Newborn Screening Act Sheet
[Decreased Alpha-L-Iduronidase]
Mucopolysaccharidoses Type I (MPS I)

Differential Diagnosis: Hurler syndrome (MPS IH), Scheie syndrome (MPS IS), and Hurler-Scheie syndrome (MPS IH/S).

Condition Description: MPS I is a lysosomal storage disorder (LSD) caused by a defect in alpha-L-iduronidase activity, resulting in accumulation of glycosaminoglycans (also known as mucopolysaccharides) within the lysosome. This accumulation results in cell enlargement and subsequent dysfunction. There is variability in severity and age of onset. MPS I is an autosomal recessive disorder.

You Should Take the Following Actions:

- Contact family to inform them of the newborn screening result and ascertain clinical status (umbilical and/or inguinal hernia, macrocephaly, macroglossia, hepatosplenomegaly, coarse facial features).
- Consult with Clinical Genomics (4-8198, off-hours via the clinic operator at 4-2511).
- Evaluate the newborn (presence of hernia, liver/spleen size, head size, cardiac status, respiratory status, facial features, joints). If any sign is present or infant is ill, transport to hospital for further evaluation/treatment in consultation with Clinical Genomics.
- Initiate timely confirmatory/diagnostic testing and management, as recommended by Clinical Genomics.
- Provide family with basic information about MPS I.

Diagnostic Evaluation: Confirmatory alpha-L-iduronidase enzyme assay, urine mucopolysaccharides. Patients with low alpha-L-iduronidase activity should have IDUA gene analysis.

Clinical Expectations: The clinical presentation and severity of symptoms of MPS I are variable, ranging from severe disease to attenuated variants (historically known as Hurler-Scheie disease and Scheie disease) that generally present with a later onset and a milder clinical presentation. In general, symptoms may include coarse facies, progressive dysostosis multiplex, hepatosplenomegaly, corneal clouding, hearing loss, mental retardation or learning difficulties, and cardiac valvular disease. MPS I is caused by mutations in the IDUA gene and has an estimated incidence of approximately 1 in 30,000 live births. Treatment options include hematopoietic stem cell transplantation and enzyme replacement therapy.

Additional Information:

Genetics Home Reference
Genetic Testing Registry
Baby's First Test

Referral:
Testing
Mayo test 60617, IDSBS, Alpha-L-Iduronidase, Blood Spot
Mayo test 60618, IDSWB, Alpha-L-Iduronidase, Blood
Mayo test 84464, MPSSC, Mucopolysaccharides Screen (MPS), Urine
Mayo test 35465, MPS1Z, Hurler Syndrome, Full Gene Analysis

Clinical
Clinical Genomics at 4-8198, off-hours via the clinic operator at 4-2511

Local Resources:
Mayo Clinic Biochemical Genetics Laboratory (BGL)
Mayo Clinic Department of Clinical Genomics
Minnesota Department of Health (MDH)
**NBS for MPS I Follow-up**

Decreased alpha-L-iduronidase (IDUA) & 2nd tier test abnormal

Alpha-L-Iduronidase, Blood Spot #60617 – IDSBS or Alpha-L-Iduronidase, Blood #60618 - IDSWB Mucopolysaccharides Screen, Urine #84464 - MPSSC

- IDUA activity – deficient
  - Urine MPS – normal or abnormal
    - Hurler Syndrome, Full Gene Analysis #35465 – MPS1Z
      - Genotype consistent with MPS I
        - Referral to Genetics Specialist
      - One mutation identified
        - IDUA deletion/duplication
          - Genotype suggestive of MPS I
          - Testing consistent with carrier status
          - Negative
      - No mutations identified
        - Not MPS I*

- IDUA activity – normal
  - Urine MPS – normal or abnormal

**Abbreviations:**
MPS I – Mucopolysaccharidosis type I
IDUA – Alpha-L-Iduronidase
MPS - mucopolysaccharides

* Consult with Genetics Specialist if clinical suspicion for MPS I or other condition is high

Actions are shown in shaded boxes; results are in the unshaded boxes.