Clinical Policy: Nusinersen (Spinraza)

Reference Number: PA.CP.PHAR.327
Effective Date: 01/18
Last Review Date: 07/18

Coding Implications
Revision Log

Description
The intent of the criteria is to ensure that patients follow selection elements established by Pennsylvania Health and Wellness® clinical policy for Nusinersen (Spinraza™).

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

Policy/Criteria
It is the policy of health plans affiliated with Pennsylvania Health and Wellness® that Spinraza is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Spinal Muscular Atrophy (must meet all)**:**

1. Diagnosis of spinal muscular atrophy (SMA) Types I, II, or III;
2. Genetic testing confirming 1, 2, 3, or 4 copies of SMN2 gene;
3. Genetic testing confirms the presence of one of the following (a, b or c):
   a. Homozygous deletions of SMN1 gene (e.g., absence of the SMN1 gene);
   b. Homozygous mutation in the SMN1 gene (e.g., biallelic mutations of exon 7);
   c. Compound heterozygous mutation in the SMN1 gene (e.g., deletion of SMN1 exon 7 (allele 1) and mutation of SMN1 (allele 2));
4. Prescribed by or in consultation with a pediatric neurologist;
5. Documentation of baseline Hammersmith Infant Neurological Examination (HINE) Section 2 motor milestone score (total 26 points) for ages 0-2 years or Hammersmith functional motor scale expanded (HFMSE) score (total 66 points) for ages 2 years and above;
6. Total dose does not exceed 4 doses of 12 mg, prescribed for intrathecal use.

Approval duration: 6 months

II. Continued Therapy

A. Spinal Muscular Atrophy (must meet all)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Provider submits documentation of the number of categories of improvement and decline in motor milestones based on the HINE or HFMSE score since the most recent approval
3. If request is for a dose increase, new dose does not exceed 12 mg every 4 months prescribed for intrathecal use.
4. Member is receiving a clinical benefit based on the prescriber's assessment.

Approval duration: 12 months

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

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
Updated specialist requirement to pediatric neurologist. Added HFMSE baseline score for age >2 yo. Expanded indication to SMA types 1-3 with SMN2 copies up to 4. References reviewed and updated	02/18	

References
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5. Maitre NL, Chorna O, Romeo DM, and Guzzetta A. Implementation of the Hammersmith Infant Neurological Examination in a High-Risk Infant Follow-Up Program. Pediatric Neurology 2016; 65:31-38.
6. 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.

7. 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.
8. Mercuri E, Finkel RS, Kirschner J, et al. Efficacy and Safety of Nusinersen in Children with Later-Onset Spinal Muscular Atrophy (SMA): End of Study Results from the Phase 3 CHERISH Study. 2017 Annual Spinal Muscular Atrophy Conference. July 2, 2017. Available at: http://ir.ionispharma.com/static-files/8f38823c-b92d-49bb-9792-e78841bda551. Accessed November 9 ,2017.
9. Darras BT, Royden Jones H Jr, Ryan MM, et al. Neuromuscular Disorders of Infancy, Childhood, and Adolescence: A Clinician's Approach. 2nd ed. London, UK: Elsevier; 2015.