GUIDELINES
This policy does not certify benefits or authorization of benefits, which is designated by each individual policyholder contract. Paramount applies coding edits to all medical claims through coding logic software to evaluate the accuracy and adherence to accepted national standards. This guideline is solely for explaining correct procedure reporting and does not imply coverage and reimbursement.

DESCRIPTION
Spinal muscular atrophy (SMA) is a severe neurodegenerative disorder characterized by a loss of anterior horn cells in the spinal cord. Subsequently, patients with SMA experience significant hypotonia, proximal muscle weakness, and muscular atrophy. Reflexes are typically diminished or absent while sensation is preserved.

SMA is classified based on the age of onset and severity of clinical symptoms. The most severe form is SMA type I, also called Werdnig-Hoffman disease. It is associated with severe, generalized muscle weakness and loss of muscle tone at birth or within the first three months of life. Respiratory failure and subsequent death usually occurs by the age of two. This type accounts for 60% to 70% of the cases. Children with SMA type II, which is diagnosed between 6 and 18 months of age, may be able to sit but are unable to stand or walk without assistance. They may survive beyond age 4, but scoliosis and problems with swallowing and coughing are common. SMA type III, also known as Kugelberg-Welander disease, is characterized by proximal muscle weakness that manifests after 18 months. SMA type III may also be subdivided into types IIIa (with onset before age 3) and IIIb (with onset after age 3). Individuals with SMA type III learn to walk independently but eventually experience frequent falls and difficulty with stairs; disease progression may also result in the need for a wheelchair in adulthood. Finally, some clinicians will diagnose patients with SMA type IV, if the onset of symptoms is after age 30, the muscle weakness is mild, and the respiratory system is not involved.

SMA is inherited in an autosomal recessive manner and is caused by alterations in the survival motor neuron 1 (SMN1) gene located on chromosome 5 at band q12.2 to q13.3. Approximately 95% of SMA patients have the condition as a result of a homozygous deletion involving at least exon 7 of SMN1. SMN2, a gene nearly identical in sequence to SMN1, is located in the same highly repetitive region on chromosome 5. Although it does not cause SMA, it has been shown to modify the phenotype of the condition; those with the milder SMA types II or III tend to have more copies of SMN2 than those with the severe type I.

The American College of Obstetricians and Gynecologists (ACOG, 2017) recommends that “Screening for spinal muscular atrophy should be offered to all women who are considering pregnancy or are currently pregnant.” The guidelines state that, “in patients with a family history of spinal muscular atrophy, molecular testing reports of the affected individual and carrier testing of the related parent should be reviewed, if possible, before testing. If the reports are not available, SMN1 deletion testing should be recommended for the low-risk partner.”

POLICY
Genetic testing for spinal muscular atrophy (SMA) requires prior authorization for all product lines.

HMO, PPO, Individual Marketplace, Elite, Advantage
Paramount considers genetic testing for SMN1 medically necessary for the following indications:

- Individual to be tested exhibits symptoms of SMA (eg, symmetrical proximal muscle weakness, absent or markedly decreased deep tendon reflexes); or
- Carrier screening when the individual to be tested is asymptomatic and any of the following criteria are met:
  - Individual has a family history of SMA or SMA-like disease*; or
  - Individual has an affected or carrier blood relative in whom a disease-causing SMA mutation has been identified. (Testing Strategy: Test for familial mutation); or
  - Individual is the reproductive partner of an individual affected with or carrier of SMA or SMA-like disease; or
- The prenatal diagnosis or preimplantation genetic diagnosis of SMA in the pregnancy of two known carriers.

*Note: SMA includes arthrogryposis multiplex congenita-SMA (AMC-SMA), congenital axonal neuropathy (CAN), SMA0, SMA I (Werdnig-Hoffmann disease), SMA II, SMA III (Kugelberg-Welander disease) and SMA IV.
Paramount considers SMN2 gene testing medically necessary when ALL of the following criteria are met:

- Individual to be tested exhibits onset of clinical signs and symptoms consistent with SMA at six months of age or younger; AND
- Therapy with Spinraza (nusinersen) is being considered

For information regarding Spinraza (nusinersen), please refer to Spinraza Pharmacy Coverage Policy.

Paramount considers genetic testing for spinal muscular atrophy (SMA) experimental and investigational in the general population and for all other indications because there is inadequate evidence in the published peer-reviewed clinical literature regarding its effectiveness.

**CODING/BILLING INFORMATION**

The appearance of a code in this section does not necessarily indicate coverage. Codes that are covered may have selection criteria that must be met. Payment for supplies may be included in payment for other services rendered.

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| 81400    | Molecular pathology procedure, Level 1 (eg, identification of single germline variant [eg, SNP] by techniques such as restriction enzyme digestion or melt curve analysis) [when specified as the following]:
  - SMN1 (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy), exon 7 deletion |
| 81401    | Molecular pathology procedure, Level 2 (eg, 2-10 SNPs, 1 methylated variant, or 1 somatic variant [typically using nonsequencing target variant analysis], or detection of a dynamic mutation disorder/triplet repeat)
  - SMN1/SMN2 (survival of motor neuron 1, telomeric/survival of motor neuron 2, centromeric) |
| 81403    | Molecular pathology procedure, Level 4 (eg, analysis of single exon by DNA sequence analysis, analysis of >10 amplicons using multiplex PCR in 2 or more independent reactions, mutation scanning or duplication/deletion variants of 2-5 exons) [when specified as the following]:
  - SMN1 (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy), known familial sequence variant(s) |
| 81405    | Molecular pathology procedure, Level 6 (eg, analysis of 6-10 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 11-25 exons, regionally targeted cytogenomic array analysis) [when specified as the following]:
  - SMN1 (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy), full gene sequence |

**ICD-10 CODES**

- G12.0 Infantile spinal muscular atrophy, type I [Werdnig-Hoffmann]
- G12.1 Other inherited spinal muscular atrophy

**TAWG REVIEW DATES:** 04/21/2017, 04/26/2018

**REVISION HISTORY EXPLANATION**

- **04/21/17:** Policy created to reflect most current clinical evidence per The Technology Assessment Working Group (TAWG).
- **04/26/18:** Removed codes 81404, 81406, 81408, & 81479. Added ICD-10 codes G12.0 & G12.1. Policy reviewed and updated to reflect most current clinical evidence per The Technology Assessment Working Group (TAWG).

**REFERENCES/RESOURCES**

Centers for Medicare and Medicaid Services, CMS Manual System and other CMS publications and services
Ohio Department of Medicaid http://jfs.ohio.gov/
Centers for Medicare and Medicaid Services, Healthcare Common Procedure Coding System, HCPCS Release and Code Sets
Industry Standard Review
Hayes, Inc.