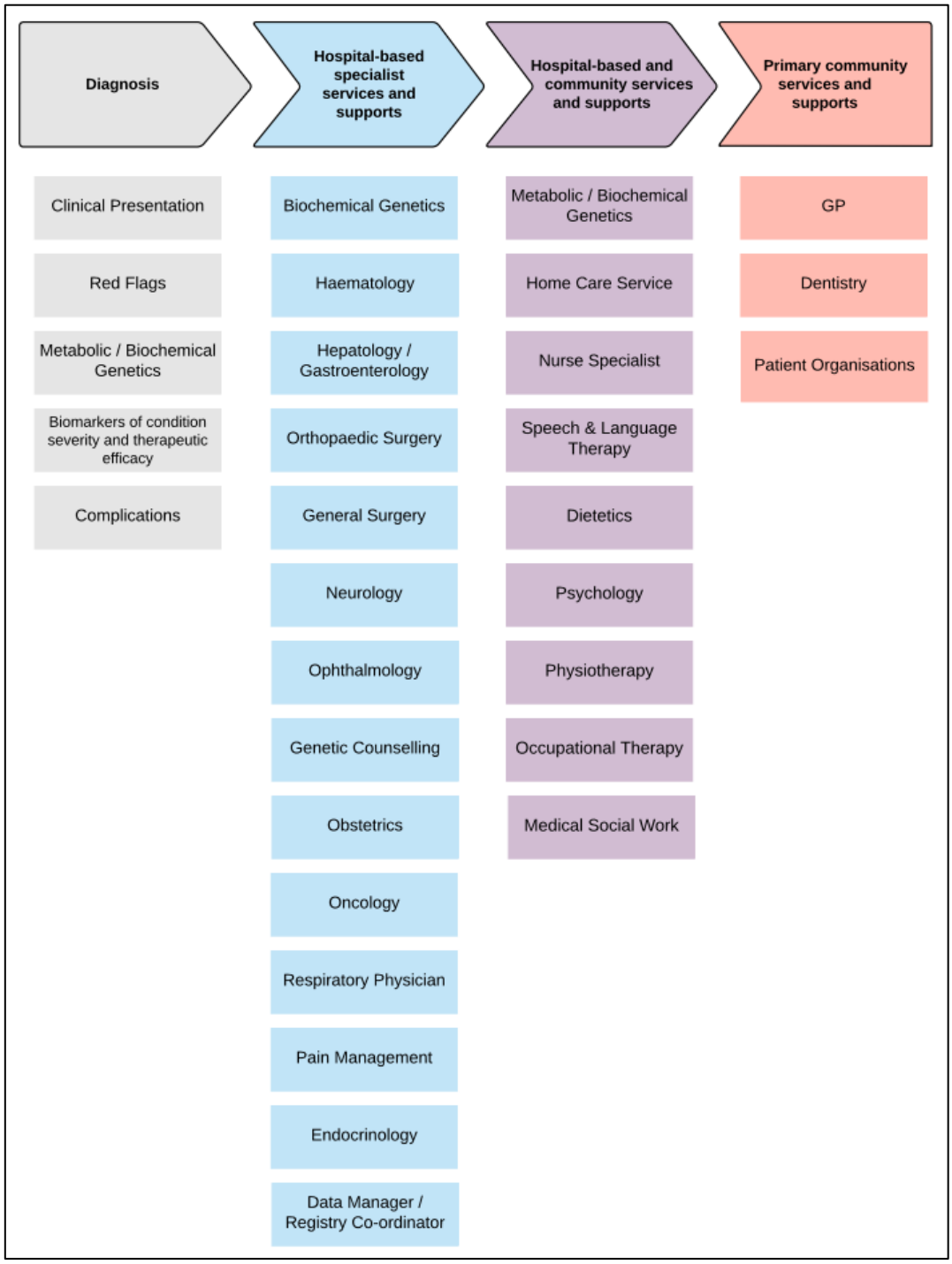
Gaucher Disease

Adult Care Pathway

HSE National Rare Diseases Office

Gaucher Disease (GD) Adult Care Pathway



Clinical Characteristics

Orphacode: 335

Disease Definition: Gaucher disease (GD) is a lysosomal storage disorder encompassing three main forms (types 1, 2 and 3), a foetal form and a variant with cardiac involvement (Gaucher disease - ophthalmoplegia - cardiovascular calcification or Gaucher-like disease). Glucocerebrosidase enzyme deficiency results in excessive build-up of lipid in the liver, spleen, lungs, bone marrow and with less frequency in the brain. Severity can vary between individuals and depending on GD type, but for many patients if left untreated, GD progression can cause significant disability

Acid beta-glucosidase = Glucocerebrosidase = Glucosylceramidase = EC 3.2.1.45) deficiency

Diagnosis	Clinical Presentation	**There are three major clinical subtypes of Gaucher Disease: CDI, GDII, GDIII** GDI is the most common type and is characterised by the absence of primary central nervous system conditions along with the presence of clinical or radiographic evidence of bone conditions, hepatosplenomegaly, anaemia, thrombocytopenia, lung conditions. Persons with GDI may have peripheral neuropathy and Parkinson disease (PD). GDII and GDIII are characterised by the presence of primary neurologic conditions (Bulbar signs, Pyramidal signs, Oculomotor apraxia, Generalized tonic-clonic seizures and progressive myoclonic epilepsy, Dementia). GDII is the most severe form. It is found in infants and no effective treatment is available. Persons with GDII usually do not live beyond 4 years. GDIII is generally identified in childhood. It has CNS complications and is linked to severe systemic conditions. ERT will relieve the systemic symptoms, but not the neurological effects. **Prognosis:** Type 1: very variable condition severity; Type 2 (acute neuronopathic): rapidly progressive with death during infancy; Type 3 (subacute neuronopathic): less rapidly progressive neurovisceral involvement, causing death in childhood or early adulthood
Diagnosis	Red Flags	**When to Test for Gaucher disease?** Thrombocytopenia+/- Bone pain +/- Hepatomegaly +/- Anaemia +/- Splenomegaly +/- MGUS +/-
Diagnosis	Metabolic/ Biochemical Genetics	Measurement of leukocyte β-glucosidase leukocyte (BGL) levels DNA analysis - Acid β-glucosidase genotyping. The four most common variants are: 1. c.84dupG 2. c.115+1G>A

		3. p. Asn409Ser (c.122A>G) 4. p.Leu483Pro (c.1448T>C)
Diagnosis	Biomarkers of condition severity and therapeutic efficacy	Lyso GB1 is the most sensitive and predictive biomarker of GD symptoms such as thrombocytopenia and splenomegaly. To date, there is no gold standard biomarker that can confidently predict the key features of GD
Diagnosis	Complications	Avascular necrosis of the hip and bone crises; Splenic rupture; Cirrhosis; Pulmonary infiltration by Gaucher cells may lead to overt lung conditions; Haematological abnormalities: anaemia, thrombocytopenia and leukopenia; Hypergammaglobulinaemia, T-lymphocyte deficiency in the spleen and reduced neutrophil chemotaxis; Persons with GD may be at increased risk of developing other conditions later in life, usually after age 50. e.g. Parkinson disease (PD), osteoporosis, some cancer types, including liver cancer and myeloma
Hospital-based specialist services and supports	Biochemical Genetics	Establish diagnosis and coordinate treatment plan Genetic testing/ Counselling; Monitor response to treatment and suggest referral to specialists Coordinate the support of person with GD in the hospital and in primary services; Enzyme replacement therapy and substrate reduction therapy (adults) are currently the standard of support for the treatment of symptomatic Type 1 and Type 3 GD but bone marrow; transplantation and gene therapy have been used. Note: Cytochrome P450 activity testing is required to determine for Eliglustat; Management also includes treatment of complications such as anaemia, thrombocytopenia, bleeding tendency, skeletal conditions, liver or lung involvement and organomegaly
Hospital-based specialist services and supports	Haematology	Early diagnosis and monitor/ management of haematological manifestations related to GD such as anaemia, clotting conditions and haematological cancers; Transfusion of blood products; Anticoagulants in individuals with severe thrombocytopenia and/or coagulopathy
Hospital-based specialist services and supports	Hepatology/ Gastroenterology	Early diagnosis and management of liver fibrosis, cirrhosis, portal hypertension, oesophageal and gastric varices, gallbladder conditions, hepatocellular carcinoma, splenomegaly and other GI symptoms
Hospital-based specialist services and supports	Orthopaedic Surgery	Early diagnosis and treatment of orthopaedic complications - fractures, dislocations and avascular necrosis; Joint replacement surgery. Release of spinal cord or nerve root compression, CTS

Hospital-based specialist services and supports	General Surgery	Splenectomy and management of spleen infarctions
Hospital-based specialist services and supports	Neurology	Investigate and manage neurological effects including symptoms of Parkinson's disease (PD), dementia and neuropathy
Hospital-based specialist services and supports	Ophthalmology	Diagnose and treat corneal opacities and other manifestations
Hospital-based specialist services and supports	Genetic Counselling	Autosomal Recessive; In some locations carrier-screening for individuals of Ashkenazi Jewish descent to identify couples at risk of having a child affected with GD is available; It is appropriate to offer testing to asymptomatic at-risk relatives so that those with glucocerebrosidase enzyme deficiency or biallelic pathogenic variants can benefit from early diagnosis and treatment if indicated
Hospital-based specialist services and supports	Obstetrics	Close liaison between metabolic and obstetric team during pregnancy; Pregnancy can exacerbate pre-existing symptoms and trigger new features in affected women. Those with severe thrombocytopenia and/or clotting abnormalities are at increased risk for bleeding around the time of delivery
Hospital-based specialist services and supports	Oncology	Management of multiple myeloma, lymphoma, malignant melanoma, hepatocellular carcinoma
Hospital-based specialist services and supports	Respiratory Physician	Management of air space and/or interstitial conditions, pulmonary vascular conditions, pulmonary hypertension, small lung volumes (due to hepatosplenomegaly and spinal deformities)
Hospital-based specialist services and supports	Pain Management	Pain management (if required)
Hospital-based specialist services and supports	Endocrinology	Osteoporosis
Hospital-based specialist services and supports	Data Manager / Registry Co-ordinator	Create and maintain database of service users; Record service user biographical, clinical and research data; Audit and quality improvement; Ensure minimum data set standards for ERN registry
Hospital-based and community services and supports	Metabolic/ Biochemical Genetics	Enzyme replacement therapy (ERT) infusion Substrate reduction therapy (SRT)
Hospital-based and community services and supports	Home Care Service	ERT Home Infusion by Nurse Specialist

Hospital-based and community services and supports	Nurse Specialist	Service user and family education, advice and support; Liaise with health service professionals; Link for the family and between all teams to acute and community nursing services; Main point of contact for service user and family; Co-ordination of services and supports; Link to patient organisations
Hospital-based and community services and supports	Speech & Language Therapy	Assess and support speech, language and communication needs (SLCN) and / or feeding, eating, drinking & swallowing needs based on individual needs / priorities; Dementia, motor, muscular and cognitive difficulties and oncology treatment may impact SLCN / FEDS; Chronic changes may require referral to community SLT for ongoing support
Hospital-based and community services and supports	Dietetics	Dietary advice to support bone health, manage GI symptoms, Metabolic syndrome in persons with GD on long term treatment and weight management (if indicated); Nutrition assessment and support for persons with GD with failure to thrive/ nutrition risk / malnourished ; Nutritional management of complications that may arise in adults - Parkinson disease (PD), osteoporosis, some cancer types
Hospital-based and community services and supports	Psychology	Diagnose and monitor psychosocial issues particularly depression, anxiety and distress, in persons with GD and their family members; Support for chronic condition; bereavement and grief intervention
Hospital-based and community services and supports	Physiotherapy	Hypoxia secondary to pulmonary infiltration: long term oxygen therapy; Restrictive lung condition/pulmonary hypertension: pulmonary rehabilitation; Respiratory muscle weakness, dysfunctional breathing, retained secretions: chest physiotherapy Parkinsonian syndrome / peripheral neuropathy: Falls prevention – balance and gait training, strength training, provision of brace/mobility aid Lymphoedema management: manual lymph drainage, compression bandaging / garments Bone infarction (femoral head necrosis) / Lytic lesions: Rehab post fracture - restoration of joint/muscle function, rehab post joint replacement surgery / IM nailing; Collapse of vertebral bodies (Red flags - profound motor/sensory weakness in lower extremities, bowel/bladder dysfunction, saddle distribution sensory disturbance):

		Rehabilitation post spinal fixation surgery, management of spinal cord compression, provision of brace / mobility aid, gait training, postural advice, strength training; Promotion of exercise therapy for weight management (weight gain associated with ERT) and mental well-being Exercise advice: No contact sports, avoid high impact sport (post TKR/THR), recommend swimming/hydrotherapy
Hospital-based and community services and supports	Occupational Therapy	Assessment/review of daily living skills: functional transfers, functional mobility, feeding, self-care, accessing the community Postural management and specialist seating including powered mobility Environmental adaptations in the home and school including housing adaptation support and recommendations Specialist equipment for feeding, aids for independence, assistive walking devices, hoists, shower chairs, slings Pain/fatigue management Assistive technology
Hospital-based and community services and supports	Social Work	Psychosocial support: Assess social and family supports, safeguarding Link with community supports as required e.g GP, Public Health Nurse, Primary Care SW, Local authority SW, Mental Health SW, Disability SW, TUSLA Offer 1-1 counselling or GP referral to Counselling in primary care (CIPC) www.hse.ie/eng/services/list/4/mental-health-services/counsellingpc/ Financial support (as required): Patient advocacy, support applications for Medical card, Disability allowance, Supplementary Welfare allowance, Exceptional Needs payment, Long-term illness card, direct to Citizens' information www.citizensinformation.ie/ Housing and/or mobility issues: Advocacy and support - request adapted room if required. Facilitate housing transfer Home Care Packages: if issues with activities of daily living - arrange application for inpatients, liaise with Public Health Nurse to arrange for out-patients Respite Care: liaise with public health nurse or community disability services to arrange

		Employment issues: Link to Intreo public employment and EmployAbility services www.gov.ie/en/campaigns/fb84c0-intreo/ www.gov.ie/en/service/8578c4-access-the-employability-service/
Primary community services and supports	GP	Track bone density in coordination with Gaucher specialist Diagnose other issues related to GD e.g., gallstones and gallbladder conditions Management of bone pain, anaemia, osteopenia, GI symptoms Coordination of local services and supports Refer / communicate across services Management of inter-current conditions
Primary community services and supports	Dentistry	Diagnosis and management of dental manifestations e.g., bony involvement of the mandible and the maxilla, dental extractions and other dental surgery, bleeding tendency, and bisphosphonate therapy
Primary community services and supports	Patient Organisations	Advocacy, support, information Gaucher Association (www.gaucher.org.uk) US National Gaucher Foundation (www.gaucherdisease.org) Rare Diseases Ireland (www.rdi.ie) Rare Ireland Family Support Network (www.rareireland.ie)

CLINICAL LEAD:

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