UNEXPLAINED CKD?

IT COULD BE FABRY DISEASE

Recognize the signs and symptoms to make an early diagnosis[1-6]

Fabrazyme®
agalsidase beta

INDICATION AND USAGE

Fabrazyme® (agalsidase beta) is indicated for use in patients with Fabry disease. Fabrazyme reduces globotriaosylceramide (GL-3) deposition in capillary endothelium of the kidney and certain other cell types.

The reduction of GL-3 inclusions suggests that Fabrazyme may ameliorate disease expression; however, the relationship of GL-3 inclusion reduction to specific clinical manifestations of Fabry disease has not been established.

SANOFI GENZYME

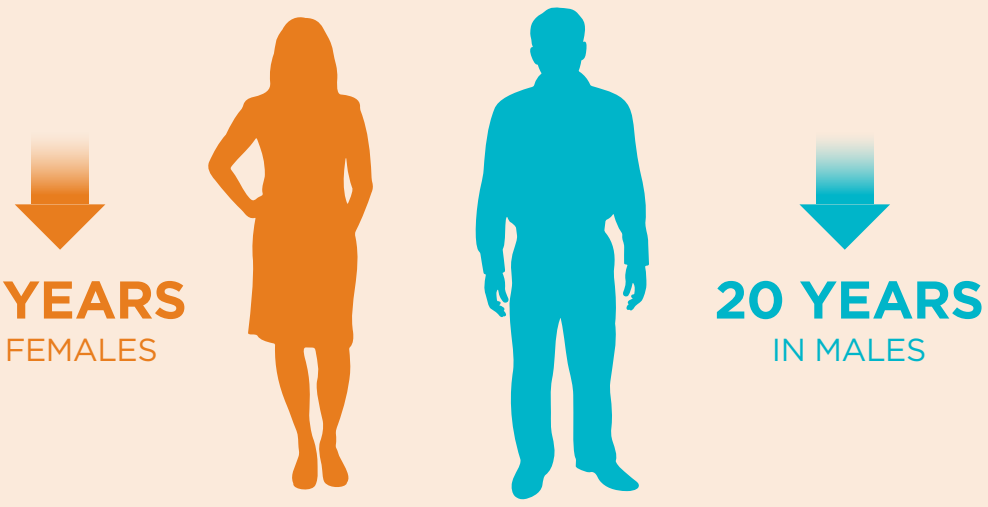
Please see Important Safety Information on pages 18–19 and full Prescribing Information.

NEPHROLOGISTS CAN PLAY A CRITICAL ROLE IN THE EARLY DETECTION OF FABRY DISEASE.

Fabry disease: Progressive. Often life threatening.[1-5]

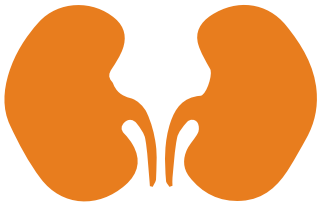
- A multisystemic disease that impacts essential organs, such as the kidney, heart, and brain[7,8]
- An X-linked disorder that affects men, women, and children[1,2]

Undiagnosed and unmanaged, Fabry disease can reduce life expectancy[9,10]



FABRY DISEASE CAN HAVE A SERIOUS IMPACT ON ESSENTIAL ORGANS, INCLUDING THE KIDNEYS.[7,8]

Patients with Fabry disease are at high risk of progressing to ESRD at a young age[2,11]



In the Fabry Registry, female and male patients with ESRD required their first dialysis or transplantation at a median age of **38 years**[12]:

Podocyte damage

can be seen as early as the first decade of life, often silent to clinical measures and before overt symptom onset[2]

Renal failure

is one of the main causes of death in patients with Fabry disease[13]

The prevalence of Fabry disease in the dialysis population is

80x–480x[14-16]
HIGHER IN MEN

10x–108x[17,18]
HIGHER IN WOMEN

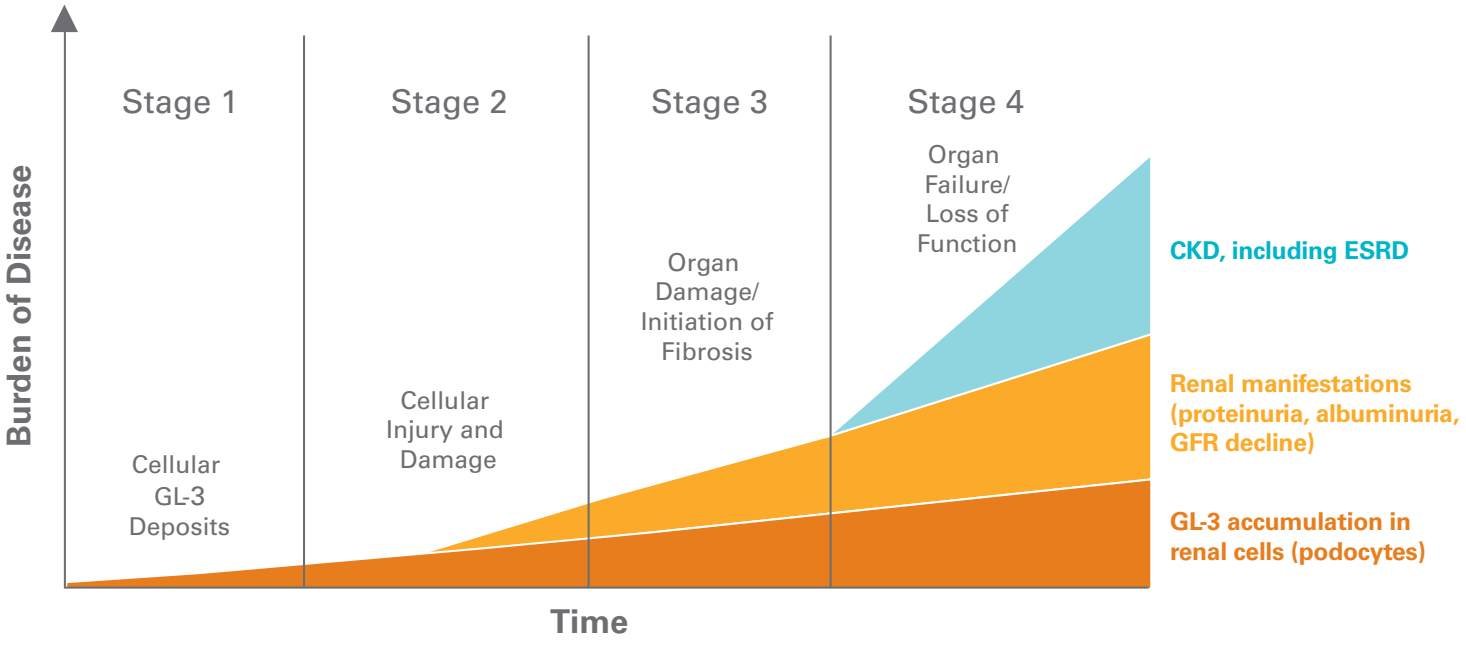
than in the general population[4,19]

ESRD=end-stage renal disease.

THE HALLMARK OF FABRY DISEASE IS GL-3 ACCUMULATION.[13]

- Fabry disease is caused by mutations in the *galactosidase alpha (GLA)* gene that cause complete or partial deficiency of α-galactosidase (α-GAL A)[20]
- This results in lifelong, progressive cellular accumulation of globotriaosylceramide (GL-3) throughout the body[20]
- GL-3 buildup starts in utero and continues throughout life[21-24]

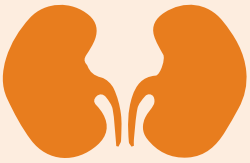
Renal damage as a result of GL-3 accumulation often precedes laboratory abnormalities and clinical symptom onset[5,25]



GFR=glomerular filtration rate.

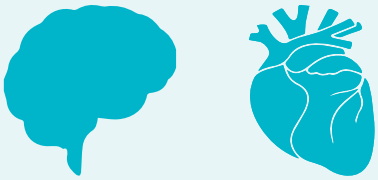
Adapted from Eng CM, Fletcher J, Wilcox WR, et al. *J Inherit Metab Dis*. 2007;30(2):192 and Schiffmann R, Hughes DA, Linthorst GE, et al. *Kidney Int*. 2017;91(2):284-293.

NEPHROLOGISTS CAN IDENTIFY FABRY DISEASE BEFORE SERIOUS COMPLICATIONS OCCUR.[6]



Renal manifestations may include[26]:

- Proteinuria
- Elevated serum creatinine
- Podocyte injury
- Glomerular sclerosis
- Fibrosis
- Renal failure/ESRD



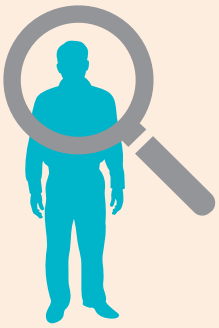
Nonrenal manifestations may include[2]:

- Neuropathic pain in the hands and feet
- Impaired sweating
- Heat/cold intolerance
- Angiokeratomas
- Early cardiac disease
- Early TIA/stroke

TIA=transient ischemic attack.

RULE OUT FABRY DISEASE IN YOUR PATIENTS WITH UNEXPLAINED CKD.

Renal Best Practice Guidelines recommend screening patients with unexplained CKD[27]



Screening **MALES** <50 years of age with unexplained CKD

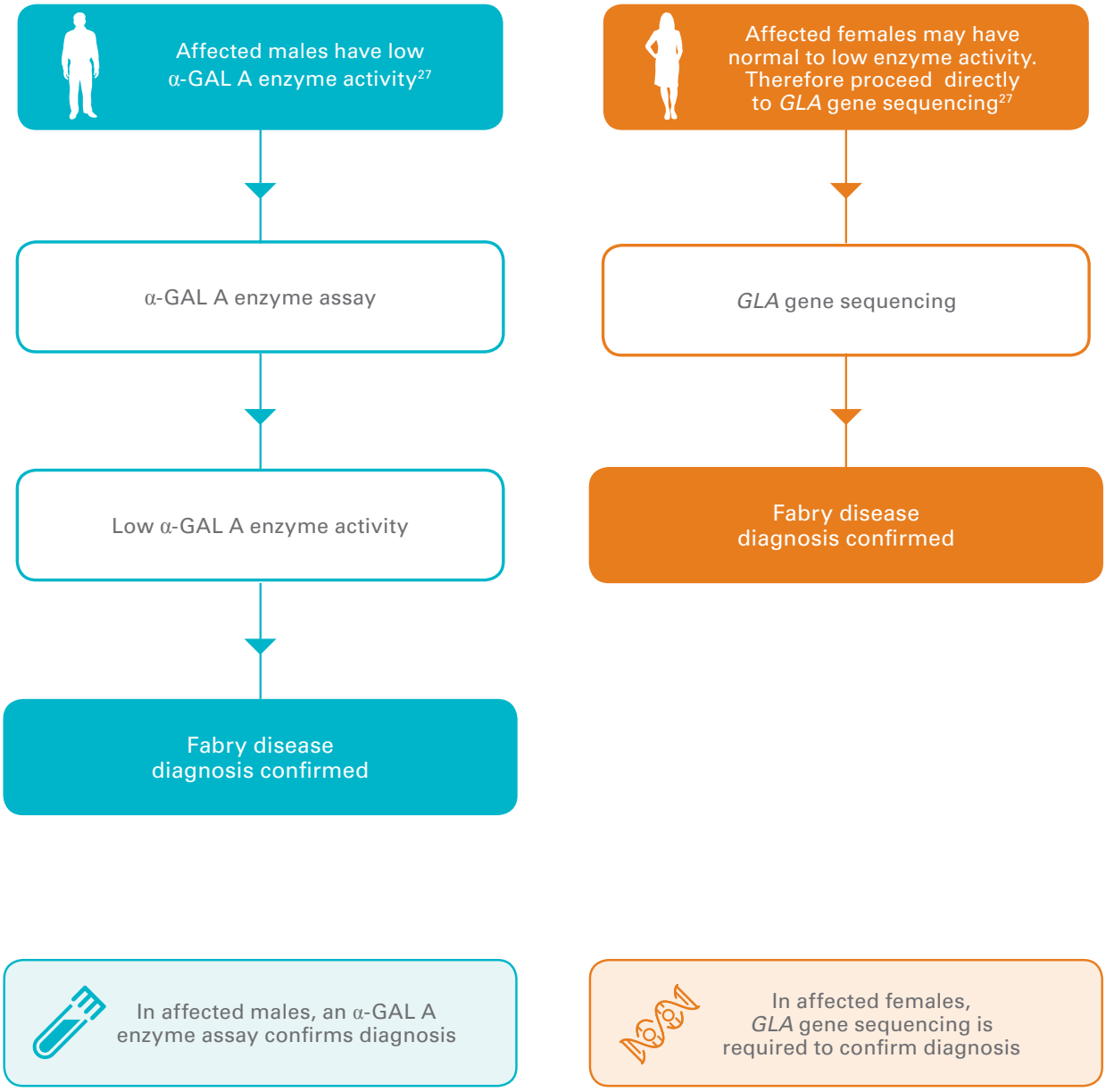
Screening **FEMALES** at any age with unexplained CKD and other symptoms associated with Fabry disease

FABRY DISEASE AFFECTS FAMILIES

For every index patient diagnosed, an average of **5 additional affected family members** may be identified[19]

TESTING FOR FABRY DISEASE IS SIMPLE.

Diagnostic testing can be easily incorporated into standard clinical practice



CAN YOU SOLVE THIS DIAGNOSTIC CHALLENGE?

CASE STUDY: Ben, a 32-year-old man presenting with unexplained proteinuria

Nonspecific signs and symptoms that overlap with more common diseases often make diagnosis of rare diseases a challenge. Additionally, diagnosis can be delayed when manifestations affect multiple organ systems, if they are considered in isolation rather than holistically.

Ben presented with unexplained proteinuria

Clinical History

SINCE TEENS	IN 20s	OVER PAST 2 YEARS
Impaired sweating and heat/temperature intolerance	Reduced exercise tolerance, recurrent abdominal pain, episodes of diarrhea and constipation	Polyuria and development of pain and numbness in arms/legs following heavy exercise

Do you know a patient like Ben?

CAN YOU SOLVE THIS DIAGNOSTIC CHALLENGE?

CASE STUDY: Ben, a 32-year-old man presenting with unexplained proteinuria (continued)

Pertinent clinical and laboratory findings

CLINICAL FINDINGS	LABORATORY FINDINGS
BP 125/85 mmHg	eGFR 80 mL/min/1.73 m^2
BMI and HR in normal ranges	Proteinuria (0.75 g/24 hours)
Abdominal, pelvic, and genital angiokeratomas	

↓

Based on clinical and laboratory findings, the nephrologist suspects Fabry disease

↓

Diagnosis of Fabry disease is confirmed by low plasma α-GAL A activity of 0.08 nmol/hr/mL

↓

Family screening was conducted after Ben tested positive for Fabry disease

eGFR=estimated GFR.

Ben exhibited signs and symptoms of Fabry disease since childhood but remained undiagnosed for ~15 years

An earlier diagnosis of Fabry could have helped better manage the disease and identify other affected family members

THE PROGRESSION AND MANAGEMENT OF FABRY DISEASE IN CHILDREN AND MEN[1,2]

CHILDREN

In the Fabry Registry:

- **77%** of boys and **51%** of girls reported symptoms (N=352)[28]
- Median ages of symptom onset were **6 and 9 years** in boys and girls, respectively (N=352)[28]
- **53%** of boys and **87%** of girls with symptoms that warrant treatment remain untreated[28]

ERT should be considered in symptomatic pediatric patients[29]*

SIGNS AND SYMPTOMS WARRANTING TREATMENT[29]

NEUROLOGIC	• Neuropathic pain crises • Fabry neuropathy
RENAL	• Decline in eGFR • Pathological albuminuria • Pathological proteinuria • Creatinine elevation • Cellular GL-3 accumulation • Evidence of tissue damage, such as podocyte effacement
CARDIAC	• Cardiomyopathy • Arrhythmia, including sinus bradycardia attributable to Fabry disease
GI	• Recurrent abdominal pain and diarrhea (excluding alternative causes)
OTHER	• Exercise intolerance and impaired sweating

MEN

In the Fabry Registry:

- Male patients experienced a high frequency of symptoms at an early age[12]
- Median age at time of diagnosis was **24 years**[12]
- Men experienced a mean delay of **14 years** from symptom onset to diagnosis[12]

ERT should be considered for men at time of diagnosis[6]

Classic Fabry mutation (symptomatic or asymptomatic):

- ERT should be considered and is appropriate
- Treatment decisions may be influenced by advanced age of the patient and severe comorbidity

Nonclassic Fabry mutation or missense *GLA* VUS:

- ERT should be considered and is appropriate if there is laboratory, histological, or imaging evidence of injury to the kidney, heart, or the CNS, even in the absence of typical Fabry symptoms
- The abnormalities should be attributable to Fabry disease; this may require histological assessment or biochemical evidence of GL-3 accumulation
- The advice of an expert in genetics and management of Fabry disease should be sought for interpretation of the pathogenicity of any VUS

VUS=variants of unknown significance.

*Patients younger than 8 years of age were not included in clinical studies of Fabrazyme. The safety and efficacy of Fabrazyme in patients younger than 8 years of age have not been evaluated.

Fabrazyme (agalsidase beta) reduces globotriaosylceramide (GL-3) deposition in capillary endothelium of the kidney and certain other cell types. The reduction of GL-3 inclusions suggests that Fabrazyme may ameliorate disease expression; however, the relationship of GL-3 inclusion reduction to specific clinical manifestations of Fabry disease has not been established.[20]

THE PROGRESSION AND MANAGEMENT OF FABRY DISEASE IN WOMEN[1,2]

WOMEN

In the Fabry Registry:

- Nearly **70%** reported having signs and symptoms (N=1077)[12]
- **66%** of women with symptoms that warrant treatment remain untreated (N=1077)[12]

ERT should be considered upon early signs of Fabry disease in women[6,30]

SIGNS AND SYMPTOMS WARRANTING TREATMENT[6,30]

	Classic Symptomatic Signs/symptoms suggesting major organ involvement	**Classic Asymptomatic OR Nonclassic†** Lab/histological/imaging evidence of injury to kidney, heart, or CNS
RENAL	Proteinuria/albuminuria not attributable to other causes, evidence of renal impairment	GFR <90 mL/min/1.73 m^2 for age >40 years, albuminuria >30 mg/g Podocyte foot process effacement on renal biopsy Moderate or severe GL-3 inclusions in a range of renal cell types
CARDIAC	Symptomatic cardiac disease not due to other causes (dyspnea, palpitation, syncope, chest pain)	Asymptomatic cardiac disease (cardiomyopathy or arrhythmia, cardiac fibrosis on contrast cardiac MRI)
CNS	Stroke/TIA	Silent strokes, cerebral white matter lesions (on brain MRI)
PAIN	Neuropathic pain, pain crises, Fabry disease neuropathy	
GI	Recurrent diarrhea; chronic, disabling GI dysfunction (excluding alternative causes)	
OTHER	Exercise intolerance and impaired sweating	

VUS=variants of unknown significance.

†Nonclassic or missense GLA VUS have the same recommendation for males and females.

Fabrazyme (agalsidase beta) reduces globotriaosylceramide (GL-3) deposition in capillary endothelium of the kidney and certain other cell types. The reduction of GL-3 inclusions suggests that Fabrazyme may ameliorate disease expression; however, the relationship of GL-3 inclusion reduction to specific clinical manifestations of Fabry disease has not been established.[20]

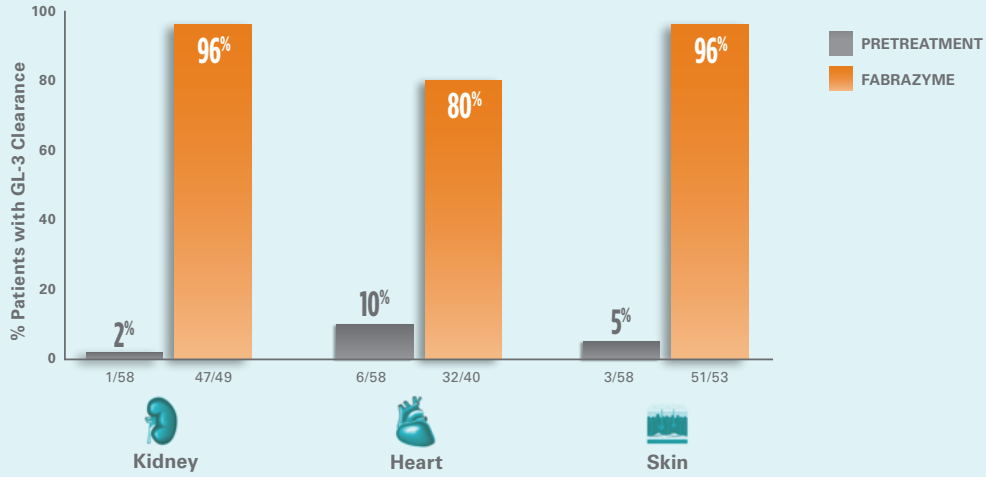
COUNT ON FABRAZYME®.

Fabrazyme® agalsidase beta

FABRAZYME cleared GL-3 as quickly as 5 months in the capillary endothelium of the kidney, heart, and skin[20]

- Study 1: At 5 months, a GL-3 inclusion score of 0 was achieved in the capillary endothelium of the kidney by 20 (69%) Fabrazyme patients compared with 0 (0%) placebo patients
- Similar reductions in GL-3 inclusions were also achieved in the capillary endothelium of the heart and skin, in 21 (72%) Fabrazyme patients compared with 1 (3%) placebo patient, and 29 (100%) Fabrazyme patients compared with 1 (3%) placebo patient, respectively
- Study 1 open-label extension: At 6 months, the majority of patients treated with Fabrazyme had a GL-3 inclusion score of 0 in the capillary endothelium of the kidney, heart, and skin

Fabrazyme-treated patients with GL-3 clearance at 6 months in the extension study[7,20*†]



In the Study 1 open-label extension[20]:

- **GL-3 decreased to normal or near-normal levels in mesangial cells, glomerular capillary endothelium, interstitial cells, and noncapillary endothelium**
- **GL-3 was reduced in vascular smooth muscle cells and renal cells, including tubular epithelium and podocytes**

*Study 1: Randomized, 1:1, double-blind, placebo-controlled study. 58 patients with Fabry disease (56 males, 2 females), 16 to 61 years, all naive to ERT. Patients received either 1 mg/kg of Fabrazyme or placebo every 2 weeks for 5 months. Inclusion severity ranged from 0 (normal or near normal) to 3 (severe inclusions). All 58 patients in Study 1 participated in the Study 1 extension, a 54-month, open-label extension trial.

† Placebo patients began Fabrazyme treatment at entry into the open-label extension. This graph represents pooled results from all patients in the study (Fz/Fz and Pl/Fz).

SELECTED IMPORTANT SAFETY INFORMATION

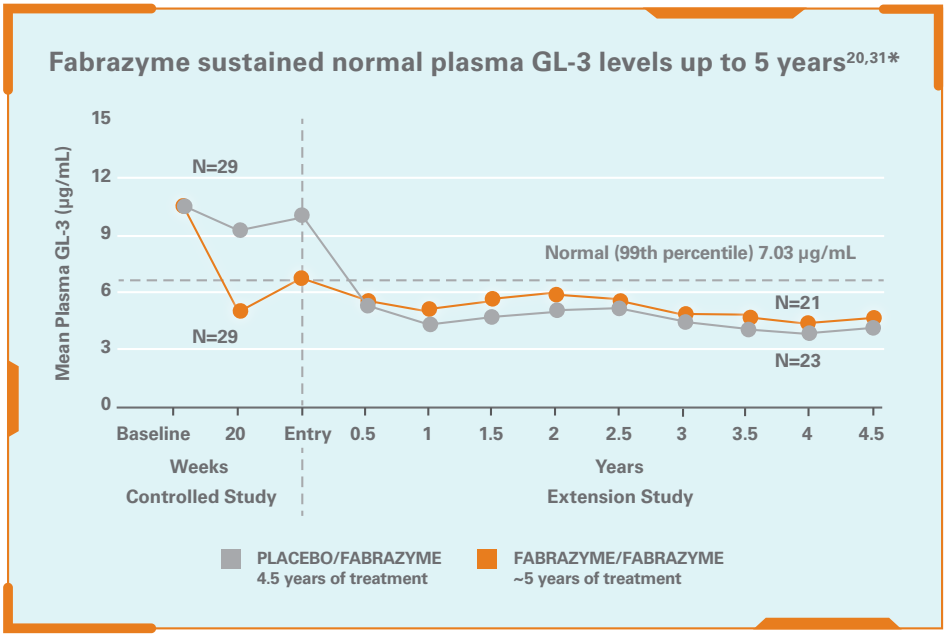
WARNINGS AND PRECAUTIONS

Anaphylaxis and Allergic Reactions: Life-threatening anaphylactic and severe allergic reactions have been observed in patients during Fabrazyme infusions. In clinical trials and postmarketing safety experience, approximately 1% of patients developed anaphylactic or severe allergic reactions during Fabrazyme infusions.

COUNT ON FABRAZYME.

Fabrazyme® agalsidase beta

FABRAZYME rapidly normalized plasma GL-3 and maintained it for up to 5 years[20,31]



- Similar long-term responses were seen in a majority of patients, with sustained GL-3 clearance in the capillary endothelium of the kidney (8/8), heart (6/8) and skin (31/36) at 4.5 years[20]
- The reduction of GL-3 inclusions suggests that Fabrazyme may ameliorate disease expression; however, the relationship of GL-3 inclusion reduction to specific clinical manifestations of Fabry disease has not been established[20]

Fabrazyme Also Cleared GL-3 in Pediatric Populations ≥8 years[20†]

- In 12 male patients, Fabrazyme achieved GL-3 inclusion scores of 0 in the capillary endothelium of the skin at 24 weeks and 48 weeks. Two male patients had no measurable GL-3 inclusions at baseline
- In 14 male patients, Fabrazyme normalized plasma GL-3 levels at 24 weeks and sustained levels at 48 weeks

†Study Design: Open-label, uncontrolled, multinational, multicenter study to evaluate safety, pharmacokinetics, and pharmacodynamics of Fabrazyme treatment in pediatric patients. Study Population: 16 pediatric patients (14 males, 2 females) aged 8 to 16 years at first treatment. Study Dose: Fabrazyme 1 mg/kg every 2 weeks for up to 48 weeks.

Female patients had no measurable GL-3 inclusions and had normal plasma GL-3 levels at baseline, which remained normal through 48 weeks.

SELECTED IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (continued)

- Reactions have included localized angioedema (including swelling of the face, mouth, and throat), bronchospasm, hypotension, generalized urticaria, dysphagia, rash, dyspnea, flushing, chest discomfort, pruritus, and nasal congestion.
- Interventions have included cardiopulmonary resuscitation, oxygen supplementation, IV fluids, hospitalization, and treatment with inhaled beta-adrenergic agonists, antihistamines, epinephrine, and IV corticosteroids.
- If severe allergic or anaphylactic reactions occur, immediately discontinue administration of Fabrazyme and provide necessary emergency treatment. Because of the potential for severe allergic reactions, appropriate medical support measures should be readily available when Fabrazyme is administered.

COUNT ON FABRAZYME®. COUNT ON EXPERIENCE.

Fabrazyme® agalsidase beta

FABRAZYME is the longest-studied Fabry disease therapy[32]

OVER 15 YEARS

Over **15 years** of real-world experience[32]

Chosen for more than **4500 patients** worldwide[32]

Can be used for patients regardless of genotype or disease severity[20]

Heather and Cindy, *Fabry patients*

Alexsia, *Fabry patient*

SELECTED IMPORTANT SAFETY INFORMATION

Infusion-Associated Reactions: In clinical trials with Fabrazyme, 59% of patients experienced infusion-associated reactions, some of which were severe.

- In patients experiencing infusion-associated reactions, pretreatment with an antipyretic and antihistamine is recommended. Infusion-associated reactions occurred in some patients after receiving pretreatment.
- If an infusion-associated reaction occurs, decreasing the infusion rate, temporarily stopping the infusion, and/or administrating additional antipyretics, antihistamines, and/or steroids may ameliorate the symptoms.

COUNT ON OPTIONS.

Fabrazyme® agalsidase beta

FABRAZYME can be administered in multiple treatment settings

PHYSICIAN OFFICES

INFUSION CENTERS

HOME

- Choice of treatment setting is at the discretion of the physician
- Because of the potential for severe infusion-associated reactions, appropriate medical support measures should be readily available

Charles and Amanda, *Fabry patients*

Braulio and Clara, *Fabry patients*

SELECTED IMPORTANT SAFETY INFORMATION

- If severe infusion-associated reactions occur, immediate discontinuation of the administration of Fabrazyme should be considered, and appropriate medical treatment should be initiated. Severe reactions are generally managed with administration of antihistamines, corticosteroids, intravenous fluids, and/or oxygen when clinically indicated. Because of the potential for severe infusion-associated reactions, appropriate medical support measures should be readily available when Fabrazyme is administered.

COUNT ON THE WELL-ESTABLISHED SAFETY PROFILE OF FABRAZYME®.

Fabrazyme® agalsidase beta

The safety of FABRAZYME has been assessed in 4 clinical trials involving 162 patients with over 473 patient-years of experience[20,32]

- Approximately 1% of patients in clinical trials and postmarketing safety experience developed life-threatening anaphylactic or severe allergic reactions
- In clinical trials, 59% of patients experienced infusion-associated reactions during Fabrazyme treatment, some of which were severe
- Over time Fabrazyme, infusion-associated reactions tended to decline during clinical trials; however, they may still occur despite extended duration of treatment
- A standard pretreatment approach with an antipyretic and antihistamine is recommended for patients experiencing infusion-associated reactions; however, in clinical trials, infusion-associated reactions occurred in some patients after receiving pretreatment
- Patients with advanced Fabry disease may have compromised cardiac function, which may predispose them to a higher risk of severe complications from infusion-associated reactions, and these patients should be monitored closely during Fabrazyme administration
- Re-administration of Fabrazyme to patients who have previously experienced severe or serious allergic reactions to Fabrazyme should be done only after careful consideration of the risks and benefits of continued treatment, and only under the direct supervision of qualified personnel and with appropriate medical support measures readily available

Charles, Heather, and Amanda, *Fabry patients*

Please see Important Safety Information on pages 18–19 and full Prescribing Information.

SUMMARY OF COMMON ADVERSE REACTIONS IN CLINICAL TRIALS

Fabrazyme® agalsidase beta

Occurring in at least 5% of FABRAZYME-treated patients at an incidence >2.5% compared with placebo-treated patients[20]

Adverse Reaction	Fabrazyme (n=80) %	Placebo (n=60) %
Upper respiratory tract infection	44	30
Chills	43	12
Pyrexia	39	22
Headache	39	28
Cough	33	25
Paresthesia	31	18
Fatigue	24	17
Peripheral edema	21	7
Dizziness	21	8
Rash	20	10
Pain in extremity	19	8
Nasal congestion	19	15
Lower respiratory tract infection	18	7
Pain	16	13
Back pain	16	10
Myalgia	14	5
Hypertension	14	5
Feeling cold	11	2
Pruritus	10	3
Tachycardia	9	3

Adverse Reaction	Fabrazyme (n=80) %	Placebo (n=60) %
Sinusitis	9	3
Excoriation	9	2
Increased blood creatinine	9	5
Tinnitus	8	3
Dyspnea	8	2
Respiratory tract congestion	8	2
Toothache	6	3
Pharyngitis	6	2
Fall	6	3
Burning sensation	6	0
Anxiety	6	3
Depression	6	2
Wheezing	6	0
Hypoacusis	5	0
Chest discomfort	5	2
Fungal infection	5	0
Viral infection	5	0
Muscle spasms	5	2
Hot flush	5	0

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IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Anaphylaxis and Allergic Reactions: Life-threatening anaphylactic and severe allergic reactions have been observed in patients during Fabrazyme infusions. In clinical trials and postmarketing safety experience, approximately 1% of patients developed anaphylactic or severe allergic reactions during Fabrazyme infusions.

- Reactions have included localized angioedema (including swelling of the face, mouth, and throat), bronchospasm, hypotension, generalized urticaria, dysphagia, rash, dyspnea, flushing, chest discomfort, pruritus, and nasal congestion.
- Interventions have included cardiopulmonary resuscitation, oxygen supplementation, IV fluids, hospitalization, and treatment with inhaled beta-adrenergic agonists, antihistamines, epinephrine, and IV corticosteroids.
- If severe allergic or anaphylactic reactions occur, immediately discontinue administration of Fabrazyme and provide necessary emergency treatment. Because of the potential for severe allergic reactions, appropriate medical support measures should be readily available when Fabrazyme is administered.

Infusion-Associated Reactions: In clinical trials with Fabrazyme, 59% of patients experienced infusion-associated reactions, some of which were severe.

- In patients experiencing infusion-associated reactions, pretreatment with an antipyretic and antihistamine is recommended. Infusion-associated reactions occurred in some patients after receiving pretreatment.
- If an infusion-associated reaction occurs, decreasing the infusion rate, temporarily stopping the infusion, and/or administrating additional antipyretics, antihistamines, and/or steroids may ameliorate the symptoms.
- If severe infusion-associated reactions occur, immediate discontinuation of the administration of Fabrazyme should be considered, and appropriate medical treatment should be initiated. Severe reactions are generally managed with administration of antihistamines, corticosteroids, intravenous fluids, and/or oxygen when clinically indicated. Because of the potential for severe infusion-associated reactions, appropriate medical support measures should be readily available when Fabrazyme is administered.

Compromised Cardiac Function: Patients with advanced Fabry disease may have compromised cardiac function, which may predispose them to a higher risk of severe complications from infusion-associated reactions. Patients with compromised cardiac function should be monitored closely if the decision is made to administer Fabrazyme.

Immunogenicity and Rechallenge: In clinical trials, a few patients developed IgE or skin test reactivity specific to Fabrazyme. Physicians should consider testing for IgE in patients who experienced suspected allergic reactions. Re-administration of Fabrazyme to patients who have previously experienced severe or serious allergic reactions to Fabrazyme should be done only after careful consideration of the risks and benefits of continued treatment, and only under the direct supervision of qualified personnel and with appropriate medical support measures readily available.

IMPORTANT SAFETY INFORMATION (continued)

Fabrazyme® agalsidase beta

ADVERSE REACTIONS

- Common adverse reactions reported (≥20% and >2.5% compared to placebo) were upper respiratory tract infection (44% vs 30%), headache (39% vs 28%), cough (33% vs 25%), paresthesia (31% vs 18%), fatigue (24% vs 17%), dizziness (21% vs 8%), peripheral edema (21% vs 7%), and rash (20% vs 10%).
- Serious and/or frequently occurring (≥ 5% incidence) related adverse reactions based on a pooled analysis of 150 patients treated with Fabrazyme in double-blind and open-label clinical studies consisted of one or more of the following: chills, fever, feeling hot or cold, dyspnea, nausea, flushing, headache, vomiting, paresthesia, fatigue, pruritus, pain in extremity, hypertension, chest pain, throat tightness, abdominal pain, dizziness, tachycardia, nasal congestion, diarrhea, edema peripheral, myalgia, back pain, pallor, bradycardia, urticaria, hypotension, face edema, rash, and somnolence.
- Other serious adverse events reported in clinical studies included stroke, pain, ataxia, bradycardia, cardiac arrhythmia, cardiac arrest, decreased cardiac output, vertigo, and nephrotic syndrome. These adverse events also occur as manifestations of Fabry disease; an alteration in frequency or severity cannot be determined from the small numbers of patients studied.
- Adverse reactions (regardless of relationship) resulting in death reported in the postmarketing setting with Fabrazyme treatment included cardiorespiratory arrest, respiratory failure, cardiac failure, sepsis, cerebrovascular accident, myocardial infarction, renal failure, and pneumonia. Some of these reactions were reported in Fabry disease patients with significant underlying disease.

The safety and efficacy of Fabrazyme in patients younger than 8 years of age have not been evaluated.

REFERENCES

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RULE OUT FABRY DISEASE IN YOUR PATIENTS WITH UNEXPLAINED CKD.

Fabrazyme® agalsidase beta

- Fabry disease can have a serious impact on essential organs, including the kidney[7,8]
- Renal damage as a result of GL-3 accumulation can start as early as the first decade of life, often preceding laboratory abnormalities and clinical symptom onset[5,25]
- Renal Best Practice Guidelines recommend screening patients with unexplained CKD for Fabry disease[27]
- Nephrologists are in a unique position to identify early signs of Fabry disease, which can help lead to timely diagnosis[6]

COUNT ON FABRAZYME®.

The longest-studied Fabry disease therapy[32]

Over 15 years of real-world experience[32]

Chosen for more than 4500 patients worldwide[32]

- Can be used in patients regardless of genotype or disease severity[20]
- Cleared GL-3 as quickly as 5 months in the capillary endothelium of the kidney, heart, and skin in Study 1[20*]
- Normalized plasma GL-3 and sustained clearance for approximately 5 years in the Study 1 open-label extension[20,31]
- Has a well-established safety profile[20]

*At 5 months, GL-3 clearance was observed in the capillary endothelium of the: **Kidney:** 20 (69%) Fabrazyme patients compared with 0 (0%) placebo patients; **Heart:** 21 (72%) Fabrazyme patients compared with 1 (3%) placebo patient; **Skin:** 29 (100%) Fabrazyme patients compared with 1 (3%) placebo patient.

SELECTED IMPORTANT SAFETY INFORMATION

- If an infusion-associated reaction occurs, decreasing the infusion rate, temporarily stopping the infusion, and/or administrating additional antipyretics, antihistamines, and/or steroids may ameliorate the symptoms.
- If severe infusion-associated reactions occur, immediate discontinuation of the administration of Fabrazyme should be considered, and appropriate medical treatment should be initiated.
- Severe reactions are generally managed with administration of antihistamines, corticosteroids, intravenous fluids, and/or oxygen when clinically indicated.

INDICATION AND USAGE

Fabrazyme® (agalsidase beta) is indicated for use in patients with Fabry disease.
Fabrazyme reduces globotriaosylceramide (GL-3) deposition in capillary endothelium of the kidney and certain other cell types.

The reduction of GL-3 inclusions suggests that Fabrazyme may ameliorate disease expression; however, the relationship of GL-3 inclusion reduction to specific clinical manifestations of Fabry disease has not been established.

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