YOUR GUIDE TO REPLAGAL®
(agalsidase alfa)

This leaflet has been developed for patients who have been prescribed REPLAGAL®.

This leaflet is not a substitute for the Patient Information Leaflet (PIL) which is provided with your medicine - please ensure you read the PIL.

The PIL is also available at www.medicines.org.uk/emc/files/pil.9186.pdf. The information provided in this leaflet is general educational information and does not take the place of professional medical advice. Always follow your doctor/nurse's instructions and talk with them about any questions or problems you have regarding your health and treatment.

A patient guide initiated and funded by Takeda UK Ltd.

WHAT IS FABRY DISEASE?

Fabry disease is a rare, inherited condition caused by reduced levels of an enzyme called α-galactosidase A. This enzyme breaks down lipids, which are fat-like substances. Without this enzyme, a lipid known as globotriaosylceramide (Gb3) builds up in your cells, causing damage to tissues, organs and the walls of blood vessels.

The build-up takes place in the lysosomes of cells, which act like waste bins by helping to clear lipids. Fabry disease is therefore often referred to as a 'lysosomal storage disorder'.

If left untreated, vital organs such as the kidneys, heart and brain start to deteriorate and severe complications can arise and a wide range of symptoms can develop.

WHAT ARE THE SYMPTOMS?

Fabry disease is a complex condition and each patient can be affected in a different way, experiencing varying degrees and combinations of symptoms. Symptoms can begin in childhood, although most appear during adolescence or early adulthood.

The most common signs and symptoms include:

Early symptoms

- Pain and burning sensation in hands and feet
- Spotted, dark red rashes, mostly between the belly button and knees
- Reduced ability to sweat, resulting in over-heating and difficulty exercising
- Changes on the cornea of the eye, without the vision being affected
- Stomach pain, diarrhoea, nausea and vomiting

Symptoms that develop later

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

Potentially serious complications

- Stroke
- Kidney disease, leading to 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

WHO IS AFFECTED BY FABRY DISEASE?

Fabry disease is very rare. It is estimated to affect 1 in 40,000–60,000 males and 1 in 20,000 females in the general population.

Fabry disease is not contagious. It is a hereditary condition that children can genetically inherit from their parents. It affects both men and women of all ethnic backgrounds in all parts of the world, although it affects men and women differently. It is passed through the X chromosome, so whether it is the mother or the father who has the Fabry gene will determine how many of their children will have the faulty gene.

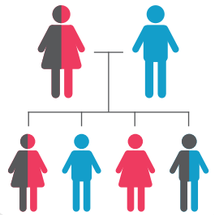
Women with Fabry

- Women have two X chromosomes, only one of which will have a copy of the faulty gene
- Symptoms in females may be no less severe but tend to appear at an older age than in males
- 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

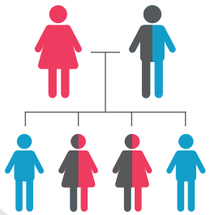
Men with Fabry

- Men only have one X 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. However, if they have a daughter, they will pass on their X chromosome and a copy of the faulty gene

Female heterozygotes
Pass the Fabry gene to their sons or daughters



Men with Fabry disease
Pass the Fabry gene to their sons or daughters



The average age of diagnosis for people with Fabry disease is 29 years old, but it varies greatly from person to person. Many people are diagnosed after many years of suffering from symptoms. Without any family history of the disease, people tend to be diagnosed late because symptoms like skin rashes and pain are non-specific symptoms.

WHAT DOES THIS MEAN FOR PEOPLE WITH FABRY?

Fabry disease can be painful, distressing and disabling for sufferers who, if left untreated, 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.

Current treatments have improved the outlook for people with Fabry disease. 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.

YOUR FABRY TREATMENT

Your doctor has prescribed REPLAGAL® for you, which is used to treat adults, adolescents and children from the age of 7 years, who have been diagnosed with Fabry disease. It is used as long-term treatment when your enzyme level is either too low or missing altogether.

REPLAGAL® is given as an intravenous infusion and is usually used alongside other treatments to manage specific symptoms (which are tailored to the individual).

WHAT IS REPLAGAL®?

REPLAGAL® has been used to treat patients with Fabry disease for over 20 years. It contains an active substance called agalsidase alfa, which is a form of the human enzyme α-galactosidase A.

REPLAGAL® is made by switching on the gene for α-galactosidase A in a human cell line. The enzyme is then removed from the cells and turned into a sterile concentrate that can be made up into a solution for infusion when needed.

HOW DOES REPLAGAL® WORK?

REPLAGAL® contains 1 mg of agalsidase alfa per millilitre (mL), which supports the low levels of the enzyme α-galactosidase A in patients with Fabry disease, which reduces the build-up of the Gb3 lipid in many types of cell.

HOW MUCH REPLAGAL® WILL I TAKE?

Your dose of REPLAGAL® will be 0.2 mg per kg of body weight. Your doctor will calculate the dose you need and prescribe you the correct amount.

HOW DO I TAKE MY REPLAGAL® TREATMENT?

You will receive an intravenous infusion every other week. Intravenous means that it will be delivered straight into your bloodstream through a vein.

Your infusion will initially be given in your hospital or clinic and will only take **40 minutes.**

If your infusions in hospital go well, it is likely that you can have your REPLAGAL® infusion at home to make things easier for you.

Depending on your situation, you may be able to have a healthcare professional visit you to give you your infusion or you may be able to be trained to perform the infusion yourself.

Your doctor will work with you to find the best way to administer the infusion for you.

WHAT TO EXPECT

As with many medications that are given by infusion, reactions due to hypersensitivity have been reported. More than 1 in 10 patients may have a reaction during or following an infusion of REPLAGAL®.

The most common side effects were:

- Swelling in the tissue (e.g. legs, arm)
- Tingling or numbness or pain in fingers or toes
- Ear ringing
- Palpitations
- Sore throat
- Abdominal pain, diarrhoea
- Rash
- Back or limb pain, muscle pain, joint pain
- Chest pain, cold symptoms, fever, feeling sick
- Change in the taste of food, prolonged sleep
- Eyes tearing
- Increased ear ringing
- Increased heart rate, heart rhythm problems
- Increased blood pressure, low blood pressure, facial flushing (redness)
- Hoarseness, or tight throat, runny nose
- Abdominal discomfort
- Acne, red or itchy or mottled skin, excessive sweating
- Muscle and bone discomfort, swelling of the extremities or joints
- Hypersensitivity
- Infusion-related reaction (for example chills, headache, nausea, fever, tiredness, unsteadiness, difficulty breathing, shaking, cough and vomiting)
- Chest tightness, increased feeling lack of energy, feeling cold or hot, flu-like symptoms, discomfort

If you do experience any side effects, talk to your doctor, pharmacist or nurse.

Further information on less frequent side effects can be found in the Patient Information Leaflet. If you notice any of these effects during or after an infusion you should tell your doctor immediately:

- High fever, chills, sweating or fast heart rate
- Vomiting
- Light-headedness
- Hives (rash)
- Swelling in your hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing

Severe life-threatening allergic reactions ('anaphylactoid reactions') have been reported in some patients.

If you do experience any of these symptoms, your doctor may stop the infusion temporarily (5–10 minutes) until the symptoms go away and then begin the infusion again.

Your doctor may also treat the symptoms with other medicines (antihistamines or corticosteroids).

Most of the time you can still be given REPLAGAL® even if these symptoms occur.

MANAGING FABRY SYMPTOMS

Many people with Fabry disease report their pain as being the worst aspect of their condition, and it is often one of the most difficult symptoms to treat.

Many sufferers find that pain symptoms can be made worse by certain triggers, and that by avoiding these and other triggers they can help to gain some control over their own symptoms.

Triggers can include:

- Exercise
- Stress
- Alcohol consumption
- Fever
- Variations in temperature

The next page contains some tips on how to avoid pain and other symptom triggers in Fabry disease.

REDUCING THE RISK OR SEVERITY OF PAIN*

- Avoid changes in temperature or humidity – layering clothing can help keep the body temperature steady
- Drink plenty of fluids after periods of activity
- Avoid excessive physical exertion and stressful situations
- Minimise your alcohol intake
- Do not allow yourself to get over-tired – take frequent rests if you can
- Consider the use of cold compresses on painful areas of skin
- Keep away from sources of infection and visit your doctor regularly

REDUCING THE INCIDENCE AND SEVERITY OF GASTROINTESTINAL SYMPTOMS

- Eat smaller meals more often – please do not be afraid to eat
- Keep a food diary and identify which foods cause the most severe symptoms
- Make healthy food choices
- Reduce the amount of fat in your diet

*May not affect all patients.

HEALTHY LIVING

Choosing a healthy lifestyle can help your condition and help to protect you from other serious illnesses. Five factors that most people consider important to stay as healthy as possible:

Don't smoke: If you smoke, stopping smoking can be the single most effective thing you can do to reduce your risk of future illness.

Regular physical activity: At least 30 minutes of physical activity on most days is advisable for most individuals. People with Fabry disease often find it impossible to do so, as exercise triggers or worsens symptoms, but if you can find an activity that you enjoy that doesn't cause discomfort, that would be ideal.

Good diet: People with Fabry disease are often fearful of food because eating can trigger abdominal symptoms. Nevertheless, eating a healthy diet is still important for you, so you should try and follow these guidelines, even if you have adapted the way you eat to suit your illness.

Try to achieve your ideal weight: Many people with Fabry disease are under-weight, probably because they don't absorb nutrients from food as well as others, and because food can be a symptom trigger. Finding out what the ideal weight for your height should be, and working towards achieving it, may help.

Don't drink too much alcohol: A small amount of alcohol is usually fine, if it doesn't trigger your symptoms. But drinking too much can be harmful. Men and women should drink no more than 14 units per week (and no more than 3 units in any one day).

REMEMBER, YOU'RE NOT ALONE

Having a long-term illness like Fabry disease, with its unpredictable, often disabling, symptoms, can mean you need to push yourself a little harder than most – sometimes when you really don't feel like it.

A good support network can really help. It is reassuring to know that there are people around to share the good times, offer comfort during the bad times and be a reliable back-up when practical help is needed.

So a strong team of people around you – who understand your illness and what you might need from them – can provide valuable support. Friends, family and of course your medical team, can make a really big difference to how well you cope with having Fabry disease.

Many people with Fabry disease gain great support from other patients. And thanks to the internet, Fabry patients around the world can join together and share their stories.

There are multiple Internet forums and social media groups devoted to Fabry disease.

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.co.uk
www.mpssociety.org.uk

Want to find out more about **Fabry disease** and **REPLAGAL®** (agalsidase alfa)?

Visit
REPLAGALPATIENTWEBSITE.co.uk
or scan the QR code below

The REPLAGAL® patient website contains helpful information, support and sources of advice, including:

- Information about how REPLAGAL® works
- Guides to living with Fabry disease for you and your friends and family
- Videos from other people with Fabry disease
- Information on who to contact for further advice and support

REPLAGAL®
agalsidase alfa

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in the package leaflet. You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

By reporting side effects you can help provide more information on the safety of this medicine.

Takeda

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