AAVBC
AMERICAN ACADEMY OF VALUE BASED CARE

Lysosomal Storage Disorders

Quick Reference Guide

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1 CLINICAL SNAPSHOT

Definition: Lysosomal storage disorders (LSDs) are a heterogeneous group of more than 50 rare inherited metabolic diseases caused by deficient or absent lysosomal enzymes, transporters, or related proteins. The resulting inability to degrade specific substrates leads to progressive intracellular accumulation of sphingolipids, glycosaminoglycans, glycogen, or other macromolecules.[1,2] Over time, this accumulation produces multisystem organ dysfunction involving the **central nervous system, liver, spleen, heart, kidneys, lungs, bones, eyes, and peripheral nerves**. Although many LSDs are recognized in childhood, attenuated or late-onset forms may first present in adulthood with nonspecific findings such as **neuropathic pain, tremor, parkinsonism, cardiomyopathy, renal dysfunction, hepatosplenomegaly, skeletal disease, or progressive cognitive and functional decline**. Common examples include **Gaucher disease, Fabry disease, Pompe disease, acid sphingomyelinase deficiency, and the mucopolysaccharidoses**.[3-5]

ICD-10 Codes:

Code the most specific confirmed LSD subtype supported by enzyme testing, biomarker analysis, molecular testing, or specialist documentation. Major code families include **E75 —** disorders of sphingolipid metabolism and other lipid storage disorders, **E76 —** disorders of glycosaminoglycan metabolism, and **E74.0 —** glycogen storage disease.[6] Examples include **E75.21** Fabry disease**, E75.22** Gaucher disease**, E75.23** Krabbe disease**, E75.24** Niemann-Pick disease**, E75.25** metachromatic leukodystrophy**, E75.11** mucolipidosis IV**, E76.01** Hurler syndrome**, E76.02** Hurler-Scheie syndrome**, E76.03** Scheie syndrome**, E76.1** Hunter syndrome**, E76.21** Morquio A**, E76.22** Sanfilippo syndrome**, and E74.02** Pompe disease. Avoid broad unspecified codes when the subtype is known. Do not use an LSD code for carrier status, family history, or an unconfirmed biochemical abnormality.[6]

Prevalence and disease burden: Collectively, lysosomal storage disorders affect approximately **1 in 5,000 live births**, although prevalence varies widely by disease, ancestry, and screening practices.[7-9] Gaucher disease is substantially more common among Ashkenazi Jewish populations, while Fabry and Pompe diseases remain individually rare.[10,12] Because attenuated and late-onset forms may remain unrecognized for years, true prevalence is likely underestimated. Diagnostic delays are common in Fabry, Gaucher, and other LSDs and may permit irreversible organ damage to accumulate before treatment begins.[3,4] Targeted therapies—particularly lifelong enzyme-replacement therapy—carry substantial treatment, infusion, access, and care-coordination burdens.
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Late-onset LSDs may present in older adults as otherwise unexplained multisystem disease. Gaucher disease may cause cytopenias, bone disease, hepatosplenomegaly, or parkinsonism; recent registry data estimate Parkinson disease in approximately **4.0% of patients with Gaucher disease type 1 by age 60 and 12.2% by age 80**.[13,14] Fabry disease may present with left-ventricular hypertrophy, arrhythmia, stroke, neuropathic pain, or chronic kidney disease, while late-onset Pompe disease may cause progressive proximal, axial, or respiratory muscle weakness.[15-17] When these findings cluster, PCPs should consider an LSD and coordinate **enzyme testing, molecular confirmation, genetic counseling, and specialty referral** before irreversible organ injury develops.[18,19]