foundation

Supporting your life with Fabry disease

WHAT IS FABRY DISEASE?

PRACTICAL MINI-GUIDE 1

This leaflet is not intended to replace medical advice or care.

Provided and funded by Takeda UK Ltd.

WHAT IS FABRY DISEASE?

Fabry disease (sometimes known as Anderson–Fabry disease after the two scientists who discovered it) is a rare genetic disorder caused by the deficiency of an important enzyme called alpha-galactosidase A

- Normally, the enzyme alpha-galactosidase A is present in most cells of the body and helps to break down fat-like substances called lipids
- People with Fabry disease have inherited a faulty gene, which leads to reduced levels of, or poorly functioning, alpha-galactosidase A. This causes a build up of a fatty substance called globotriaosylceramide (Gb3) in parts of the cells referred to as lysosomes
- Because Gb3 starts to accumulate in the lysosomes of cells, Fabry disease is often referred to as a `lysosomal storage disorder'
- Gb3 tends to build up most in kidney, heart and nerve cells, and in the walls of blood vessels. Eventually, the cells and tissues begin to deteriorate, and symptoms start to appear
- The tissues and organs most severely affected by Fabry disease are the skin, eyes, kidneys, heart and brain

WHO GETS FABRY DISEASE?

- Fabry disease affects men and women of all ethnic backgrounds in all parts of the world
- Symptoms can begin in childhood, although most appear during adolescence or early adulthood
- Although Fabry disease is one of the most common lysosomal storage disorders, it is classified as a rare disease, affecting an estimated 1 in 40,000–60,000 males and 1 in 20,000 females in the general population

HOW IS FABRY DISEASE INHERITED?

- People with Fabry disease have a faulty gene, which means that the body's cells cannot produce a fully working version of the enzyme alpha-galactosidase A
- The gene responsible for Fabry disease lies on the X chromosome – one of the two chromosomes that determine an individual's sex
- This means that there are differences between how Fabry disease affects men and women, and how it is passed on to their children

"Obviously, I am worried and upset about the boys having Fabry disease but I think there are a lot worse things that could happen. We have really good lives and we just have to make the most of them." Mandy – A Fabry patient

Anecdotal quote for illustrative purposes.
Patient name and picture are not real

For more information about how Fabry disease is inherited, please contact the MPS Society for their booklet on inheritance www.mpssociety.org.uk

WOMEN

- Women have two X chromosomes, so if a woman has Fabry disease, one of these will have a copy of the faulty gene (unless both parents pass on X chromosomes containing copies of the faulty gene)

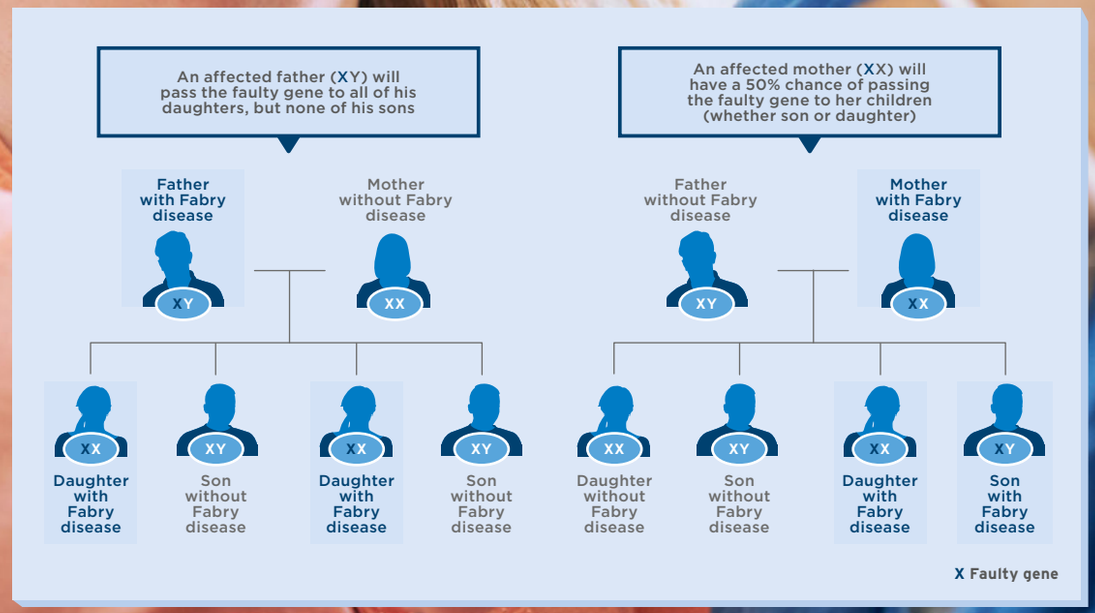
- Females with Fabry disease have a 50% chance of passing on the faulty gene to their children, regardless of whether the child is a boy or girl because they will pass on an X chromosome to their son or their daughter

- Females may have less severe disease manifestation than men but this is not always the case. The reason for this is that females have two X chromosomes, one of which will be active and one inactive. It is a matter of chance which chromosome is active in a particular cell. If the pattern of activation is skewed in favour of the X chromosome with the faulty gene, then a female is likely to have more severe symptoms

MEN

- Men only have one X chromosome (and one Y chromosome), so if it contains the faulty Fabry gene, they will more than likely develop symptoms of Fabry disease

- Men pass on their Y chromosome to their son, so they cannot pass on the condition to their son. However, if they have a daughter, they will pass on their X chromosome and a copy of the faulty gene



WHAT ARE THE SYMPTOMS OF FABRY DISEASE?

Symptoms can vary daily, and from person-to-person. Some people may have only mild symptoms, while others suffer severe symptoms from an early age.

Symptoms tend to appear at a younger age in boys than in girls

- Because of the lack of disease-specific symptoms, the diagnosis of Fabry disease is often delayed, with a mean delay from onset to diagnosis of 13.7 years in men and 16.3 years in women
- Diagnosis tends to be late (in the absence of a family history of the disease) because skin rashes tend to be overlooked while patients reporting symptoms of pain are often misdiagnosed as suffering from neuropathic pain

Early symptoms (sometimes appearing for the first time in childhood) include:

- Pain and discomfort in the hands and feet, often brought on by hot weather or exercise
- Spotted, dark red rashes (called angiokeratomas) seen mostly between the belly button and knees
- A decreased ability to sweat (perspire), resulting in over-heating and decreased tolerance to heat
- Characteristic changes on the cornea of the eye, without the vision being affected
- Abdominal pain, diarrhoea, nausea and vomiting

"My hands and feet get unbearably painful, especially if they're touched by hot or cold water. The pain prevents me from immersing myself and I shower at a specific temperature that keeps the trauma to my body at a minimum" George – A Fabry patient

Anecdotal quote for illustrative purposes. Patient name and picture are not real.

As Fabry disease progresses with time, additional symptoms may appear, including:

- Fatigue (often extreme and disabling)
- Abdominal cramping, frequent bowel movements shortly after eating, diarrhoea and nausea
- Headaches
- Hearing loss or tinnitus (ringing in the ears)
- Swelling of the ankles
- Chest pain or palpitations

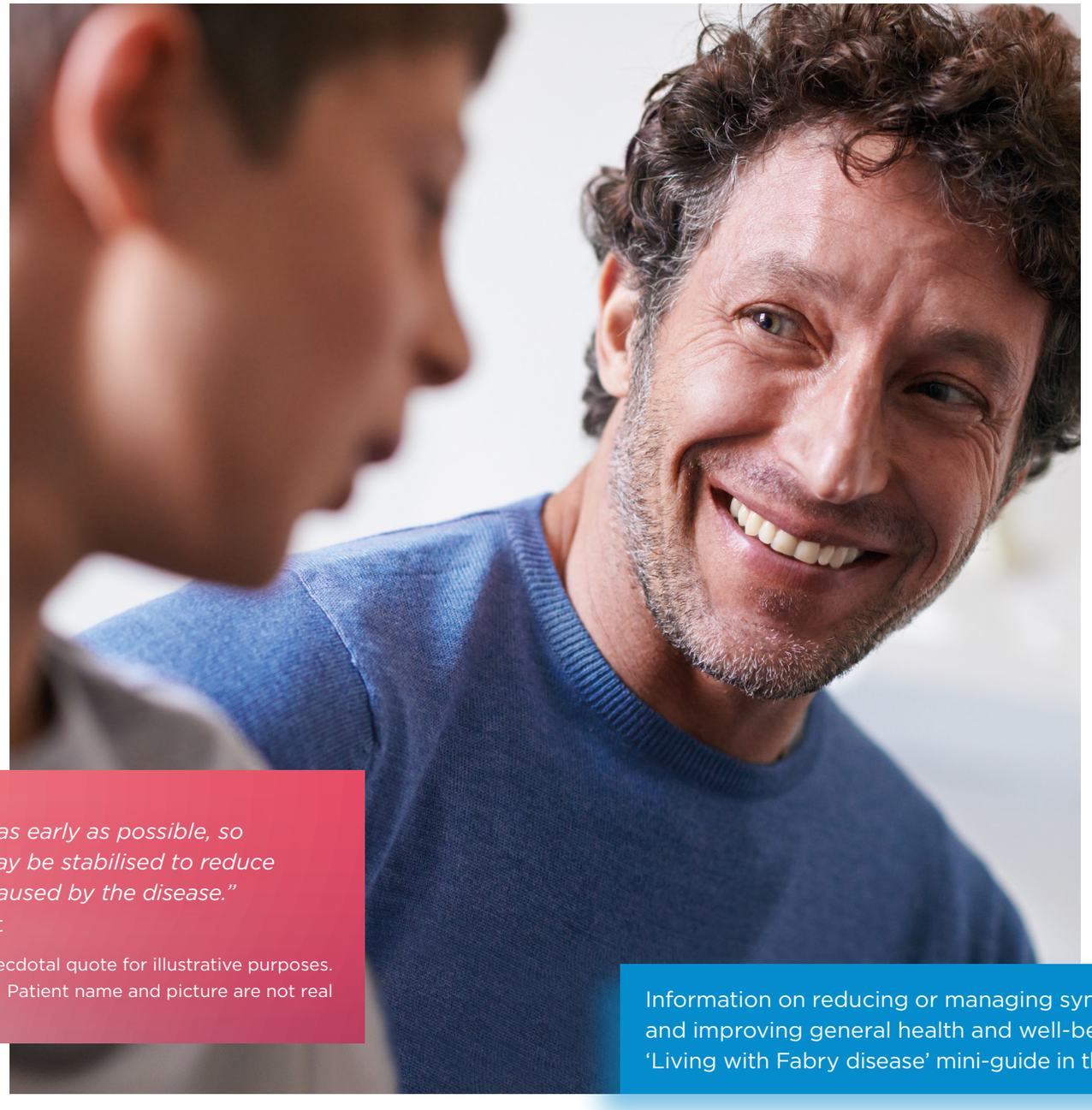
Potentially serious complications associated with Fabry disease include:

- Kidney disease, leading to loss of protein in the urine (proteinuria) and possible kidney failure
- Heart conditions, including changes in the shape and function of the heart, irregular heartbeat, and leaky heart valves
- Disruption to normal blood flow in the brain. This can cause dizziness and, in some cases, strokes

- All of these symptoms result from the gradual build up of the fatty substance, Gb3, in the cells and tissues. If left untreated, vital organs eventually start to deteriorate, and severe, sometimes life-threatening, complications can arise
- The good news is that progression of the disease can be slowed with effective treatments

WHAT IS THE OUTLOOK FOR PEOPLE WITH FABRY DISEASE?

- Fabry disease can be painful, distressing and disabling, and if left untreated, people with Fabry disease report feeling depressed, anxious, tired and frustrated
- Symptoms can be made worse by the fear of serious complications and the risk of potentially life-threatening events such as heart attacks and strokes. Life expectancy for people with Fabry disease has, in the past, been estimated to be around 15–20 years shorter than the general population if left untreated. Current treatments have improved life expectancy by about 15 years compared with untreated patients
- Doctors and researchers have gained a better understanding of the causes and consequences of Fabry disease, and made great progress in the way the condition is now diagnosed and treated



"It is vital to get help as early as possible, so that the condition may be stabilised to reduce the damage that is caused by the disease."
Ted – A Fabry patient

Anecdotal quote for illustrative purposes.
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There are two basic approaches to the management of Fabry disease:

- Treatment to manage symptoms or the impact of the disease
- Treatments designed to replace or supplement the alpha-galactosidase A enzyme activity.
  - Enzyme replacement therapy (ERT), uses regular infusions to replace the missing enzyme
  - Chaperone therapy is an oral treatment to help restore the activity of the defective enzyme. Genetic testing will show whether a patient is expected to respond to this treatment option

- Many experts believe that earlier diagnosis and better treatment hold the potential to change the natural course of Fabry disease
- Put simply, the outlook for people with Fabry disease has never been brighter, thanks to the continuing work of thousands of scientists, doctors, and patients around the world

Information on reducing or managing symptoms of Fabry disease, and improving general health and well-being can be found in the 'Living with Fabry disease' mini-guide in this series

OTHER MINI-GUIDES IN THIS SERIES INCLUDE:

Living with Fabry disease

This mini-guide offers suggestions and practical guidance on how to live more comfortably with Fabry disease. Topics covered include how to avoid symptom triggers, how to cope with school, college or work, and how to build a support network.

Do you know someone with Fabry disease?

A practical guide to offer to your support network to aid their understanding of Fabry disease.

THE MPS SOCIETY

The MPS Society is a UK charity supporting individuals and families affected by mucopolysaccharide and lysosomal storage diseases, including Fabry Disease, throughout the UK. It offers a unique opportunity for people affected by Fabry disease to get in touch with other people in similar circumstances and it provides up-to-date information on management, treatment and living with Fabry disease.

For further information about the MPS Society please, contact:

MPS Society Helpline:
+44 (0) 345 389 9901

Email: mps@mpssociety.org.uk
Web: www.mpssociety.org.uk

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