Prior Authorization Review Panel

CHC-MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: PA Health & Wellness	**Submission Date: 02/01/2021**
Policy Number: PA.CP.PHAR.327	**Effective Date: 01/01/2018** **Revision Date: 01/2021**
Policy Name: Nusinersen (Spinraza)	

Type of Submission – Check all that apply:

- ☐ **New Policy**
- ☐ **Revised Policy***
- ✓ **Annual Review - No Revisions**
- ☐ **Statewide PDL -** *Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.*

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any changes or clarifying information for the policy below:

1Q 2021 annual review: references reviewed and updated.

Name of Authorized Individual (Please type or print): **Auren Weinberg, MD**	**Signature of Authorized Individual:** 

Clinical Policy: Nusinersen (Spinraza)

Reference Number: PA.CP.PHAR.327
Effective Date: 01/2018
Last Review Date: 01/2021

Coding Implications
Revision Log

Description
Nusinersen (Spinraza™) is a survival motor neuron-2 (SMN2)-directed antisense oligonucleotide.

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

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval 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. Prescribed by or in consultation with a pediatric neurologist;
3. Genetic testing confirming 1, 2, 3, or 4 copies of SMN2 gene;
4. 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));
5. Documentation of one of the following baseline scores (*see Appendix D*) (a or b):
   a. For age < 2 years: Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorder (CHOP-INTEND) score or Hammersmith Infant Neurological Examination (HINE) Section 2 motor milestone score;
   b. For age ≥ 2 years: Hammersmith functional motor scale expanded (HFMSE) score;
6. Spinraza is not being initiated simultaneously with Zolgensma®;
7. If the member has a history of treatment with Zolgensma, must meet the following (a and b):
   a. Provider must submit evidence of poor response to Zolgensma (e.g., sustained decrease in CHOP-INTEND score over a period 6 months);
   b. Documentation of provider attestation of clinical deterioration;
8. Dose does not exceed 12 mg per dose, prescribed for intrathecal use.

Approval duration: 12 months (up to 6 doses)

B. Other diagnoses/indications: Refer to PA.CP.PMN.53

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 CHOP-INTEND, HINE, or HFMSE score (based on member's age) since the most recent approval (*see Appendix D*);
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

B. Other diagnoses/indications (1 or 2):

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to PA.CP.PMN.53

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CHOP-INTEND: Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorder
FDA: Food and Drug Administration
HFMSE: Hammersmith functional motor scale expanded
HINE: Hammersmith Infant Neurological Examination
SMA: spinal muscular atrophy
SMN: survival motor neuron

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: General Information

- 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 are 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.
- SMN2 gene copy and SMA types
  - SMN2 gene copy numbers are variable in individuals with spinal muscular atrophy. Higher numbers typically correlate with less severe disease.
  - More than 95% of individuals with spinal muscular atrophy retain at least 1 copy of the SMN2 gene
  - About 80% of individuals with Type I spinal muscular atrophy have 1 or 2 copies of the SMN2 gene
  - About 82% of individuals with Type II spinal muscular atrophy have 3 copies of the SMN2 gene
  - About 96% of individuals with Type III spinal muscular atrophy have 3 or 4 copies of the SMN2 gene
- The CHOP-INTEND score is a validated 16-item, 64-point scale shown to be reliable and sensitive to change over time for SMA Type 1. In a prospective cohort study of SMA type I patients (n = 34), the mean rate of decline in the CHOP-INTEND score was 1.27 points/year (95% CI 0.21-2.33, p = 0.02).
- The HINE Section 2 motor milestone exam is an easily performed and relatively brief standardized clinical neurological examination that is optimal for infants aged between 2 and 24 months with good inter-observer reliability. This endpoint evaluates seven different areas of motor milestone development, with a maximum score between 2-4 points for each, depending on the milestone, and a total maximum score of 26 points.
- The HFSME score combines the Hammersmith Functional Motor Scale with a 13-item expansion module for ability to distinguish motor skills among individuals who may be

older or with SMA types II and III. Each item is graded from 0 to 3, with 0 signifying no response, with a total of 66 points.

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
SMA	**Initial** (4 loading doses): 12 mg intrathecally every 14 days for 3 doses (loading doses); then, a fourth loading dose of 12 mg intrathecally 30 days after the third loading dose **Maintenance**: 12 mg intrathecally every 4 months	12 mg intrathecally every 4 months

V. Product Availability

Solution for intrathecal injection: 12 mg/5 mL

VI. References

1. Spinraza Prescribing Information. Cambridge, MA: Biogen Inc.; June 2020. Available at: https://www.spinraza-hcp.com/. Accessed August 20, 2020.
2. 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.
3. 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.
4. 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.
5. Finkel RS, Mercuri E, Darras BT, et al. Nusinersen versus sham control in infantile-onset spinal muscular atrophy. N Engl J Med 2017; 377:1723-32. DOI: 10.1056/NEJMoa1702752
6. 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.
7. Mercuri E, Darras BT, Chiriboga CA, et al. Nusinersen versus sham control in later-onset spinal muscular atrophy. N Engl J Med 2018; 378:625-35. DOI: 0.1056/NEJMoa1710504
8. 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.
9. Finkel RS, McDermott MP, Kaufmann P, et al. Observational study of spinal muscular atrophy type I and implications for clinical trials. Neurology 2014; 83:810-817.
10. Dunaway Young S, Montes J, Kramer SS, et al. Six-minute walk test is reliable and valid in spinal muscular atrophy. *Muscle and Nerve.* 2016. 54: 836-842.
11. Ramsey D, Scoto M, Mayhew A, et al. Revised Hammersmith Scale for Spinal Muscular Atrophy: A SMA Specific Clinical Outcome Assessment Tool. *PLoS ONE*. 2017; 12(2): e0172346. https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0172346.

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	
1Q 2019 annual review: references reviewed and updated.	01/19	
1Q 2020 annual review: removed requirement for documentation of number of categories of improvement for continued approval; added criteria preventing concurrent prescribing of Zolgensma; added criteria requiring medical justification, attestation, and evidence of clinical deterioration in members with a history of Zolgensma administration; added that member does not have respiratory insufficiency; Changed initial approval duration from 6 months to 12 months and added quantity limit of 4 doses to allow for interruptions in administration of initial loading doses while still requiring an evaluation prior to transition into maintenance therapy; references reviewed and updated.	01/2020	
1Q 2021 annual review: references reviewed and updated.	01/2021	