What are the next steps if you are interested in being tested?

If you would like to know more about Fabry, or be tested, the next step is to go and see a healthcare professional. Depending on your individual situation this might be:

- **Your relative's doctor, genetic counsellor or a member of their healthcare team**
- **Someone your relative's doctor refers you to**
- **Taking the tear-off section in this leaflet to your own doctor, who may refer you on**

Have a discussion with a healthcare professional, who should assess your risk of having Fabry; explain the nature of the genetic tests including potential advantages and disadvantages; and arrange for a test if it is appropriate and should you wish it.

If you consent, a genetic test can be performed to look for Fabry associated mutations.[6] The test is usually done on a cheek swab, blood or other tissue sample.[14]

If a Fabry mutation is found, your medical team will talk to you more about the disease, any potential implications and how to manage it, including the treatment options.

Getting support

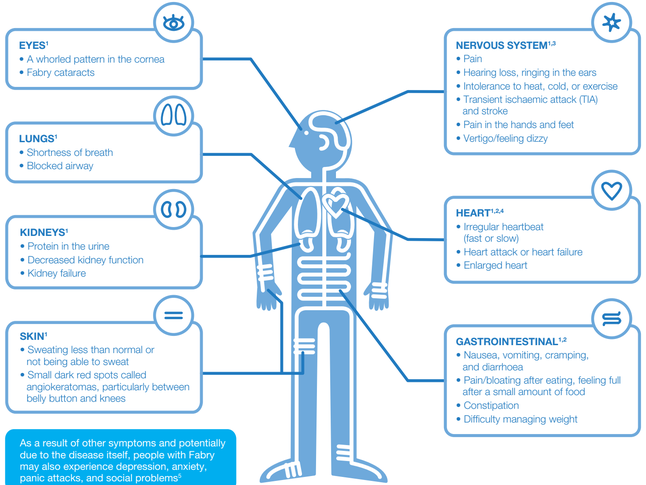
If you would like to know more about Fabry and its genetics, please visit **www.fabryfamilytree.com**

There are also organisations for people and families with Fabry who may be able to offer support.

Talk to a healthcare professional about your risk of Fabry.

Tear-off for your doctor

What are the symptoms of **Fabry**?



As a result of other symptoms and potentially due to the disease itself, people with Fabry may also experience depression, anxiety, panic attacks, and social problems[5]

Amicus Therapeutics

Talk to a healthcare professional about who in your family may be at risk of Fabry

Disclaimer: This leaflet was sent to you because it is possible that you could be at risk of Fabry based on how Fabry is passed down in families and your relative's family tree. However, this does not necessarily mean you have the disease, and it does not in any way suggest a diagnosis of Fabry disease. Any concerned individual should speak to a healthcare professional.

References

1. Germain DP. Orphanet J Rare Dis. 2010;5:30 **2.** Oritz A, et al. Mol Genet Metab. 2018;123(4):416–427 **3.** Cammarata G, et al. Biomed Res Int. 2015;504784 **4.** Laney DA. Mol Genet Metab. 2019:126(2):S90-91 **5.** Yamamoto S et al. Intern Med. 2019;58(4):603-607 **6.** Laney DA, et al. J Genet Couns. 2013;22(5):555-564 **7.** DNA, genes, chromosomes and mutations. Genetic Alliance UK. Available at: https://www.geneticalliance.org.uk/information/learn-about-genetics/dna-genes-chromosomes-and-mutations/ [Last accessed August 2019] **8.** Yousef Z et al. Eur Heart J. 2013;34(11):802-808 **9.** Desnick RJ et al. Ann Intern Med. 2003;138(4):338-346 **10.** Hilz MJ et al. Dig Liver Dis. 2018:50(5):429-437 **11.** Hoffmann B & Mayatepek E. Dtsch Arztebl Int. 2009;106(26):440-447 **12.** Mehta A & Hughes DA. Fabry disease. GeneReviews®. Available at: https://www.ncbi.nlm.nih.gov/books/NBK1292/ [Last accessed August 2019] **13.** Germain DP et al. Clin Genet. 2019;96(2):107-117. **14.** How is genetic testing done? Genetics Home Reference. Available at: https://ghr.nlm.nih.gov/primer/testing/procedure [Last accessed August 2019]

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Our **family** & **Fabry**

Amicus Therapeutics

You are receiving this leaflet because someone in your family has been diagnosed with Fabry disease. Fabry is a genetic condition that can be passed down the generations of a family. Based on how Fabry is passed down and your relative's family tree, it is possible that you could be at risk of Fabry. However, this does not necessarily mean you have the disease.

What is **Fabry**?

Fabry affects everyone differently, some people with Fabry experience no symptoms, others are severely affected, and everyone else falls somewhere in-between. [1]

Fabry has the potential to affect most of the body, but the experience of symptoms can vary between individuals – even those within the same family. [1-6] Symptoms can develop and worsen over time, potentially resulting in serious or life-threatening complications – although this won't be the case for everyone.[1]

If you have Fabry you may or may not have experienced symptoms yet.

What causes the symptoms of **Fabry**?

People with Fabry have genetic mutations (variants) that result in a certain enzyme (a-galactosidase A) not working properly. [1,6] Normally the enzyme helps break down certain sugary-fatty substances (glycosphingolipids) in the cells of our body. [1,6]

In those with Fabry, the sugary-fatty substances build up, causing problems and the symptoms of Fabry. [1,6]

What are genetic mutations? [7]

Genetic information is stored in DNA, providing instructions that tell every cell in your body what to do. Mutations can occur in DNA, these are errors in the instructions

For more information about Fabry and how it is passed down in families please visit **www.fabryfamilytree.com**, or speak to a healthcare professional

Why should you consider being tested for **Fabry**?

You may want to consider talking with a healthcare professional about being tested for Fabry. This is because it has been identified in a relative and based on how it is passed down in families and your relative's family tree, it is possible you could be at risk of Fabry. However, this does not necessarily mean you have the disease.

Fabry symptoms can be hard to recognise due to how varied they can be, their overlap with more common conditions and how rare Fabry is. [1,10,11] This means some people may never receive a diagnosis, others have to see multiple specialists and may be misdiagnosed before the correct Fabry diagnosis is given. [1,10,11]

Long delays to diagnosis are common with Fabry, an average delay is 15 years – being tested could save you from this diagnostic odyssey. [1,10,11]

As Fabry can get worse over time, knowing about it sooner and receiving help may also mean that you can slow the disease worsening, potentially leading to a healthier future. [2,12,13]

The advantages and disadvantages of being tested can be discussed with healthcare professionals.

If you choose not to be tested, it's still important for you to know that Fabry is in your family and you should always tell your healthcare team if you have any health issues of your own. Sharing that Fabry disease is in the family with a medical team could help prompt a diagnosis.

Talk to a healthcare professional about who in your family may be at risk of Fabry

next steps

What are the next steps if you are interested in being tested?

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Getting support

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There are also organisations for people and families with Fabry who may be able to offer support.

Talk to a healthcare professional about your potential risk of Fabry.

You can take the tear-off letter to the right to your own doctor. As Fabry is rare they may not have heard of it, but this should help start a conversation.[9]

Amicus Therapeutics

Dear Doctor,

Your patient has been highlighted as potentially at risk of Fabry disease through a pedigree analysis of their relative who has been diagnosed with Fabry.

Fabry is a genetic disorder with X-linked inheritance. [1] It is a progressive, multisystemic disorder and may cause serious morbidity and mortality in both men and women. [1,2]

Fabry can be difficult to diagnose due to its rarity, overlap with more common conditions and variability of symptoms – even within a family. [1,3-7] It may be underdiagnosed and is often misdiagnosed with an average diagnostic delay of 15 years. [1,3,4] Due to its progressive nature, early intervention is thought to help prevent disease progression and may lead to improved health outcomes. [2,8,9]

For more information about Fabry please visit **www.fabryfamilytree.com**

Based on the above you may want to begin the process of investigating for Fabry, either directly or by referral. Predictive genetic testing is available. It may be advisable that the patient's risk of Fabry be reviewed, and where possible genetic counselling be provided.

References: 1. Germain DP. Orphanet J Rare Dis. 2010;5:30 **2.** Ortiz A, et al. Mol Genet Metab. 2018;123(4):416-427 **3.** Hoffmann B & Mayatepek E. Dtsch Arztebl Int. 2009;106(26):440-447 **4.** Hilz MJ, et al. Dig Liver Dis. 2018;50(5):429-437 **5.** Cammarata G, et al. Biomed Res Int. 2015;504764 **6.** Yamamoto S et al. Intern Med. 2019;58(4):603-607 **7.** Laney DA. Mol Genet Metab. 2019;126(2):S90-91 **8.** Mehta A & Hughes DA. Fabry disease. GeneReviews®. Available at: https://www.ncbi.nlm.nih.gov/books/NBK1292/ [Last accessed August 2019] **9.** Germain DP et al. Clin Genet. 2019;96(2):107-117.