A TAKEDA SUMMARY

Fabry disease: recognise and refer

Fabry disease is a rare but life-threatening X-linked inherited lysosomal storage disorder that is **underdiagnosed.**[1-3] The disease progresses with increasingly severe symptoms that, in advanced cases, can lead to premature death.[1,4]

Approximately **1,000** people in the UK

are living with Fabry disease, although the true number is likely higher due to underdiagnosis and late-onset forms.[1,3,5,6]

Lack of clinician awareness of Fabry disease means it is often not recognised and is misdiagnosed in over a quarter of patients; some wait as long as 20 years for a correct diagnosis.[4,7]

Fabry may be more common than you think; for example, it has been found in as many as **3% of patients with unexplained LVH.**[8]

Early recognition and prompt referral for treatment are essential to prevent irreversible organ damage.[1,4,8]

Contact your local centre to refer any suspected patients or for further information. Click or scan the QR codes to find your nearest specialised centre:[9-11]

Adult

Paediatric

Please note these will take you to an external website that is not owned, or controlled by Takeda Ltd.

SIGNS AND SYMPTOMS TO LOOK OUT FOR

You may already have affected patients in your practice. Consider referring any patients with unexplained cardiac, renal or neurological symptoms for further evaluation.[4,9]

Fabry is a progressive, multi-organ disease with two primary clinical forms: classical and late-onset.[4]

The earliest signs in children are

neuropathic pain, which occurs in **60–80% of patients**

and skin abnormalities, found in **50–78% of patients**

In late-onset or advanced Fabry, the most severe symptoms are cardiac manifestations, such as **LVH**; these occur in **40–60% of patients**

Here are some signs and symptoms from each subtype:

	Classical disease (manifesting in children)[4,7]	Advanced and late-onset (manifesting in adults)[4,7]
Peripherial neurologic	Neuropathic pain (acroparaesthesia), pain crises, hearing loss, tinnitus, vertigo	Present or past experience of neuropathic pain, hearing loss, vertigo
Dermatological	Skin abnormalities (angiokeratomas), sweating abnormalities (anhidrosis or hypohidrosis)	Skin abnormalities (hypohidrosis or hyperhidrosis), linear telangiectasia, lymphedema
Gastrointestinal	Nausea, vomiting, diarrhoea	Nausea, vomiting, diarrhoea
Cerebrovascular	Cerebral microvascular ischemic involvement	White matter lesions, TIAs, ischemic strokes
Renal	Microalbuminuria, proteinuria	Albuminuria, renal impairment, end-stage renal disease
Cardiac	Shortened PR interval, arrhythmias	LVH, HCM, arrhythmias, valvular disease
Ocular	Corneal deposits (cornea verticillata)	Corneal deposits, lenticular opacities

These manifestations **significantly reduce HRQoL**, affecting mobility, daily activities, and emotional well-being – but they are **often mistaken for symptoms caused by other diseases.**[4,12]

THINK FABRY[4,8]

- ? Family history of Fabry disease
- ? Family history of sudden cardiac death
- ? Renal conditions with no cardiovascular risk factors
- ? Unexplained LVH or stroke
- ? Unexplained GI symptoms and pain

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RARE DISEASE HUB

A TAKEDA SUMMARY

FABRY DISEASE MYTHS AND FACTS

"Only men are affected because it is X-linked."

The Fabry Outcomes Survey, which was a global disease registry funded by Takeda from 2001 until its closure in September 2022, demonstrated that females can experience significant organ involvement challenging the notion of a milder disease course in women.[7]

"If the patient has survived into adulthood without problems, they don't have Fabry disease."

Late-onset Fabry disease may not cause any symptoms until the third to fourth decade of the patient's life, often with predominant cardiac involvement.[1]

Inheritance

Fabry disease is X-linked; **hemizygous men are consistently affected**, whereas **heterozygous women may be as severely affected as men** or remain asymptomatic for life.[2]

AFFECTED MEN

All daughters will inherit the mutation, while sons will remain unaffected.[2]

AFFECTED WOMEN

There is a **50%** chance of passing the mutation to sons and daughters.[2]

Family members may also be at risk: once a pathogenic variant is identified, family members should be considered for clinical examination and molecular genetic testing.[2]

Treatment

Fabry disease is a chronic condition caused by mutations in the *GLA* gene on the X chromosome, leading to a deficiency or absence of the enzyme α-Gal A. Guidelines recommend lifelong treatment.[1,2,5]

Enzyme replacement therapy

ERT provides recombinant α-Gal A to compensate for any enzyme deficiency.[1]

Lifelong infusions are typically required; treatment may be administered in a hospital, or at home under appropriate supervision if well tolerated.[1,5,13]

Oral chaperone therapy

In some patients, misfolded α-Gal A may be stabilised by chaperone therapy; such mutations are termed amenable.[1]

Approximately

35–50% of patients

have an amenable variant, making them eligible for this treatment.[1,4]

Referral

Refer any patients with suspected Fabry disease directly to a specialist metabolic centre, by phoning, emailing or writing a letter to your nearest centre.[9-11]

All treatments are delivered through designated specialist centres and funded by highly specialised commissioning, relieving costs from local practices.[9,14]

Click on the links or scan the QR code below to find your nearest specialised metabolic centre:

Click to find your nearest adult centre

Click to find your nearest paediatric centre

Please note these will take you to an external website that is not owned, or controlled by Takeda Ltd.

ABBREVIATIONS: α-Gal A, α-galactosidase A; ERT, enzyme replacement therapy; HCM, hypertrophic cardiomyopathy; HRQoL, health-related quality of life; LVH, left ventricular hypertrophy; TIA, transient ischaemic attack.

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