PROVIDER POLICIES & PROCEDURES

SPINRAZA® (NUSINERSEN)

The primary purpose of this document is to assist providers enrolled in the Connecticut Medical Assistance Program (CMAP) with the information needed to support a medical necessity determination for Spinraza (nusinersen). By clarifying the information needed for prior authorization of services, HUSKY Health hopes to facilitate timely review of requests so that individuals obtain the medically necessary care they need as quickly as possible.

Spinraza (nusinersen) is a prescription medication used to treat Spinal Muscular Atrophy (SMA) in pediatric and adult patients.

CLINICAL GUIDELINE

Coverage guidelines for the use of Spinraza (nusinersen) will be made in accordance with the DSS definition of Medical Necessity. The following criteria are guidelines *only*. Coverage guidelines are based on an assessment of the individual and their unique clinical needs. If the guidelines conflict with the definition of Medical Necessity, the definition of Medical Necessity shall prevail. The guidelines are as follows:

Initial Requests

Spinraza (nusinersen) may be considered medically necessary as an intrathecal injection for individuals with SMA Type 1, 2 or 3 when the following criteria is met:

A. Spinraza (nusinersen) has been ordered by or in consultation with a physician specializing in the management of SMA or other neuromuscular disorders; **AND**
B. The diagnosis of SMA has been made by or in consultation with a physician with expertise in diagnosing SMA; **AND**
C. Genetic testing has been performed and has confirmed documentation of homozygous deletion, homozygous mutation, or compound heterozygous mutations of the SMN1 gene on chromosome 5q; **AND**
D. The patient is not dependent on permanent ventilatory support (defined as invasive ventilation/tracheostomy or non-invasive ventilatory support for at least 16 hours per day for > 21 days in the absence of an acute reversible event); **AND**
E. A baseline motor exam has been completed by a physician or physical therapist (specializing in SMA motor exam evaluations and supervised by a neurologist or physiatrist) experienced in treating SMA and utilizing at least one of the following exam instruments:
    - Hammersmith Infant Neurological Exam, Section 2 (HINE - 2)
    - Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND)
    - Hammersmith Functional Motor Scale Expanded (HFMSE)
    - Revised Upper Limb Module (RULM);

    Other standardized tests may be considered appropriate based on an assessment of the individual and will be reviewed based on submitted medical documentation; **AND**
F. One of the following criteria is met:

1. The patient has not previously received gene replacement therapy (e.g., Zolgensma [onasemnogene abeparvovec]) for SMA; **OR**
2. The patient has previously received gene therapy replacement for SMA and has experienced a decline in clinical status; **AND**

G. The patient is not on concurrent gene-based SMA therapy (e.g., Evrysdi [risdiplam]); **AND**
H. Spinraza (nusinersen) administration will follow the current FDA Spinraza (nusinersen) labeling for dosing protocol; **AND**
I. A description of the benefits, risks and treatment expectations has been provided to the individual, parent or guardian.

Requests to Continue

Note: Members who previously received Spinraza (nusinersen) and subsequently administered gene therapy replacement (e.g., Zolgensma) must meet all initial nusinersen criteria prior to re-starting therapy on nusinersen.

Spinraza (nusinersen) will continue to be authorized in six (6) month intervals* when the following criteria is met**:**

A. The individual has:
1. Demonstrated a clear response. There is an improved motor ability in repeat motor testing after the 5th dose **(required for first re-authorization only).** Improvement when using the following tests is defined as:

HINE-2	Infants must improve in one or more milestones and show more milestones with improvement than worsening
CHOP INTEND	At least a 4 point increase in score from pretreatment baseline
HFMSE	At least a 3 point increase in score from pretreatment baseline
RULM	At least a 2 point increase in score from pretreatment baseline

OR

2. Achieved and maintained any new motor skills from pretreatment baseline when they would otherwise be unexpected to do so; **OR**
3. Maintained all prior motor skills and has not declined in functional status; **OR**
4. Demonstrated a decline in functional status. In these instances, a letter from the treating physician explaining why the medication should be continued along with supporting documentation from the medical literature; **AND**

B. One of the following criteria are met:
1. The patient has not received gene replacement therapy (e.g., Zolgensma [onasemnogene abeparvovec]) since Spinraza (nusinersen) therapy was originally approved; **OR**
2. The patient was prescribed Spinraza (nusinersen) due to clinical worsening after receiving gene replacement therapy (e.g., Zolgensma) and there is documentation of stabilization or improvement in clinical status with Spinraza (nusinersen) therapy (e.g., impact on motor milestones); **AND**

C. The patient is not on concurrent gene-based SMA therapy (e.g., Evrysdi [risdiplam]); **AND**

D. The patient is not dependent on permanent ventilatory support (defined as invasive ventilation/tracheostomy or non-invasive ventilatory support for at least 16 hours per day for > 21 days in the absence of an acute reversible event); **AND**
E. Documentation shows that the benefits of treatment continue to outweigh the risks (i.e., continued intrathecal injections).

*The 6 month periodic re-examination must be done by the same examiner as the baseline exam. If this is not possible, the re-examination must be done by another physician or physical therapist (specializing in SMA motor exam evaluations and supervised by a neurologist or physiatrist) experienced in treating SMA who must use the same exam instrument unless it is determined that the original exam instrument is no longer age appropriate.

SMA Type 0 and 4
Spinraza (nusinersen) is considered investigational in the treatment of SMA Types 0 and 4 and therefore not medically necessary.

NOTE: EPSDT Special Provision
Early and Periodic Screening, Diagnosis, and Treatment (EPSDT) is a federal Medicaid requirement that requires the Connecticut Medical Assistance Program (CMAP) to cover services, products, or procedures for Medicaid enrollees under 21 years of age where the service or good is medically necessary health care to correct or ameliorate a defect, physical or mental illness, or a condition identified through a screening examination. The applicable definition of medical necessity is set forth in Conn. Gen. Stat. Section 17b-259b (2011) [ref. CMAP Provider Bulletin PB 2011-36].

PROCEDURE
Prior authorization of Spinraza (nusinersen) is required. Coverage determinations will be based upon a review of requested and/or submitted case-specific information.

The following information is needed to review requests for Spinraza™ (nusinersen):
1. Fully completed State of Connecticut, Department of Social Services HUSKY Health Program Spinraza (nusinersen) Prior Authorization Request form (to include physician's order and signature);
2. Clinical information supporting the medical necessity of the treatment as outlined in the *Clinical Guideline* section of this policy to include genetic testing and baseline motor exam results and medical record documentation from the treating neurologist; and
3. Other information as requested.

Requesting Authorization
Requests for the prior authorization of Spinraza (nusinersen) must be submitted by the ordering physician and faxed to the number listed on the request form. Questions regarding this form should be directed to the HUSKY Health Program Utilization Management Department at 1.800.440.5071 (select option for medical authorizations).

Initial Authorization
Initial approval of Spinraza (nusinersen) will be for 5 doses ONLY (4 initial loading doses and 1 maintenance dose) to be given in accordance with the current Spinraza (nusinersen) FDA label instructions.

Re-authorization
After the initial 5 doses have been administered, the individual must be re-evaluated as outlined in the *Clinical Guideline* section of this policy.

This re-examination must be done by the same examiner as the baseline exam. If this is not possible, the re-examination must be done by another physician who is experienced in treating SMA) or a physical therapist (specializing in SMA motor exam evaluations and supervised by a neurologist or physiatrist).

EFFECTIVE DATE
This Policy for the prior authorization of Spinraza (nusinersen) for individuals covered under the HUSKY Health Program is effective November 1, 2017.

LIMITATIONS
Not Applicable

CODE:

Code	Definition
J2326	Injection, nusinersen, 0.1mg

DEFINITIONS

1. **Current Procedural Terminology (CPT):** The most recent edition of a listing, published by the American Medical Association, of descriptive terms and identifying codes for reporting medical services performed by providers.
2. **HUSKY A**: Connecticut children and their parents or a relative caregiver; and pregnant women may qualify for HUSKY A (also known as Medicaid). Income limits apply.
3. **HUSKY B**: Uninsured children under the age of 19 in higher income households may be eligible for HUSKY B (also known as the Children's Health Insurance Program) depending on their family income level. Family cost-sharing may apply.
4. **HUSKY C**: Connecticut residents who are age 65 or older or residents who are ages 18-64 and who are blind, or have another disability, may qualify for Medicaid coverage under HUSKY C (this includes Medicaid for Employees with Disabilities (MED-Connect), if working). Income and asset limits apply.
5. **HUSKY D**: Connecticut residents who are ages 19-64 without dependent children and who: (1) do not qualify for HUSKY A; (2) do not receive Medicare; and (3) are not pregnant, may qualify for HUSKY D (also known as Medicaid for the Lowest-Income populations).
6. **HUSKY Health Program**: The HUSKY A, HUSKY B, HUSKY C, HUSKY D and HUSKY Limited Benefit programs, collectively.
7. **HUSKY Limited Benefit Program or HUSKY, LBP**: Connecticut's implementation of limited health insurance coverage under Medicaid for individuals with tuberculosis or for family planning purposes and such coverage is substantially less than the full Medicaid coverage.
8. **Medically Necessary or Medical Necessity**: (as defined in Connecticut General Statutes § 17b-259b) Those health services required to prevent, identify, diagnose, treat, rehabilitate or ameliorate an individual's medical condition, including mental illness, or its effects, in order to attain or maintain the individual's achievable health and independent functioning provided such services are: (1)

Consistent with generally-accepted standards of medical practice that are defined as standards that are based on (A) credible scientific evidence published in peer-reviewed medical literature that is generally recognized by the relevant medical community, (B)recommendations of a physician-specialty society, (C) the views of physicians practicing in relevant clinical areas, and (D) any other relevant factors; (2) clinically appropriate in terms of type, frequency, timing, site, extent and duration and considered effective for the individual's illness, injury or disease; (3) not primarily for the convenience of the individual, the individual's health care provider or other health care providers; (4) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the individual's illness, injury or disease; and (5) based on an assessment of the individual and his or her medical condition.

9. **Prior Authorization**: A process for approving covered services prior to the delivery of the service or initiation of the plan of care based on a determination by CHNCT as to whether the requested service is medically necessary.

ADDITIONAL RESOURCES AND REFERENCES:

1. Chiriboga CA, Swoboda KJ, Darras BT, et al. Results from a phase 1 study of nusinersen (ISIS-SMN(Rx)) in children with spinal muscular atrophy. Neurology. 2016 Mar 8;86(10):890-7.
2. De Vivo DC, et al. Nusinersen in Presymptomatic Infants with Spinal Muscular Atrophy: Interim Efficacy and Safety Results from Phase 2 of NURTURE Study. Presented at the CureSMA Conference; 2018; Dallas, TX.
3. Finkel RS, Chiriboga CA, Vajsar J, et al. Treatment of infantile-onset spinal muscular atrophy with nusinersen: a phase 2, open-label, dose-escalation study. Lancet. 2017 Dec 17; 388(10063):3017-3026.
4. Finkel RS, Mercuri E, Darras BT, et al. Nusinersen versus Sham Control in Infantile-Onset Spinal Muscular Atrophy. N Engl J Med. 2017;377(18):1723-1732**.**
5. Glanzman AM, O'Hagen JM, McDermott MP, et al. Validation of the Expanded Hammersmith Functional Motor Scale in spinal muscular atrophy type II and III. J Child Neurol. 2011; 26(12):1499-507.
6. Haataja L, Mercuri E, Regev R, et al. Optimality score for the neurologic examination of the infant at 12 and 18 months of age. J Pediatr. 1999 Aug;135(2 Pt 1):153-61.
7. Ionis Pharmaceuticals, Inc. A Study to Assess the Efficacy and Safety of IONIS-SMN Rx in Infants with Spinal Muscular Atrophy. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000-[cited 2017 Jan 6]. Available from: https://clinicaltrials.gov/show/NCT02193074
8. Ionis Pharmaceuticals, Inc. A Study to Assess the Efficacy and Safety of IONIS-SMN Rx in Patients with Later-onset Spinal Muscular Atrophy. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000-[cited 2017 Jan 6]. Available from: https://clinicaltrials.gov/show/NCT02292537
9. Lunn MR, Wang CH. Spinal muscular atrophy. Lancet. 2008 Jun 21;371(9630):2120-33.
10. Markowitz JA, Singh P, Darras BT. Spinal Muscular Atrophy: A Clinical and Research Update. Pediatric Neurology 46 (2012) 1-12.
11. Mercuri E, Darras BT, Chiriboga CA, et al. Nusinersen versus Sham Control in Later-Onset Spinal Muscular Atrophy. N Engl J Med. 2018;378(7):625-635.
12. O'Hagen JM, Glanzman AM, McDermott MP, et al. An expanded version of the Hammersmith Functional Motor Scale for SMA II and III patients. Neuromuscular disorders: NMD. 2007; 17(9-10):693-7.

13. Prior TW, Snyder PJ, Rink BD, et al. Newborn and carrier screening for spinal muscular atrophy. Am J Med Genet A. 2010 Jul;152A(7):1608-16.
14. Spinraza [package insert]. Cambridge, MA: Biogen, Inc., revised February 2023.
15. Sugarman EA, Nagan N, Zhu H, et al. Pan-ethnic carrier screening and prenatal diagnosis for spinal muscular atrophy: clinical laboratory analysis of >72,400 specimens. Eur J Hum Genet 2012; 20:27-32.
16. Walter MC, Wenninger S, Thiele S, et al. Safety and treatment effects of nusinersen in longstanding adult 5q-SMA type 3 – A prospective observational study. J Neuromuscul Dis. 2019;6(4):453-465.
17. Yeo CJJ, Simeone SD, Townsend EL, et al. Prospective cohort study of nusinersen treatment in adults with spinal muscular atrophy. J Neuromuscul Dis. 2020;7(3):257-268.

PUBLICATION HISTORY

Status	Date	Action Taken
Original publication	October 2017	Approved by DSS on October 23, 2017. Approved by the Clinical Quality Subcommittee on December 18, 2017.
Update	July 2018	Code Update. HCPCS code C9489 deleted by CMS effective January 1, 2018. New code *J2326 - Injection, nusinersen, 0.1 mg*, effective January 1, 2018, added. Approved at the July 25, 2018 Medical Policy Review Committee Meeting. Change approved by the CHNCT Clinical Quality Subcommittee on September 17, 2018. Approved by DSS on September 19, 2018.
Update	June 2019	Update to *Clinical Guideline* section. Added SMA types 2 and 3 Added language indicating that treatment with Spinraza is considered investigational for those with SMA type 0 or 4. Created new guidelines for individuals who are presymptomatic Added guidelines for individuals who do not clearly respond to treatment Updated guidelines for reauthorization requests. Changed HINE exam to HINE-2 Changed ULM test to RULM test Added language that other standardized motor tests may be appropriate and will be reviewed based on submitted documentation. Added need for a description of benefits, risks and treatment expectations to be provided to patient or parent/guardian Update to *Additional Resources and References* section Changes approved at the June 12, 2019 Medical Reviewer meeting. Changes approved by the CHNCT Clinical Quality Subcommittee on June 19, 2019. Approved by DSS on June 21, 2019.
Update	June 2020	Added criteria related to previous gene therapy. Change approved at the May 13, 2020 Medical Reviewer meeting. Change approved by the CHNCT Clinical Quality Subcommittee on June 15, 2020. Approved by DSS on June 19, 2020.

Update	June 2021	Removed criteria requiring the individual to have at least 2 copies of the SMN2 gene. Revised criteria to add the following: individual has not previously been treated with Zolgensma and not on concurrent gene based therapy for SMA. Changes approved at the April 14, 2021 CHNCT Medical Reviewer meeting. Changes approved at the June 21, 2021 CHNCT Clinical Quality Subcommittee meeting. Approved by DSS on June 28, 2021.
Update	June 2022	Updated Clinical Guideline section for *Requests to Continue* for symptomatic patients with SMA Types 1, 2, or 3. Formatting updates. Added indication for individuals previously treated with Zolgensma who have demonstrated clinical worsening. Changes approved at the May 11, 2022 CHNCT Medical Reviewer meeting. Changes approved by the CHNCT Clinical Quality Subcommittee on June 20, 2022. Approved by DSS on July 5, 2022.
Update	June 2023	Updated Clinical Guideline section. Removed pre-symptomatic criteria and reorganized remaining criteria. Added statement regarding individuals who previously were treated with Zolgensma. Added additional statements in the “requests to continue” section with regards to achieving and maintaining new motor milestones. Moved the statement regarding ventilatory support in the “requests to continue” section into criteria. Updated Reference section. Changes approved at the May 10, 2023, CHNCT Medical Reviewer meeting. Changes approved by the CHNCT Clinical Quality Subcommittee on June 19, 2023. Approved by DSS on June 28, 2023.
Reviewed	May 2024	Reviewed and approved with no changes at the May 22, 2024 CHNCT Medical Reviewer meeting. Approved by the CHNCT Clinical Quality Subcommittee on June 17, 2024. Approved by DSS on June 26, 2024.