



Spinraza™ (nusinersen) (Intrathecal)

Document Number: IC-0291

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I. Length of Authorization

Coverage will be provided annually and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Loading: 1 vial on D1, D15, D29, and D59
- Maintenance: 1 vial every 112 days

B. Max Units (per dose and over time) [HCPCS Unit]:

- Loading: 120 billable units on D1, D15, D29, and D59
- Maintenance: 120 billable units every 112 days

III. Initial Approval Criteria¹⁻⁷

- Submission of medical records related to the medical necessity criteria is **REQUIRED** on all requests for authorizations. Records will be reviewed at the time of submission. Please provide documentation via direct upload through the PA web portal or by fax.

Coverage is provided in the following conditions:

Spinal Muscular Atrophy (SMA) † Φ

- Patient must not have previously received treatment with SMA gene therapy (i.e., onasemnogene abeparvovec-xioi); **AND**
- Patient will not use in combination with other agents for SMA (e.g., onasemnogene abeparvovec, risdiplam, etc.); **AND**
- Patient must have the following laboratory tests at baseline and prior to each administration*: platelet count, prothrombin time; activated partial thromboplastin time, and quantitative spot urine protein testing; **AND**

- Patient retains meaningful voluntary motor function (e.g. manipulate objects using upper extremities, ambulate, etc.); **AND**
- Patient must have a diagnosis of 5q spinal muscular atrophy confirmed by either homozygous deletion of the *SMN1* gene or dysfunctional mutation of the *SMN1* gene; **AND**
- Patient must have one of the following SMA phenotypes:
 - SMA I confirmed by one of the following:
 - Patient must have 1-2 copies of the *SMN2* gene; **OR**
 - Patient has 3 copies of the *SMN2* gene in the absence of the c.859G>C single base substitution modification in exon 7; **OR**
 - SMA II with symptomatic disease (i.e., impaired motor function and/or delayed motor milestones); **OR**
 - SMA III with symptomatic disease (i.e., impaired motor function and/or delayed motor milestones); **AND**
- Baseline documentation of one or more of the following:
 - Motor function/milestones, including but not limited to, the following validated scales: Hammersmith Infant Neurologic Exam (HINE), Hammersmith Functional Motor Scale Expanded (HFMSE), Children’s Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND), 6-minute walk test (6MWT), upper limb module (ULM), etc.
 - Respiratory function tests [e.g., forced vital capacity (FVC), etc.]
 - Exacerbations necessitating hospitalization and/or antibiotic therapy for respiratory infection in the preceding year/timeframe
 - Patient weight (for patients without a gastrostomy tube)

SMA phenotype 1 (aka Werdnig-Hoffman disease) has a natural history characterized by onset of symptoms (i.e. severe weakness) prior to 6 months of age, inability to sit without support, and an average life span of less than 2 years (in patients without prior therapy to increase SMN protein). SMA phenotype 2 is characterized by symptom onset between 6 and 18 months of age and failure to walk independently. SMA phenotype 3 is characterized by symptom onset after 18 months of age and an ability to walk independently at some point. Deficiency of SMN protein, due to homozygous deletion/mutation in the *SMN1* gene, results in loss of motor neurons in the spinal cord and brain stem manifesting clinically as atrophy and weakness. Copy number of the *SMN2* gene, which produces approximated 5-10% functional SMN protein, are positively correlated with milder phenotype.

- Approximately 80% of patients with SMA1 have 1 or 2 copies of the *SMN2* gene; approximately 20% have 3 copies (estimated percentages vary)
- The c.859G>C single base substitution modification in exon 7 of the *SMN2* gene is predictive of a milder phenotype

Nusinersen is a modified antisense oligonucleotide that binds to a specific sequence within the SMN2 pre-messenger RNA, thereby modifying the splicing of the SMN2 pre-messenger RNA to promote the expression of full-length SMN protein.

*Laboratory tests should be obtained within several days prior to administration

† FDA-labeled indication(s), ‡ Compendia recommended indication(s); ◊ Orphan Drug

IV. Renewal Criteria¹

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Absence of unacceptable toxicity which would preclude safe administration of the drug. Examples of unacceptable toxicity include the following: significant renal toxicity, thrombocytopenia, coagulation abnormalities, etc.; **AND**
- Patient has responded to therapy compared to pretreatment baseline in one or more of the following:
 - Stability or improvement in net motor function/milestones, including but not limited to, the following validated scales: Hammersmith Infant Neurologic Exam (HINE), Hammersmith Functional Motor Scale Expanded (HFMSSE), Children’s Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND), 6-minute walk test (6MWT), upper limb module (ULM), etc.
 - Stability or improvement in respiratory function tests [e.g., forced vital capacity (FVC), etc.]
 - Reduction in exacerbations necessitating hospitalization and/or antibiotic therapy for respiratory infection in the preceding year/timeframe
 - Stable or increased patient weight (for patients without a gastrostomy tube)
 - Slowed rate of decline in the aforementioned measures

V. Dosage/Administration

Indication	Dose
Spinal Muscular Atrophy	12 mg administered, as an intrathecal bolus injection over 1 to 3 minutes using a spinal anesthesia needle, per administration. Prior to administration, 5 mL of cerebrospinal fluid should be removed. Imaging guidance and sedation may be required for administration.
	<u>Initiation</u>
	Four loading doses: the first three loading doses should be administered at 14-day intervals. The 4 th loading dose should be administered 30 days after the 3 rd dose.
	<u>Maintenance</u>
	One dose every 112 days thereafter

Store refrigerated at 2°C to 8°C; warm to room temperature prior to administration

VI. Billing Code/Availability Information

HCPCS code:

J2326 –Injection, nusinersen, 0.1 mg; 1 billable unit = 0.1 mg

NDC:

Spinraza 12 mg/5 mL solution for injection; single-dose vial: 64406-0058-xx

VII. References

1. Spinraza [package insert]. Cambridge, MA; Biogen, Inc.; June 2020. Accessed June 2020.
2. Wang CH, Finkel RS, Bertini ES, et al. Consensus statement for standard of care in spinal muscular atrophy. *J Child Neurol.* 2007 Aug;22(8):1027-49.
3. Prior TW, Finanger E. Spinal muscular atrophy. GeneReviews. www.ncbi.nlm.nih.gov/books/NBK1352/ (Accessed on June 10, 2019).
4. Finkel RS, Mercuri E, Darras BT, et al; for the ENDEAR Study Group. Nusinersen versus sham control in infantile-onset spinal muscular atrophy. *N Engl J Med.* 2017;377(18):1723-1732. Finkel RS, Mercuri E, Darras BT, et al; for the ENDEAR Study Group. Nusinersen versus sham control in infantile-onset spinal muscular atrophy. *N Engl J Med.* 2017;377(18):1723-1732.
5. Mercuri E, Darras BT, Chiriboga CA, et al; for the CHERISH Study Group. Nusinersen versus sham control in later-onset spinal muscular atrophy. *N Engl J Med.* 2018;375:625-635.
6. Dabbous O, Maru B, Jansen JP, et al. Survival, Motor Function, and Motor Milestones: Comparison of AVXS-101 Relative to Nusinersen for the Treatment of Infants with Spinal Muscular Atrophy Type 1. *Adv Ther.* 2019 May;36(5):1164-1176.
7. Kichula E, Duong T, Glanzman A, et al. Children’s Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND) Feasibility for Individuals with Severe Spinal Muscular Atrophy II (S46.004). *Neurology* Apr 2018, 90 (15 Supplement) S46.004
8. Novitas Solutions, Inc. Local Coverage Determination (LCD): Nusinersen (Spinraza) (L38682). Centers for Medicare & Medicaid Services, Inc. Updated on 11/15/2019 with effective date 11/21/2019. Accessed June 2020.
9. Novitas Solutions, Inc. Local Coverage Article (LCA): Billing and Coding: Nusinersen (Spinraza) (A56860). Centers for Medicare & Medicaid Services, Inc. Updated on 12/19/2019 with effective date 12/26/2019. Accessed June 2020.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
G12.0	Infantile spinal muscular atrophy, type I [Werdnig-Hoffmann]
G12.1	Other inherited spinal muscular atrophy
G12.25	Progressive spinal muscle atrophy
G12.8	Other spinal muscular atrophies and related syndromes

ICD-10	ICD-10 Description
G12.9	Spinal muscular atrophy, unspecified

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: <http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx>. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA):

Jurisdiction(s): H,L	NCD/LCD/Article Document (s): L37682
https://www.cms.gov/medicare-coverage-database/search/lcd-date-search.aspx?DocID=L37682&bc=gAAAAAAAAAAAA	

Jurisdiction(s): H,L	NCD/LCD/Article Document (s): A56860
https://www.cms.gov/medicare-coverage-database/search/article-date-search.aspx?DocID=A56860&bc=gAAAAAAAAAAAA	

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto Government Benefit Administrators, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC