Newborn Screening ACT Sheet

[Exon 7 Deletion (Pathogenic Variant) in Survival Motor Neuron Gene (*SMN1*)] Spinal Muscular Atrophy (SMA)

Condition Description: Spinal muscular atrophy (SMA) is an autosomal recessive neurodegenerative motor neuron disease caused by pathogenic changes in the Survival Motor Neuron 1 gene (*SMN1*) gene. Newborn screening (NBS) aims to identify patients with homozygous deletions in SMN1, which represents ~95% of cases. SMA is clinically variable, with age of onset ranging from birth to adulthood. SMA type I accounts for more than half of cases and presents at or shortly after birth with hypotonia, breathing and feeding difficulties. Disease severity is attenuated by the number of copies of a related gene, SMN2. Individuals with three or more copies of SMN2 present with later infantile (SMA type 2), childhood (SMA type 3) or adult-onset SMA. For infants identified via NBS with two or three copies of *SMN2*, rapid confirmation of genetic diagnosis, assessment and treatment initiation prior to six weeks of age is critical for optimal outcome. The most severe form (SMA type 0) is associated with larger deletion in Exon 7 or the entire gene.

YOU SHOULD TAKE THE FOLLOWING IMMEDIATE ACTIONS:

- Contact family to inform them of the newborn screening result, ascertain clinical status, arrange immediate clinical evaluation, and provide them with basic information about SMA.
- Take a family history
- Urgent referral to an SMA specialist (child neurologist or MDA clinic) for genetic counseling, comprehensive clinical evaluation, and initiation of treatment
- Take immediate steps to ensure rapid molecular (DNA) confirmation of the NBS result, including *SMN1* and *SMN2* gene dosage (copy number).
- Report findings to state newborn screening program.

Diagnostic Evaluation: Evaluation includes rapid molecular confirmation of *SMN1* mutations and *SMN2* copy number, and physical and neurological assessment by an experienced SMA specialist.

Clinical Considerations: Individuals with the infantile-onset forms of SMA can present with rapidly progressive symptoms at or shortly after birth. Symptoms can include hypotonia, weakness, trouble feeding or respiratory failure. Infants with three or more *SMN2* copies may not present until later childhood or even adulthood. The more severe forms of SMA are associated with high mortality unless diagnosed and treated promptly in the first weeks of life (intrathecal nusinersen or gene therapy, and possibly other emerging therapies). Standard-of-care recommendations include monitoring respiratory, developmental and nutritional status.

Additional Information:
Gene Reviews
Genetics Home Reference
Cure SMA
Muscular Dystrophy Association (MDA) Care Center Network

Referral (local, state, regional and national):
Testing
Concert
Find Genetic Services

ACMG
American College of Medical Genetics and Genomics
Translating Genes Into Health®

LOCAL RESOURCES: Insert State newborn screening program web site links

State Resource site *(insert state newborn screening program website information)*

Name	
URL	
Comments	

Local Resource Site *(insert local and regional newborn screening website information)*

Name	
URL	
Comments	

APPENDIX: Resources with Full URL Addresses
Additional Information:

Gene Reviews
https://www.ncbi.nlm.nih.gov/books/NBK1352/

Genetics Home Reference
https://ghr.nlm.nih.gov/condition/spinal-muscular-atrophy

OMIM
http://omim.org/entry/232300

Cure SMA
http://www.curesma.org/

Muscular Dystrophy Association (MDA) Care Center Network
https://www.mda.org/care/mda-care-centers

Referral (local, state, regional and national):

Testing
https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=DMD

Concert Genetics
https://www.concertgenetics.com/

Find Genetic Services
https://clinics.acmg.net

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