Clinical Policy: Nusinersen (Spinraza)

Reference Number: WA.UM.34
Effective Date: 05/17
Last Review Date: 08/17

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

The intent of the criteria is to ensure that patients follow selection elements established by the Health Care Authority clinical policy for Nusinersen (Spinraza™).

Policy/Criteria

It is the policy of Coordinated Care that Spinraza is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

1. Member must have documentation of a confirmed diagnosis of spinal muscular atrophy (SMA) defined as ONE of the following (either 1a, 1b, or 1c) genetic tests of 5q13 demonstrating:
    a. Homozygous SMN1 gene deletion; ***OR***
    b. Homozygous SMN1 gene mutation; ***OR***
    c. Compound heterozygous SMN1 gene mutation; **AND**
2. Patient has sufficient number of copies of SMN2 gene defined as ONE of the following (either 2a or 2b) genetic tests demonstrating:
    a. If a pre-symptomatic infant, then ≤ 3 copies of SMN2 gene is required; ***OR***
    b. If a symptomatic patient, then ≥ 2 copies of SMN2 gene is required AND documentation of age of onset of symptoms; **AND**
3. Nusinersen is prescribed by a provider with expertise in treating and managing SMA; **AND**
4. Nusinersen will be administered by a specialist with competency in intrathecal injections or under the supervision of a provider with expertise in performing lumbar puncture procedures; **AND**
5. The following documentation of applicable patient outcomes, measured at baseline, has been submitted:
    a. For all members:
        i. Hammersmith Functional Moto Scale Expanded (HFMSE)
        ii. Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND)
        iii. Pulmonary status (e.g. tracheostomy, hours of ventilation, CPAP, etc)

iv. Complete blood count, cystatin-C, coagulation status, urine protein, serum electrolytes including bicarbonate, liver and renal function tests

6. For infant to early childhood:
    a. Hammersmith Infant Neurological Exam (HINE)
7. For ambulatory patients:
    a. 6 Minute Walk Test (6MWT)
8. For non-ambulatory patients:
    a. Upper Limb Module (UML)

Upon review of the submitted documentation from the patient's chart and demonstration of meeting the above initial approval criteria, Nusinersen will be approved for 5 doses to be administered in a 6 month period. The first 3 doses must be administered 14 days apart, the fourth dose must be 30 days after the third dose, and the fifth dose must be four months after the fourth dose. Continued approval will be required every 6 months for doses to be administered every 4 months.

Approval duration: 6 months

II. Continued Therapy

1. Currently receiving medication via CCW benefit or member has previously met initial approval criteria; **AND**
2. Absence of serious infections, deterioration in kidney function, thrombocytopenia, severe hyponatremia, low serum bicarbonate levels, measured prior to each maintenance dose; **AND**
3. The following documentation of applicable patient outcomes, measured prior to each maintenance dose, has been submitted:
4. For non-ambulatory patients:
    a. Upper Limb Module (UML)
5. For ambulatory patients:
    a. 6 Minute Walk Test (6MWT)
6. For infant to early childhood:
    a. Hammersmith Infant Neurological Exam (HINE)
7. For all patients:
    a. Hammersmith Functional Moto Scale Expanded (HFMSE)
    b. Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND)
    c. Pulmonary status (e.g. tracheostomy, hours of ventilation, CPAP, etc)
    d. **AND**
8. Documentation has been submitted demonstrating medical necessity:

a. Improvement or maintenance of functional status from baseline functional tests (HFMSE, CHOP-INTEND, Pulmonary status, HINE, 6MWT, or UML); **OR**
b**.** Member has achieved and maintained new motor milestones from pretreatment baseline functional tests (HFMSE, CHOP-INTEND, Pulmonary status, or HINE); ***OR***
c. Disease progression is slower than what would otherwise be unexpected in this population using the following tools:

i. HFMSE:
   a. At least 3 points increase in score from pretreatment baseline
ii. CHOPD-INTEND:
   a. At least a 4 point increase in score from the pretreatment baseline
iii. If infant or early childhood: HINE:
   a. 1. Patient has demonstrated improvement in more categories than decline; AND
   b. At least 2 points (or maximum score) in ability to kick; OR
   c. At least 1 point in any other HINE milestone (e.g. head control, rolling, sitting, crawling, etc.)
iv. If ambulatory: 6MWT:
   a. 1. At least a 30 meter increase from pretreatment baseline
v. If non-ambulatory: ULM:
   a. At least a 2 point increase in score from the pretreatment baseline

Upon review of the submitted documentation from the member's chart and demonstration of meeting the above continuation criteria, Nusinersen will be approved for an additional 6 month period. Continued approval will be required every 6 months for doses to be administered every 4 months.

Approval duration: 12 months

Exclusion Criteria:

1. Nusinersen is considered not medically necessary for the treatment of SMA without 5q mutations or deletions or in pre-symptomatic patients with > 3 copies of the SMN2 gene.

Background
Description/Mechanism of Action:

Spinraza is an antisense oligonucleotide designed to treat SMA caused by mutations in chromosome 5q that lead to SMN protein deficiency. Using in vitro assays and studies in transgenic animal models of SMA, Spinraza was shown to increase exon 7 inclusion in SMN2 messenger ribonucleic acid transcripts and production of full-length SMN protein.

Formulations:
Spinraza: Intrathecal injectable formulation
Sterile, clear and colorless solution supplied as a 12 mg/5 mL (2.4 mg/mL) solution in a single-dose glass vial free of preservatives

FDA Approved Indications:
Spinraza™ is indicated for the treatment of spinal muscular atrophy (SMA) in pediatric and adult patients.

Appendices
Appendix A: Abbreviation Key
HINE: Hammersmith Infant Neurological Examination
HFMSE: Hammersmith functional motor scale expanded
SMA: Spinal muscular atrophy
SMN: Survival motor neuron

Appendix B: Spinraza/Spinal Muscular Atrophy
- SMA is an autosomal recessive genetic disorder. It is caused by mutations in the SMN1 (survival motor neuron) gene that is found on chromosome 5 (hence the name 5q-SMA). To develop SMA, an individual must inherit two faulty (deletion or mutation) SMN1 genes, one from each parent.
- There are other types of SMA that is not related to chromosome 5 or SMN. Safety and efficacy of Spinraza in non-SMN-related SMA have not been established.
- SMN-related SMA is classified as type 1 through 4 depending on time of onset. The age of disease onset of symptoms correlates with disease severity: the earlier the age of onset, the greater the impact on motor function. Children who display symptoms at birth or in infancy typically have the lowest level of functioning (type 1). SMA onset in children (types 2 and 3), teens or adults (type 4) generally correlates with increasingly higher levels of motor function.
- Efficacy of Spinraza was established primarily in infantile disease (SMA type 1). Spinraza was approved based on interim results of an unpublished Phase III study of patients with spinal muscular atrophy type I (infantile-onset). The phase III study, referred to as ENDEAR, enrolled infants diagnosed with symptomatic, genetically confirmed spinal muscular atrophy (SMA) type I with two copies of SMN2 gene. Key inclusion criteria were: genetic documentation of 5q SMA homozygous gene deletion, homozygous mutation or compound heterozygote, onset of clinical signs and symptoms consistent with SMA at ≤ 6 months, at study entry, receiving adequate nutrition and hydration) with or without gastrostomy),

seven month of age or younger at screening, body weight ≥ 3rd percentile for age, gestational age of 37 to 42 weeks. Key exclusion criteria were: Hypoxemia and signs or symptoms of SMA present at birth within the 1st week after birth

- Based on the mechanism of action of Spinraza, SMN2 must be present in sufficient amount for the production of full length SMN protein required to alleviate or minimize the symptoms of SMA.
- All subjects in the ENDEAR study had at least 2 copies of SMN2 genes (98% of the subjects in the pivotal study had 2 copies of SMN2 genes, while other had 3 or 4 copies).
- It is unknown whether patients with less than 2 copies would make sufficient SMN protein to mitigate the symptoms of SMA as the efficacy of this agent has not been demonstrated in patients with less than 2 copies of SMN 2 genes.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
N/A	

Reviews, Revisions, and Approvals	Date	Approval Date
Policy created.	5/1/2017	5/16/2017
Removed absence of infection as criteria	7/57/17	8/23/17

References

1. Spinraza™ Prescribing Information. Cambridge, MA: Biogen Inc.; December 2016. Available at: https://www.spinraza-hcp.com/. Accessed January 4, 2017.
2. Micromedex® Healthcare Series [Internet database]. Greenwood Village, CO: Thomson Healthcare. Updated periodically. Accessed January 6, 2017.
3. Wang CH, Finkel RS, Bertini ES, et al. Consensus Statement for Standard of Care in Spinal Muscular Atrophy. Journal of Child Neurology 2007; 22:1027-1049.
4. Cobben JM, de Visser M, Scheffer H, et al. Confirmation of clinical diagnosis in requests for prenatal prediction of SMA type I. J Neurol Neurosurg Psychiatry 1993; 56: 319-21.
5. Maitre NL, Chorna O, Romeo DM, and Guzzetta A. Implementation of the Hammersmith Infant Neurological Examination in a High-Risk Infant Follow-Up
6. Program. Pediatric Neurology 2016; 65:31-38.
7. Finkel RS, Kuntz N, Mercuri E, et al. Primary Efficacy and Safety Results from the Phase 3 ENDEAR Study of Nusinersen in Intants Diagnosed with Spinal Muscular Atrophy. Poster

presented at: 43rd Annual Congress of the British Paediatric Neurology Assocation; 11-13 January, 2016; Cambridge, UK.
8. Finkel RS, Chiriboga CA, Day JW, et al. Treatment of Infatile-Onset Spinal Muscular Atrophy with Nusinersen: A Phase 2, Open-Label, Dose-Escalation Study. The Lancet 2016;16:31408-8.

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.