Suggested Follow-up for Spinal Muscular Atrophy (SMA)
(Absence of *SMN1 due to homozygous deletion of Exon 7*)

Condition Description:

Spinal muscular atrophy (SMA) is an autosomal recessive neurodegenerative motor neuron disease caused by pathogenic changes in the Survival Motor Neuron 1 (*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**, also known as Werdnig-Hoffman disease, accounts for more than half of cases and presents at or shortly after birth with hypotonia, breathing, and feeding difficulties. Tongue fasciculations are present in a majority of affected individuals. Without treatment, **death typically occurs by 2 years of age**.

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 IV). For infants identified with two or three copies of *SMN2*, rapid confirmation of genetic diagnosis, assessment, and **treatment initiation prior to 6 weeks of age** is critical for optimal outcome. The most severe form (SMA type 0), is associated with a 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 and **arrange immediate clinical evaluation** within 24 hours
- Provide them with basic information about SMA and take a family history
- **Make an urgent referral** to an SMA specialist (child neurologist and/or clinical geneticist) 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 all findings to the SC DHEC Newborn Screening Program.

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

Clinical Considerations and Treatment Options:

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. The FDA has 3 currently approved medications to treat SMA: intrathecal (Spinraza®) or gene therapy (Zolgensma® and Evrysdi) and possibly other emerging therapies. Standard-of care recommendations include monitoring respiratory, developmental, and nutritional status.

The first FDA-approved prescription medicine for SMA in pediatric and adult patients was nusinersen, also known as Spinraza®. This drug is delivered directly to the central nervous system (CNS) where motor neuron loss begins. After initial loading doses, the drug is given 3 times a year.

Zolgensma® and Evrysdi® are forms of gene therapy that treat the genes involved in SMA. The *SMN1* and *SMN2* genes give the body instructions for making a protein that helps with controlling muscle movement.

Additional Resources for Healthcare Providers:

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

Genetics Home Reference - https://medlineplus.gov/genetics/condition/spinal-muscular-atrophy/

American College of Medical Genetics (ACMG) - https://clinics.acmg.net/

Cure SMA - https://www.curesma.org/

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

Resources available for Families:

https://www.babysfirsttest.org/newborn-screening/conditions/spinal-muscular-atrophy

https://www.curesma.org/

https://smafoundation.org/

Confirmatory Testing Information:

Greenwood Genetic Center (GGC) Diagnostic Lab, Greenwood, SC

https://www.ggc.org/test-finder-item/spinal-muscular-atrophy-smn1-sequencing

https://www.ggc.org/test-finder-item/spinal-muscular-atrophy-smn1-smn2-deletion-duplication-mlpa

University of North Carolina Hospital, Molecular Genetics Laboratory, Chapel Hill, NC

https://www.uncmedicalcenter.org/app/files/public/d72d8e4d-639c-40b7-9d7e-8a6ee3b6f711/pdf-mclendon-labs-mol-test-req.pdf

Mayo Clinic Laboratories, Rochester, Minnesota

https://www.mayocliniclabs.com/test-catalog/overview/65575#Specimen

https://www.mayocliniclabs.com/test-catalog/overview/65941#Specimen

Perkin Elmer Genomics

https://www.perkinelmergenomics.com/test/D5134/

https://www.perkinelmergenomics.com/test/D5231/

INVITAE/ Biogen - SMA Identified program

https://www.invitae.com/en/sma-identified/#test

CLOSEST PROVIDERS/CENTERS IN SC, NC, and GA

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Prisma Health Pediatric Neurology
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Columbia, SC 29203
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Prisma Health Pediatric Neurology
200 Patewood Drive, Suite A350
Greenville, SC 29615
Phone: 864-454-5110

Addie Stark Hunnicutt, MD
Pediatric Specialties-Spartanburg
249 North Grove Medical Park Drive, Suite 200
Spartanburg, SC 29303
Phone: 864-454-5110

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Medical University Of South Carolina
135 Rutledge Avenue
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Phone: 843-792-6735

Neena Champaigne, MD, FACMG, FAAP
Contracted Medical Biochemical Geneticist
Greenwood Genetic Center
Greenwood, SC 29646
Phone: 864-388-1064
Email: neena@ggc.org

Atrium Health: Neurology Charlotte
1010 Edgehill Road North
Charlotte, NC 28207
Phone: (704) 446-1900

Atrium Health: Wake Forest Baptist Medical Center
1 Medical Center Blvd
Winston-Salem, NC 27157
Phone: (336) 716-4101

Augusta University Neuroscience
1120 15th Street
Augusta, GA 30912
Phone: (706) 721-4581

UNC Hospitals Neurology Clinic
194 Finley Golf Course Road, Suite 200
Chapel Hill, NC 27517
Phone: (919) 966-9281

CHOA at Scottish Rite
MDA Care Center
1001 Johnson Ferry Road
Atlanta, GA 30342
Phone: (404) 785-4595

Children's Healthcare of Atlanta (CHOA)
Pediatric Neurology
1405 Clifton Rd NE
Atlanta, GA 30322
Phone: 404-785-6000

Emory University Hospital
Department of Neurology
1365 Clifton Road, Building B Neuroscience Suite, 2nd Floor
Atlanta, GA 30322
Phone: (404) 778-3444

NOTE: This list is not inclusive of all MDA Centers/Neurology/Genetic Providers.