DISEASE MONOGRAPH

Not an actual physician.

Gaucher Disease Type 1

A progressive, rare, lifelong disease that can go undiagnosed for years[1]

Skeletal | Hematologic | Visceral | Metabolic

sanofi

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Gaucher disease is a lysosomal storage disorder caused by deficient activity of the lysosomal enzyme acid ß-glucosidase (also called glucocerebrosidase and glucosylceramidase), which results in the accumulation of its substrate glucosylceramide (GL-1, also called glucocerebroside).[2]

The progressive accumulation of GL-1 in lysosomes of the macrophage system, particularly in the spleen, liver, and bone marrow, can lead to progressive spleen and liver enlargement, thrombocytopenia, and bone abnormalities.[2,3]

Estimated to affect approximately 1 in 40,000 to 1 in 60,000 individuals in the general population, Gaucher disease type 1 is especially prevalent among those of Ashkenazi Jewish ancestry, in whom it is estimated to affect approximately 1 in 850.[2,4]

Gaucher disease is a lifelong condition marked by diversity in both genotype and phenotype (including the age of onset, disease severity, as well as an unpredictable, progressive disease course).[5]

Signs, symptoms, and clinical course may even differ among individuals with the same variant(s) and within the same family.[5]

The clinical manifestations of Gaucher disease type 1 include splenomegaly (most common), hepatomegaly, anemia, thrombocytopenia, and bone disease. These patients are also at increased risk for hematological malignancies, such as multiple myeloma.[2]

The clinical presentation of Gaucher disease type 1 may range from individuals being asymptomatic or mildly symptomatic to others who may experience life-threatening progression of their disease.[2,5]

In order to enhance the understanding of the course of Gaucher disease and evaluate the effectiveness of available disease management strategies, the International Collaborative Gaucher Group (ICGG) established the Gaucher Registry in 1991. The Gaucher Registry has more than 750 participating physicians in 60 countries contributing data and is the largest database on patients with Gaucher disease. The Gaucher Registry is sponsored by Sanofi and governed by the ICGG, an international group of experts in Gaucher disease. The Gaucher Registry collects observational longitudinal data that can be retrospectively analyzed to provide a better understanding of the natural history of Gaucher disease and context for its management.

Genetics

Gaucher disease is an autosomal recessive disorder defined by the presence of 2 pathogenic variant(s) *in trans* for the acid ß-glucosidase (*GBA*) gene, localized to chromosome 1 in region q21.[2,4]

- To date, more than 300 variants that partially or entirely decrease the catalytic activity of acid ß-glucosidase, and often reduce its stability, have been identified[2,4]
- The 4 most common of these variants (*N370S*, *L444P*, *84GG*, and *IVS2+1*) account for approximately 90% of the pathogenic variants in the Ashkenazi Jewish population[4]
- Non-Jewish individuals with Gaucher disease tend to be compound heterozygotes with 1 common and 1 rare/novel pathogenic variant[4]
- The clinical features and course of the disease can vary among patients with the same variant(s)[5]

With regard to correlations between genotype and phenotype, the presence of at least 1 *N370S* variant predicts non-neuronopathic disease (ie, type 1 disease).[2]

Not an actual patient.

Biochemical, Molecular, and Cellular Bases

In healthy individuals, acid ß-glucosidase in lysosomes breaks down GL-1, which is a glycolipid arising in the membranes of worn-out cells. The activity of acid ß-glucosidase occurs within the lysosomes of cells.[2]

In individuals with Gaucher disease, the catalytic breakdown of GL-1 is insufficient, leading to accumulation of the substrate within cells of the monocyte/macrophage lineage, which are called "Gaucher cells."[2]

- These lipid-engorged cells have a distinctive appearance in which cytoplasm resembles "wrinkled tissue paper"
- These aberrant macrophages accumulate progressively, primarily in the liver, spleen, and bone marrow and occasionally in lungs, kidneys, and intestines

This accumulation may disrupt organ function and may lead to irreparable damage. Studies suggest that the engorged Gaucher cells may stimulate increased release of cytokines, such as interleukin-6, interleukin-10, and tumor necrosis factor alpha, which in turn may contribute to the pathogenesis of the disease.[2,6]

Clinical Classification

Gaucher disease has been classified into 3 types based on the presence and severity of neurologic involvement. Type 1 disease is the most prevalent type, occurring in more than 90% of patients, and does not have the central nervous system manifestations that are seen in type 2 and type 3 Gaucher disease at diagnosis.[2,7]

- Estimates are that Gaucher disease type 1 affects approximately 1 in 40,000 to 60,000 individuals[4]
- Its incidence is panethnic, but is higher among Ashkenazi Jews, with approximately 1 in 850 being affected and an estimated carrier rate of 1 in 15 for *GBA* variants[2,8]

The signs and symptoms of Gaucher disease type 1 and its clinical course are variable and may even differ among individuals with the same variant(s) and within the same family. Some patients may be asymptomatic or mildly symptomatic, while others may experience life-threatening progression. Although clinical onset may occur at any age, some patients may not experience onset until adulthood.[2,5]

Type 2 and type 3 Gaucher disease involve the central nervous system. Type 2 is also known as acute infantile neuronopathic Gaucher disease, and type 3 is also known as chronic neuronopathic Gaucher disease. Both types are rare, panethnic, progressive, and potentially fatal.[2,4,9]

Not an actual physician.

Pathogenesis, Signs, and Symptoms of Gaucher Disease Type 1

The accumulation of Gaucher cells in various organs and tissues accounts for the multisystemic nature of Gaucher disease. Signs and symptoms may include one or more of the following[2]:

Visceral Involvement

At the time of Gaucher disease type 1 diagnosis, moderate-to-severe spleen and liver enlargement are present in 86% and 65% of patients, respectively. Splenomegaly is usually characteristic of Gaucher disease type 1 and is progressive, with splenic enlargement up to 15 or more times the normal volume. Hepatomegaly is also common, with liver volumes generally increasing up to 1.25 to 2.5 or more times normal. Pulmonary involvement occurs less commonly; however, pulmonary failure can be a life-threatening consequence of Gaucher disease.[2,7,10]

Skeletal Involvement

Data on disease progression have created a heightened awareness regarding the frequency and severity of skeletal involvement in Gaucher disease type 1. Skeletal involvement is often the most debilitating aspect of Gaucher disease type 1. Some types of skeletal involvement are illustrated on the following page in Figures 1A-F.[2]

In a Gaucher Registry data analysis, radiologic evidence of bone disease at diagnosis was found in 83% of patients with bone diseases and 82% with bone marrow infiltration.[10]

At the time of diagnosis, patients with skeletal involvement may have a variety of functional and metabolic bone defects and additional major complications, including but not limited to bone marrow infiltration with Gaucher cells (Figure 1A), Erlenmeyer flask deformity (Figure 1B), pathologic fracture (Figures 1C and 1D), osteopenia (Figure 1E), and osteonecrosis (Figure 1F).[2,7]

Hematologic Abnormalities

Splenic sequestration and overactivity, along with infiltration of the bone marrow and displacement of hematopoietic elements by Gaucher cells, frequently produce laboratory and/or clinical hematological abnormalities. The involvement of the spleen and liver can have many other effects on patients, including suppressing the appetite, complications of liver and splenic involvement, and low self-esteem related to appearance. There may also be abnormalities in clotting and fibrinolytic factors. Patients with Gaucher disease type 1 frequently present with anemia and thrombocytopenia. In a Gaucher Registry data analysis, at the time of diagnosis, 35% of patients had anemia, and 59% of patients had moderate-to-severe thrombocytopenia. Anemia may lead to fatigue. Thrombocytopenia may lead to excessive bruising and bleeding, even after minor trauma.[2,3,10,11]

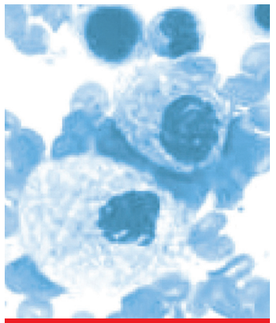


Figure 1A.
Bone marrow infiltration with Gaucher cells

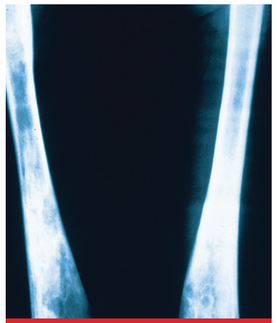


Figure 1B.
Erlenmeyer flask deformity

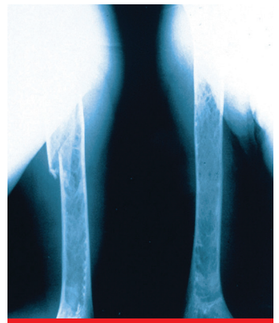


Figure 1C.
Pathologic fracture

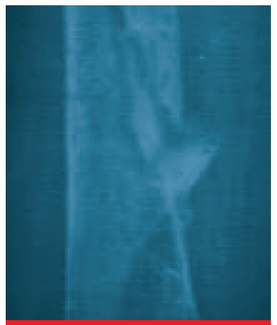


Figure 1D.
Pathologic fracture

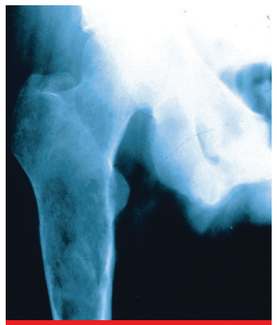


Figure 1E.
Osteopenia

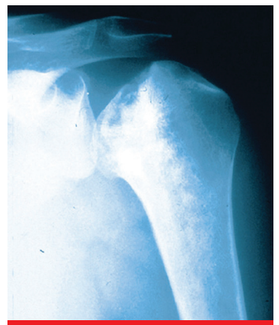


Figure 1F.
Osteonecrosis

Metabolic Disturbances and Constitutional Symptoms

Individuals with Gaucher disease have been shown to have a "resting energy expenditure" that is more than 40% greater than normal. This metabolic burden contributes to the sometimes considerable fatigue that many patients with Gaucher disease experience. It may also contribute to growth delay in children with Gaucher disease type 1. Growth retardation appears to affect both sexes equally and correlates positively with earlier onset and increased disease severity.[3,12,13]

Impact on Quality of Life

Gaucher disease can severely impair the quality of life of patients. Skeletal involvement, such as thoracic vertebral compression and osteoporosis, may lead to decreased ability to perform normal activities of daily living. Patients with bone involvement have been reported to have a significantly decreased health-related quality of life (HRQoL) relative to the general population of the United States.[3,14]

Weinreb and colleagues have shown that quality of life (SF-36) physical scores are lowest for those patients with the highest pain ratings and the most advanced bone presentation, characterized by the presence of medullary infarction, lytic lesions, and/or avascular necrosis. Complications of skeletal involvement may include excruciating acute and/or chronic pain, progressive and debilitating bone or joint destruction (often with flawed healing), kyphosis, and scoliosis. These complications in turn may require hospitalization and complex surgical interventions such as total joint replacement. Severe anemia or thrombocytopenia may require blood or platelet transfusions. When combined with skeletal complications, the symptoms associated with Gaucher disease can diminish patients' feelings of well-being and functional health and prevent them from working or pursuing family or leisure activities.[11,14-16]

Skeletal involvement in patients with Gaucher disease type 1[7,10-12,17]:

- Is very common
- May not be widely recognized as related to visceral and hematologic complications
- Often contributes to significant morbidity and diminished quality of life
- Is often associated with severe pain and considerable impairment of mobility
- Can be significant and progressive, even in patients with no apparent visceral and hematologic manifestations
- May have devastating and potentially irreversible consequences

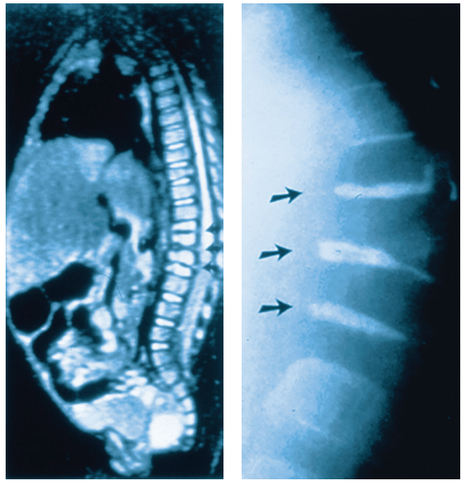


Figure 2. Thoracic vertebral compression and osteoporosis

Gaucher Disease in Childhood

In a Gaucher registry data analysis, 49% of patients with Gaucher disease type 1 were diagnosed before the age of 10, and approximately 66% of patients with Gaucher disease type 1 were diagnosed by the age of 20. Early onset is usually predictive of a more severe, rapidly progressive phenotype.[2] When disease manifests in childhood, patients often have a more severe phenotype. Disease-specific intervention may prevent the irreversible pathology.[3]

The Gaucher Registry provided statistics on the occurrence of manifestations in 887 children diagnosed with Gaucher disease type 1. Patients were younger than 18 years and had not received disease-specific management options (untreated).[12]

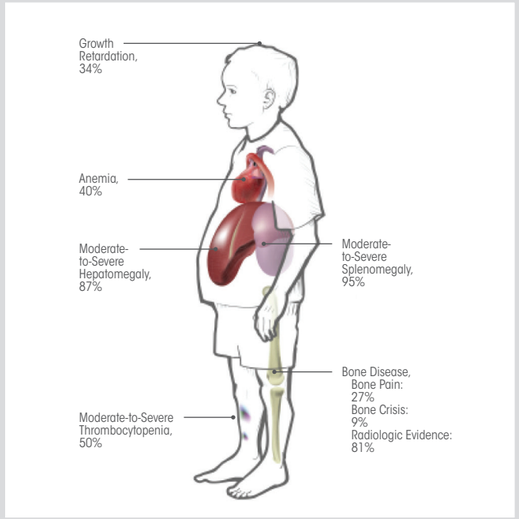
In these untreated patients, the incidence of disease manifestations was as follows (also see Figure 3)[12]:

- Splenomegaly, 95%
- Hepatomegaly, 87%
- Radiologic bone disease, 81%
- Thrombocytopenia, 50%
- Anemia, 40%
- Growth retardation, 34%
- Bone pain, 27%
- Bone crisis, 9%

For younger patients, the occurrence of anemia and more severe splenomegaly and hepatomegaly were observed, while skeletal manifestations were found more often in older children.[12]

Figure 3. Incidence of manifestations in untreated children with Gaucher disease type 1[12]

- Growth retardation refers to patients below the 5th percentile
- Anemia is defined according to age and sex references for hemoglobin concentrations as follows: <11 g/dL for boys aged 12 years and older; <10 g/dL for girls 12 years and older; <9.5 g/dL for children aged 2 to younger than 12 years; <8.5 g/dL for children aged 6 months to younger than 2 years; <9.1 g/dL for infants younger than 6 months
- Hepatomegaly (liver volume in multiples of normal) is defined as moderate (>1.25 to 2.5) to severe (>2.5)
- Splenomegaly (spleen volume in multiples of normal) is defined as moderate (>5 to 15) to severe (>15)
- Thrombocytopenia (platelet count, $x10^3/mL^3$) is defined as moderate (>60 to 120) to severe (<60)
- Radiologic evidence of bone disease may indicate Erlenmeyer flask deformity, marrow infiltration, osteopenia, avascular necrosis, infarction, lytic lesions, and/or new fractures



Diagnosis of Gaucher Disease Type 1

Due to the rarity and complexity of Gaucher disease and the lack of disease awareness among clinicians, diagnosis may be delayed for years.[1]

- In a global survey of 406 hematology-oncology specialists, only 20% considered Gaucher disease in the differential diagnosis of a sample patient exhibiting all the disease's classic symptoms (cytopenia, hepatosplenomegaly, and bone pain)
- A survey of 136 patients with Gaucher disease type 1 reported an average of 4 years from first appearance of symptoms to final diagnosis

Delayed diagnosis and management of Gaucher disease may lead to severe and sometimes irreversible complications.[1]

A definitive diagnosis of Gaucher disease is confirmed by results of laboratory testing demonstrating a deficiency of acid ß-glucosidase activity in peripheral blood leukocytes or other nucleated cells, and/or by the presence of 2 pathogenic variants *in trans* in the *GBA* gene.[18]

- Generally, a reading of 10% to 30% of normal enzyme activity is confirmation of a diagnosis, but the precise cutoff value depends on the laboratory used[19]
- Demonstration of 2 pathogenic variants *in trans* in the *GBA* gene can diagnose Gaucher disease, but should not be used for diagnosis in lieu of biochemical testing[18]

Although bone marrow biopsy specimens can help rule out hematologic malignancies, they are not reliable for establishing the presence of Gaucher cells.[19]

- Bone marrow infiltration by Gaucher cells is heterogeneous. Not detecting Gaucher cells in bone marrow samples does not rule out Gaucher disease. The presence of pseudo-Gaucher cells (ie, plasma cells that microscopically resemble Gaucher cells) in bone marrow can lead to misdiagnosis[2]
- Pseudo-Gaucher cells are also found in other disorders, such as multiple myeloma, Hodgkin disease, lymphomas, and acquired immunodeficiency syndrome (AIDS)[2]

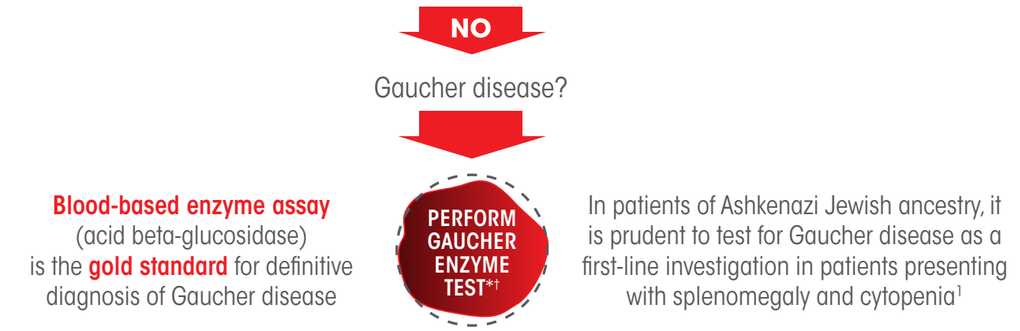
Therefore, an enzyme assay is recommended to establish a confirmatory diagnosis.[19]

Patient Identification: Key to Earlier Diagnosis and Intervention

Despite the fact that disease-specific interventions are available to patients with Gaucher disease type 1, almost 25% do not gain timely access to therapy because of delays in diagnosis. Diagnosis and management algorithms have been developed and published by Mistry and colleagues in 2011, which aim to help decrease the time to diagnosis. See Figure 4 below for a simple diagnostic algorithm adapted from the authors' recommendations.[20]

A patient with Gaucher disease may experience diagnostic delay for up to 10 years, and up to 86% of patients see a hematologist/oncologist during pursuit of their diagnosis. Therefore, greater awareness of the signs and symptoms of Gaucher disease among hematologists/oncologists, as well as other specialists, may lead to earlier identification, diagnosis, and appropriate management.[1]

Figure 4. Simple diagnostic algorithm for general population[20]



Adapted from Mistry et al. *Am J Hematol.* 2011;86(1):110-115.

Gaucher disease treatment centers provide specialized diagnostic services for patients with Gaucher disease. They are staffed by physicians and other medical professionals who specialize in the treatment of Gaucher disease, such as metabolic specialists, geneticists, hematologists, and genetic counselors. These specialists are available to offer help on this challenging condition.

*Acid-ß-glucosidase enzyme activity assays.
†Algorithm is modified from original reference.

Management, Evaluation, and Monitoring

Recommendations for the initial assessment and monitoring of patients with Gaucher disease type 1 (Table 1, page 15) have been developed by experts in the clinical management of Gaucher disease who have served as advisors of the Collaborative Gaucher Group (ICGG) Gaucher Registry.

Physicians should determine their patient's assessments and the actual frequency of necessary evaluations according to each patient's situation, including individualized therapeutic goals and routine follow-up.

- In addition to a confirmed diagnosis of enzyme deficiency and genotype determination, it is recommended that primary assessments include physical, hematologic, biochemical, visceral, and skeletal examinations and completion of the patient-reported quality of life survey (SF-36)[21]

A comprehensive assessment is recommended on at least a yearly basis, although the frequency may be dependent on treatment status and whether or not the consensus guidelines for monitoring patients, established by the ICGG, have been achieved.[21]

- Reassessment of patients is recommended when therapy has changed or in the event of the occurrence of clinical complications (Table 1)[21]
- Children should be monitored more frequently, with physical examinations at least every 6 to 12 months and 1 skeletal assessment every 1 to 2 years[17]

Hematologic Evaluations

Hematologic evaluation recommendations include the assessment of hemoglobin and platelet counts because anemia and thrombocytopenia are common in patients with Gaucher disease type 1.[21]

Biochemical Evaluations

Chitotriosidase, angiotensin-converting enzyme, and/or tartrate-resistant acid phosphatase are the recommended biochemical markers for evaluating the response to therapy. Chitotriosidase, when available as a validated procedure from an experienced laboratory, may be the most sensitive and preferred marker, although approximately 6% of patients have a variant in the gene that codes for this enzyme and may therefore not demonstrate any chitotriosidase activity. Accordingly, this marker may not be valid in some patients.[21]

Genotyping

Genotyping is highly recommended for patients with Gaucher disease type 1. Although its value is limited for prognostication and treatment decisions, it is necessary for determining the occurrence of heterozygous relatives. Currently, 7 *GBA* pathogenic variants (N370S, L444P, 84GG, IVS2+1, D409H, R463C, and V394L) appear most commonly in patients with Gaucher disease.[17,21]

Visceral Evaluations

In patients with Gaucher disease type 1 who have hepatomegaly, volumetric magnetic resonance imaging (MRI) or computed tomography (CT) is recommended for quantitative assessment of the liver volume.[22]

- Hepatomegaly is defined as liver volume greater than 1.25 x predicted normal (2.5% of total body weight)[2]

For those patients with splenomegaly, volumetric MRI or CT is recommended for quantitative assessment of spleen volume.[2]

- Ultrasonography may also be useful for identifying nodular Gaucher cell infiltration of the spleen[22]
- Splenomegaly is defined as a splenic volume greater than predicted normal (0.2%) of the total body weight[2]

Skeletal Pathology

Skeletal involvement may be the most debilitating and disabling aspect of Gaucher disease type 1 and often has the greatest impact on quality of life.[21]

Initial assessment recommendations include x-ray examination of the femora, spine, and other symptomatic areas.[21]

- T_1 and T_2-weighted MRI: evaluate marrow infiltration and some other bone abnormalities
- Plain radiographs may be used for determining the effect of disease on cortical thickness and mineral-phase lesions

Assessment recommendations also include the use of dual-energy X-ray absorptiometry (DEXA) to measure bone mineral density (BMD) for the detection of osteopenia.[21]

- DEXA is considered to be the gold standard for assessing BMD[21]
- Skeletal pathology of Gaucher disease type 1 may be focal (lytic and/or sclerotic lesions associated with infarction, thrombosis, and inflammation that may progress to osteonecrosis), local (remodeling defects and long bone deformities), or generalized (osteopenia and osteoporosis associated with an increased risk of fracture)[22]

Further recommendations for assessing and ongoing monitoring of patients, including recommendations for pulmonary evaluations and additional blood tests, are provided in Table 1.

Table 1. Schedule of assessments

Minimum Recommendations for Monitoring Adult Patients With Non-neuronopathic (Type 1) Gaucher Disease

Initial Assessment[17,21]

Blood Tests

Primary Tests	Additional Tests as Indicated[5]
Hemoglobin	AST and/or ALT
Platelet count	Alkaline phosphatase
Biochemical markers[3]	Calcium
• Chitotriosidase	Phosphorus
• ACE	PT
• TRAP	PTT
Genetic testing (DNA)	WBC
Antibody sample[4]	Total and direct bilirubin
	Albumin
	Total protein
	Serum immunoelectrophoresis
	Iron
	Iron-binding capacity
	Ferritin
	Vitamin B_{12}

Visceral[6]

Spleen volume (volumetric MRI or CT)
Liver volume (volumetric MRI or CT)

Skeletal

MRI (coronal; T_1- and T_2-weighted) of entire femora
X-ray: AP view of entire femora[7] and lateral view of spine
DEXA: lumbar spine and femoral neck
Bone age (for patients aged ≤14 years)[5]

Pulmonary[8]

ECG, chest X-ray, and Doppler echocardiogram (right ventricular systolic pressure) for patients aged >18 years

Quality of Life

Patient-reported functional health and well-being (SF-36 Health Survey)

Ongoing Monitoring[21]

	Patients Not on Therapy		Patients on Therapy			
			Not Achieved Therapeutic Goals	Achieved Therapeutic Goals		At Time of Dose Change or Significant Clinical Complication
	Every 12 Mo	Every 12-24 Mo	Every 3 Mo	Every 12 Mo	Every 12-24 Mo	
Comprehensive physical examination	X			X	X (Annual)	
SF-36 Health Survey	X			X	X (Annual)	X
Blood Tests						
Hemoglobin	X		X		X	X
Platelet count	X		X		X	X
Biochemical markers[3] • Chitotriosidase • ACE • TRAP	X		X		X	X
Additional blood tests	To be followed if abnormal, based on patient age and clinical status					
Visceral[6]						
Spleen volume (volumetric MRI or CT)	X		X		X	X
Liver volume (volumetric MRI or CT)	X		X		X	X
Skeletal[9]						
MRI (coronal; T1- & T2-weighted) of entire femora[10]	X		X		X	X
X-ray[10,11]	X		X		X	X
DEXA	X		X		X	X
Pulmonary	Recommended every 12 to 24 months for patients with borderline- or above-normal pulmonary pressures at baseline.					

ACE=angiotensin-converting enzyme; ALT=alanine aminotransferase; AP=anteroposterior; AST=aspartate aminotransferase; CT=computed tomography; DEXA=dual-energy X-ray absorptiometry; ECG=electrocardiogram; MRI=magnetic resonance imaging; PT=prothrombin time; PTT=partial thromboplastin time; TRAP=tartrate-resistant acid phosphatase; WBC=white blood cell.

1. A complete patient and family history, preferably including a pedigree, should be conducted.
2. A comprehensive physical examination should be performed at least annually.
3. One or more of these biochemical markers should be consistently monitored at least every 12 months and in conjunction with other clinical assessments of disease activity and response to treatment. Of the 3 recommended markers, chitotriosidase, when available as a validated procedure from an experienced laboratory, may be the most sensitive indicator of changing disease activity and is therefore preferred.
4. A baseline sample should be drawn and tested. A subsequent sample is suggested to be drawn at 6 months after starting enzyme therapy but is optional. Additional samples will be tested only if clinically indicated, such as for a suspected immune-mediated adverse event, prior to a switch to home therapy, or for suspected loss of effectiveness of treatment.
5. These should be followed appropriately if abnormal based on each patient's age and clinical status.
6. Obtain contiguous transaxial, 10-mm-thick sections for sum of region of interest.
7. Optimally from hips to below knees.
8. Pulmonary assessments are recommended every 12 to 24 months for patients with borderline- or above-normal pulmonary pressures at baseline.
9. Anatomical sites not included here should be evaluated if symptoms develop in such locations.
10. AP view of the entire femora (optimally from hips to below knees), and lateral view of the spine.
11. Optional in absence of new symptoms or evidence of disease progression.

The Gaucher Registry

Established more than 20 years ago, the ICGG Gaucher Registry (sponsored by Sanofi) remains the preeminent resource for data on patients with Gaucher disease. The Gaucher Registry's mission is to increase the understanding of Gaucher disease and improve outcomes for patients with this disorder.

Data from patients in over 60 countries are being used to increase knowledge about Gaucher disease and help improve outcomes for this rare disorder. Governance and scientific direction of the Gaucher Registry are set by international and regional boards of advisors with extensive experience in the management of Gaucher disease. They guide research, publications, policy, and the protocols for the Gaucher Registry.

Any person with a confirmed diagnosis of Gaucher disease is eligible to participate through their physician, regardless of disease type, treatment status, or treatment choice.

Learn more about the Gaucher Registry at www.registrynxt.com

Not actual physicians.

Resources and Support

CareConnectPSS®

CareConnectPSS, personalized support services for patients, represents Sanofi's commitment of more than 35 years to supporting the rare disease community. CareConnectPSS is designed to support each patient's unique journey.

Our Range of Support to Help Patients Living With a Rare Disease

- Programs and other offerings on a range of disease, treatment, and support topics
- Dedicated CareConnectPSS Case Managers and Patient Education Liaisons
- Disease-specific information, including genetic education and other resources
- Care coordination for moves, vacations, and more
- Assistance with understanding new or changing insurance, as well as resources to help with out-of-pocket costs for eligible patients

For more information, visit us at CareConnectPSS.com

Access to these and other services is voluntary, and your patients are not obligated to begin treatment if they contact us. You and your patients make all treatment-related decisions, and most importantly, the privacy and security of their personal information are always protected.

CareConnectPSS Co-Pay Assistance Program

The CareConnectPSS Co-Pay Program* helps eligible, US patients who are prescribed one of Sanofi's treatments pay for eligible, out-of-pocket, drug-related expenses, including co-pays and coinsurance.

The program is open to individuals who:

- Have commercial insurance
- Have prescription drug coverage
- Are prescribed one of Sanofi's treatments*
- Are residents of the United States

The program is not valid for prescriptions eligible to be reimbursed, in whole or in part, by Medicaid, Medicare (including Medicare Part D), or other federal or state programs (including any state prescription drug assistance programs).

Patients can call 1-800-745-4447, Option 3 to learn more about the program and application process

*The CareConnectPSS Co-Pay Program is available only in the United States and cannot be combined with any other rebate/coupon, free trial, or similar offer. Co-pay benefits are not transferable. This program assists patients with their out-of-pocket drug costs for their prescribed Sanofi treatment only and does not cover or provide support for the cost of MD office visits/evaluations, nursing services/observation periods, blood work, X-rays or other testing, premedications/other medications, transportation, or other related services. No claim for reimbursement of any out-of-pocket expense covered by the CareConnectPSS Co-Pay Program may be submitted to any third-party payer, whether public or private. Sanofi reserves the right to make eligibility decisions, set program maximums, and rescind, revoke, or amend this program without notice. Any savings provided by the Co-Pay Program may vary depending on patients' out-of-pocket costs. Upon registration, patients receive all program details.

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A Long-Standing Commitment to the Gaucher Community

For more than 30 years, Sanofi has been committed to helping address the needs of people living with Gaucher disease and those who care for them.

As the pioneer of Gaucher disease type 1 treatment, Sanofi brings unmatched years of research, development, and patient data to its Gaucher disease program. Sanofi will continue to serve this community for years to come and remains committed to advancing Gaucher disease type 1 care.

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450 Water Street
Cambridge, MA 02141 U.S.A.

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