make some GAA, but not enough, and/or GAA that does not function correctly.

Some people with Pompe disease have gene variants that cause Pompe disease, but the doctor still suspects Pompe disease.

The test does not detect a variant that causes Pompe disease, but the doctor still suspects Pompe disease.

The test detects a variant that causes Pompe disease.

The test detects a variant, but the doctor still suspects Pompe disease.

The test detects a variant that causes Pompe disease, but the doctor still suspects Pompe disease.

The test detects a variant that causes Pompe disease.

The person has Pompe disease.

A blood test is done.

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The person has Pompe disease.
What do these words mean?

**Autosomal recessive**: an inheritance pattern in which two copies of a gene variant must be present in order for the trait or disorder to develop

**Cell**: basic building block of all living things

**Cross-Reactive Immunological Material (CRIM)**: a measurement of natural GAA enzyme production

**Deoxyribonucleic acid (DNA)**: substance within genes that contains instructions, or code, for making proteins, including enzymes

**Diaphragm**: a thin sheet of muscle that separates the chest from the abdomen and plays a vital role in the breathing process

**Enzyme**: a special type of protein that speeds up chemical reactions that take place within a cell

**Enzyme replacement therapy (ERT)**: a treatment that replaces missing or nonfunctioning enzymes

**Gene**: the basic unit of heredity contained within each cell, made up of DNA, that group of more than 70 diseases that result from accumulation of waste products in lysosomes

**Lysosomal enzyme**: a special protein found within the lysosome of cells

**Lysosome**: a sac found in cells that contains enzymes that digest cell waste

**Neuromuscular disorder**: a disorder that affects the nerves that control voluntary muscles and the nerves that communicate sensory information back to the brain

**Sign**: objective evidence of a disease or condition that can be recognized by the patient as well as others

**Skeletal muscle**: muscle connected to the skeletal system that helps move the limbs and other parts of the body

**Sleep apnea**: a disorder in which a person's breathing stops repeatedly briefly during sleep

**Symptom**: subjective evidence of a disease or condition that can be recognized only by the patient

**Stroke**: damage to the brain resulting from blockage of blood flow or rupture of a blood vessel

Other resources that may be helpful are listed below.

**International**

International Pompe Association
worldpompe.org

The Association for Glycogen Storage Disease UK
agstd.org.uk

Australian Pompe's Association
australianpompe.com

Canadian Association of Pompe
pompecanada.com

Selbsthilfegruppe Glykogenose
Deutschland e.V.
glykogenose.de

Spierzienten Nederland
spierzienken.nl

**EUORDIS**
euordis.org

Pompe Support Network
pompe.uk

Associazione Italiana Glicogenosi (AIG)
alig-aig.it

New Zealand Pompe Network
nzpompenetwork.weebly.com

**United States**

United Pompe Foundation
unitedpompe.com

Acid Malate Deficiency Association
amda-pompe.org

Muscular Dystrophy Association
mda.org

**Resources**

Global Patient & Professional Advocacy

Please discuss any medical questions with a health-care professional (HCP).

If you would like to provide feedback on this educational resource or would like additional information please contact:
patientadvocacy@amicusrx.com.