Subject: Spinraza (nusinersen)

Background: Spinal muscular atrophy (SMA) is an autosomal recessive genetic disorder characterized by loss of motor neurons, leading to weakness and wasting of muscles. SMA is caused by mutation or deletion in the survival motor neuron 1 (SMN1) gene which results in the loss of motor neurons. This motor neuron loss often leads to wasting of muscles used for actives such as crawling, walking, sitting-up and controlling head movement. In severe cases, muscles used for breathing or swallowing are affected. SMA can be classified into four groups defined by their functional ability.

SMA Classification	Age of Onset	Highest Function
Type 1 (Severe)	0-6 months	Never sits
Type 2 (Intermediate)	7-18 months	Never stands
Type 3 (Mild)	>18 months	Stands and walks
Type 4	2nd or 3rd Decade	Walks during adult years

Spinraza (Nusinersen) is delivered by intrathecal injection, and is designed to alter the splicing of a gene (SMN2) that is nearly identical to the SMN1. Spinraza received approval from the Food and Drug Administration (FDA) on December 23rd, 2016 under the priority review to treat both pediatric and adult patients with SMA. Spinraza was also granted an orphan drug designation for the treatment of individuals with SMA. This approval was granted based in part on unpublished interim results of a randomized, placebo-controlled, phase III ENDEAR trial; in patients with infantile-onset SMA who were diagnosed before 6months of age and who were <7 months old at the time of their first dose. Results from ENDEAR trial remain unpublished. In addition to the three ongoing Phase III clinical trials (ENDEAR, CHERISH, SHINE), two phase II trials (EMRACE and NURTURE) are ongoing.

Authorization:

Prior authorization is required for all members enrolled in Harvard Pilgrim Health Care (HPHC) Commercial HMO, POS, or PPO products.

Policy and Coverage Criteria:

Harvard Pilgrim Health Care (HPHC) considers Spinraza for the treatment of spinal muscular atrophy (SMA) medically necessary for a maximum of six months of treatment when ALL the following criteria are met:

- Member is diagnosed with Type 1, 2, or 3 SMA
- Prescription is submitted by or in consultation with a board eligible/certified neurologist
- Documentation confirms the member has at least two copies of SMN2 gene
- Initial dose of Spinraza is to be administered within the same week as, preferably immediately subsequent to, a Hammersmith Infant Neurological Exam (HINE), Hammersmith Functional Motor Scale, Expanded (HFMSE) assessment Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND), or Upper Limb Module (ULM), non ambulatory, test.

Continuation of Therapy:

- Continuation of therapy beyond latest approval may be considered medically necessary for six additional months when documentation confirms significant improvement in SMA associated symptoms from pretreatment baseline status (as measured within the same week as Spinraza initiation) through ANY of the following:
    - An increase or maintenance of previous increase of at least two points from pretreatment baseline on the HFMSE, OR
    - A cumulative change of at least positive one point in all HINE section 2 categories but voluntary grasp from pretreatment baseline, OR
    - An increase or maintenance of previous increase of at least two points from pretreatment baseline on the INTEND-CHOP, OR
    - An increase or maintenance of previous increase of at least one point from pretreatment baseline on the ULM, OR
    - Documentation confirming comorbidities or injuries that would have made the member's current HFMSE/HINE/INTEND-CHOP/ULM results unexpected without Spinraza treatment.

Exclusions:

Harvard Pilgrim Health Care (HPHC) considers Spinraza experimental and investigational when the above criteria are not met, and for all other indications, including dosage and frequency beyond Food and Drug Administration (FDA) labeling. Harvard Pilgrim Health Care (HPHC) considers Spinraza not medically necessary for individuals in current treatment or previously treated with gene therapy (e.g. Zolgensma) for SMA.

Coding:

Codes are listed below for informational purposes only, and do not guarantee member coverage or provider reimbursement. The list may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible.

HCPCS Code	Description
J2326	Injection, nusinersen, 0.1 mg

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11. Paton DM. Nusinersen: antisense oligonucleotide to increase SMN protein production in spinal muscular atrophy. *Drugs Today*. 2017;53(6):327-337. doi:10.1358/dot.2017.53.6.2652413
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14. Spinraza FDA Label. Food and Drug Administration http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/209531lbl.pdf. Accessed January 21, 2019.
15. Spinraza NDA Approval Letter. Food and Drug Administration http://www.accessdata.fda.gov/drugsatfda_docs/appletter/2016/209531Orig1s000ltr.pdf. Accessed January 21, 2019.

Summary of Changes

Date	Change
2/19	**Policy updated, mutual exclusivity with Zolgensma reflected in exclusions statement**
2/18	**Policy Updated**
4/17	**New Policy**

Approved by Medical Policy Committee: 02/12/19
Approved by Clinical Policy Operational Committee: 4/17, 2/18, 02/19;
Policy Effective Date: 04/05/19
Initiated: 4/17