Mucopolysaccharidoses (MPS)

Pediatric clinical guide • November 2026

MPS are progressive lysosomal storage disorders caused by defects in glycosaminoglycan (GAG) degradation. Most are autosomal recessive. MPS II is X-linked. Clinical severity varies within each subtype. [1–5]

1. Recognize the clinical pattern

Pattern	Clues that raise suspicion
Multisystem disease	Coarse facial features, hernias, hepatosplenomegaly, recurrent ENT disease, snoring or obstructive sleep apnea, valvular disease, joint stiffness, and dysostosis multiplex.
Early neurodevelopmental involvement	Developmental plateau or regression with somatic features suggests severe MPS I or neuronopathic MPS II. Speech delay followed by behavioral and sleep problems and regression with subtle somatic findings suggests MPS III.
Skeletal-predominant disease	Disproportionate short stature, pectus carinatum, genu valgum, joint laxity and cervical instability suggest MPS IV. Joint stiffness, corneal clouding and preserved primary cognition suggest MPS VI.

2. Order biochemical and molecular testing [1–5]

Initial testing. Send urinary GAGs with age-adjusted interpretation. Request GAG fractionation or a targeted disaccharide profile by LC-MS/MS when available. Use the clinical pattern to select enzyme assays, and send these in parallel if suspicion is high.

Confirm the subtype. Arrange enzyme activity testing through a biochemical genetics laboratory, typically using leukocytes or cultured fibroblasts, and targeted molecular testing or an MPS panel. A low dried blood spot enzyme result needs diagnostic follow-up. Correlate enzyme activity, substrate results and variants to distinguish disease from pseudodeficiency.

Follow up discordant results. Normal total urinary GAGs can occur, particularly in MPS IVA. Continue subtype-specific enzyme testing if the phenotype is convincing. If a sulfatase is deficient, assay another sulfatase where appropriate to assess for multiple sulfatase deficiency.

Act early. Refer promptly after a positive newborn screen or strong clinical suspicion. In a child with suspected severe MPS I, contact the transplant team early while completing confirmation. Offer genetic counseling and targeted assessment of at-risk relatives once the subtype is established.

Subtypes and treatment

Subtype	Gene and enzyme	Disease-specific therapy
I • Hurler spectrum	IDUA · alpha-L-iduronidase	Laronidase **0.58 mg/kg IV weekly**. Early HSCT evaluation for severe MPS I. [1,7]
II • Hunter	IDS · iduronate-2-sulfatase	Idursulfase **0.5 mg/kg IV weekly** for somatic disease. See neurologic treatment below. [2]
III • Sanfilippo A–D	SGSH, NAGLU, HGSNAT, GNS	Supportive care for all subtypes. Fayuvi gene therapy is FDA-approved for neurologic manifestations in pediatric MPS IIIA with preserved neurodevelopmental function. Refer for eligibility assessment. [3,12]
IVA • Morquio A	GALNS · N-acetylgalactosamine-6-sulfatase	Elosulfase alfa **2 mg/kg IV weekly**. [4,8]
IVB • Morquio B	GLB1 · beta-galactosidase	Supportive management. The elosulfase alfa indication is for IVA. [4,8]
VI • Maroteaux–Lamy	ARSB · arylsulfatase B	Galsulfase **1 mg/kg IV weekly**. [5,9]
VII • Sly	GUSB · beta-glucuronidase	Vestronidase alfa **4 mg/kg IV every 2 weeks**. [10]

Severe MPS I and neuronopathic MPS II

Severe MPS I. Early HSCT can help preserve neurodevelopment. IV laronidase treats systemic disease and may be used around transplantation as directed by the specialist team. [1]

MPS II. In March 2026 the FDA granted accelerated approval to tividenofusp alfa-eknm (Avlayah) for neurologic manifestations when started in pediatric patients weighing at least 5 kg before advanced neurologic impairment. The approval was based on a reduction in CSF heparan sulfate. Confirmatory evidence of clinical benefit is required. [11]

Avlayah IV weekly escalation: 3 mg/kg for at least 4 weeks, then 7.5 mg/kg for at least 4 weeks, then 15 mg/kg weekly as maintenance if tolerated. Follow the label for transition from idursulfase, infusion reaction precautions and monitoring. [11]

Doses reflect U.S. prescribing references. Verify the current SFDA-approved product information, local availability and the hospital infusion protocol.

Surveillance and perioperative approach

Baseline and longitudinal assessments [1–6]

System	What to assess
Cardiac	Cardiology review, ECG and echocardiogram for valvular disease, ventricular function and other cardiac involvement.
Airway and respiratory	ENT and respiratory assessment, snoring and apneas, polysomnography as indicated, and pulmonary function when feasible.
Spine and mobility	Orthopedic and neurologic examination. Assess cervical instability and cord compression risk, particularly in MPS IVA and VI. Use specialist-directed imaging. Record mobility and functional status.
Hearing and vision	Audiology and ophthalmology. Evaluate hearing loss, corneal clouding and other subtype-specific ocular complications.
Development and daily function	Track growth, development, adaptive skills and school function. Assess sleep, behavior, pain and caregiver priorities. Coordinate physiotherapy, occupational therapy and rehabilitation.

Tailor follow-up intervals to the subtype, age, baseline findings and treatment. Track clinical function alongside biomarkers when monitoring ERT. [1–5]

Before sedation or surgery [5,6]

Flag a potentially difficult airway and cervical cord risk early. Review prior anesthesia records, mouth opening, neck mobility, obstructive sleep apnea, respiratory status, cardiac findings and available cervical imaging. Coordinate with experienced pediatric anesthesia, surgery and ENT. Arrange PICU support when indicated.

Plan airway management and extubation in advance. Maintain neutral cervical alignment when instability or stenosis is suspected. Ensure advanced airway equipment and a rescue plan are available. Choose postoperative observation based on airway risk, cardiopulmonary disease and the procedure.

Findings that warrant urgent assessment

New gait deterioration, weakness or bladder dysfunction may indicate spinal cord compression. Stridor at rest, escalating work of breathing or new desaturation warrants urgent airway and respiratory assessment. [4–6]

References

[1] GeneReviews. Mucopolysaccharidosis Type I.

[2] GeneReviews. Mucopolysaccharidosis Type II.

[3] GeneReviews. Mucopolysaccharidosis Type III.

[4] GeneReviews. Mucopolysaccharidosis Type IVA.

[5] Akyol MU et al. Recommendations for the management of MPS VI. Orphanet J Rare Dis. 2019;14:118.

[6] Walker R et al. Anaesthesia and airway management in mucopolysaccharidosis. J Inherit Metab Dis. 2013;36:211–219.

[7] Aldurazyme (laronidase). FDA prescribing information.

[8] Vimizim (elosulfase alfa). FDA prescribing information.

[9] Naglazyme (galsulfase). U.S. prescribing information.

[10] Mepsevii (vestronidase alfa). FDA prescribing information.

[11] Avlayah (tividenofusp alfa-eknm). FDA prescribing information.

[12] Fayuvi. FDA prescribing information.