BlueCross BlueShield of Texas

Medical Policies

Medical Policies - Prescription Drugs

Nusinersen (Spinraza)

Number:RX501.086

Effective Date:06-15-2017

Coverage:

CAREFULLY CHECK STATE REGULATIONS AND/OR THE MEMBER CONTRACT

Medical policies are a set of written guidelines that support current standards of practice. They are based on current peer-reviewed scientific literature. A requested therapy must be proven effective for the relevant diagnosis or procedure. For drug therapy, the proposed dose, frequency and duration of therapy must be consistent with recommendations in at least one authoritative source. This medical policy is supported by FDA-approved labeling and nationally recognized authoritative references. These references include, but are not limited to: MCG care guidelines, Hayes, DrugDex (IIb level of evidence or higher), NCCN Guidelines (IIb level of evidence or higher), NCCN Compendia (IIb level of evidence or higher), professional society guidelines, and CMS coverage policy.

Initial Therapy

Nusinersen (Spinraza™) **may be considered medically necessary** for patients with spinal muscular atrophy (SMA) who meet ALL of the following criteria:

- Diagnosis of SMA Type I, II, or III; **AND**
- Documentation of 5q SMA homozygous gene deletion, homozygous gene mutation, or compound heterozygote; **AND**
- ≤15 years of age at initiation of treatment.

Continuation Therapy

Continuation of treatment with nusinersen (Spinraza™) beyond 6 months after initiation of therapy, and every 4 months thereafter, **may be considered medically necessary** when:

- Criteria for initial therapy was met; **AND**
- There is documentation of clinically significant improvement in SMA-associated symptoms compared to the predicted natural course of the disease (e.g., progression, stabilization, or decreased decline in motor function).

Nusinersen (Spinraza™) **is considered not medically necessary** for patients who have a diagnosis of SMA when the criteria above are not met, as a clinical benefit has not been established.

Nusinersen (Spinraza™) **is considered experimental, investigational, and/or unproven** for all other indications.

Description:

Spinal muscular atrophy (SMA) is a rare autosomal recessive genetic disorder that occurs due to homozygous deletions or variant in the SMN1 gene in chromosome 5. This gene is responsible for producing the “survival of motor neuron” protein (SMN1). As a consequence of absent or low levels of SMN1, the motor neurons in spinal cord degenerate resulting in atrophy of the voluntary muscles of the limbs and trunk. During early development, these muscles are necessary for crawling, walking, sitting up, and head control. The more severe types of SMA can also affect muscles involved in feeding, swallowing, and breathing. The exact role of SMN protein in motor neurons has not been completely elucidated and levels of SMN protein required for optimal functioning are unknown. (1) SMN2 is a nearly identical modifying gene capable of producing nearly identical compensatory SMN2 protein. However, 70% to 90% of the transcripts produced from the SMN2 gene produce a truncated protein which is defective and unstable due to lack of exon 7. (2) Further, humans exhibit variability (range, 0-6) in the number of copies of SMN2 gene and copy number is inversely proportional to severity of disease. (3) These factors in tandem lead to wide variability in disease severity.

SMA is classified into 4 main categories (with additional subcategories) based on the age at the onset of symptoms. (4, 5) Generally, early onset of disease directly correlates to severity of symptom and rate of disease progression.

• Type 0: The most severe form of SMA, symptoms can often be seen in the later stages of pregnancy. Fetal movements are less than expected and after birth, the infant will have little ability to move and may not be able to breathe and swallow independently. Death occurs before the age of 6 months.

• Type I (also called infantile SMA or Werdnig-Hoffman disease and subcategorized as IA, IB and IC): Onset within 6 months of birth and symptoms progress rapidly, and the majority of infants die before one year of age from respiratory failure. About 60% of patients with SMA constitute of this phenotype. (6, 7)

• Type II (also called intermediate SMA or Dubowitz disease): Onset within 6 to 18 months with a less severe progression. Typically, a child can sit independently if positioned but is unable to walk. More than 70% of patients live beyond 25 years of age with adequate supportive care.

• Type III (also called Kugelberg-Welander disease and subcategorized as IIIA and IIIB): Onset after 18 months of age. Lifespan is not affected with a wide ranging reduction in muscle strength with a chronic course. The outcome depends primarily upon the severity of muscle weakness at presentation rather than the age of onset, but earlier onset tends to correlate with greater weakness. (8)

• Type IV (also called adult onset SMA): Usually presents in the third decade of life and is otherwise similar to SMA type III.

The birth prevalence of SMA is estimated to be between 9.1 and 10 per 100,000 live births. (9, 10) In 95% cases, both copies of the SMN1 exon 7 are absent. Remaining 5% cases are compound heterozygotes for SMN1 exon 7 deletion and small intragenic variants. The molecular diagnosis of SMA consists of the detection of the absence of exons 7 of the SMN1 gene in the majority of cases. (11)

Treatment

Nusinersen (Spinraza™) is a modified antisense oligonucleotide (a synthetic genetic material) that binds to a specific sequence in the intron downstream of exon 7 of the SMN2 transcript causing the inclusion of exon 7 in the SMN2 transcript leading to production of full length functional SMN2 protein. (12) Prior to approval of nusinersen, there were no U.S. Food and Drug Administration (FDA)-approved treatments for SMA. Medical management of SMA patients includes respiratory, digestive and musculoskeletal supportive care.

REGULATORY STATUS

In December 23, 2016, Spinraza™ (nusinersen; Biogen) was approved by the FDA through new drug application for use in spinal muscular atrophy in pediatric and adult patients.

The recommended dosing is 12mg (5mL) per intrathecal administration:

• Loading doses: first three loading doses should be administered at 14 day intervals; fourth loading dose should be administered 30 days after the third dose.

• Maintenance doses: administered once every 4 months thereafter.

Rationale:

This medical policy was originally created in February 2017 based on a search of the MEDLINE database. A summary of the identified literature is presented next.

INFANTILE-ONSET OR TYPE I SPINAL MUSCULAR ATROPHY

The evidence base is summarized in Table 1. The evidence base for patients with type I spinal muscular atrophy (SMA) consists of 2 randomized controlled trials (RCTs) and 2 early-phase open-labeled studies. Results of a phase 2 RCT trial (EMBRACE) are not available and not discussed further.

Table 1. Summary of Key Trial Characteristics in Infantile-Onset or Type I SMA Patients

Author	Study	Design	Dates	Patients (N)	Outcome	Results
Unpublished	ENDEAR	RCT	Aug 2014	Symptomatic (82)	Efficacy, safety	Available
Unpublished	EMBRACE	RCT	Aug 2015	Symptomatic (21)	Safety, tolerability	Not available
Finkel (2016)[13]	CS3A	1 arm	May 2013	Symptomatic (20)	Safety, PK	Available
Unpublished	NURTURE	1 arm	May 2015	Presymptomatic (25)	Efficacy	Available

PK: pharmacokinetics; RCT: randomized controlled trial; SMA: spinal muscular atrophy.

Symptomatic Patients

The pivotal trial was a multicenter randomized, double-blind trial (ENDEAR; NCT02193074) in which 121 infants with documented genetic diagnosis of SMA with symptom onset before 6 months of age were randomized to 2:1 to nusinersen (n=80) or sham injection (n=41). Patients were documented to have 5q SMA homozygous gene deletion, homozygous variant or compound heterozygote and 2 copies of SMN2. With a sample size of 111, the trial had 80% power to detect doubling of median time to death or permanent ventilation in nusinersen versus sham-controlled group. (14)

Nusinersen was approved on the basis of planned interim analysis that included 82 patients who completed at least 183 days of treatment or died or withdrew. Patients demographics at baseline were 44% male, 87% white, median length of

treatment 261 days (range, 6-442 days). The 2 treatment groups were balanced with respect to gestational age, birth weight, disease duration, and SMN2 copy number, except for age at symptom onset. The proportion of patients with symptom onset in the first 12 weeks of life was more in nusinersen (88%) versus sham-controlled arm (77%). The primary end point was proportion of motor milestone responders. Motor milestones were assessed according to section 2 of the Hammersmith Infant Neurologic Exam (HINE) that evaluates 7 different areas of motor milestone development, with a maximum score between 2 to 4 points for each, depending on the milestone, and a total maximum score of 26. Responder was defined as any patient with:

• At least a 2-point increase (or maximal score of 4) in ability to kick (consistent with improvement by at least 2 milestones), or at least a 1-point increase in the motor milestones of head control, rolling, sitting, crawling, standing or walking (consistent with improvement by at least 1 milestone)

• Plus improvement in more categories of motor milestones than worsening.

Multiple secondary end points related to motor improvement, survival, need for ventilation, and electrophysiology were also reported. However, the statistical plan for interim analysis did not control for multiple comparisons and therefore such results should be considered exploratory.

The results are not yet published. Results summarized in Table 2 were obtained from the U.S. Food and Drug Administration (FDA)-approved label (12) and the Academy of Managed Care Pharmacy (AMCP) dossier. (14) There was an inconsistency in the number of patients included in the interim analysis between the sponsor and FDA and therefore for the sake of clarity, information from both sources is reported side-by-side. As evident from the Table 2, the difference in the numerator was not large and results were similar between the 2 analyses. These results show that in patients with type I SMA, nusinersen showed clinically meaningful improvement in motor milestones such as independent sitting, standing and walking and other motor function that exceeded those seen in the control group. Further, the hazard ratio (HR) for event-free survival was 0.53 in favor of nusinersen versus sham controlled. (15) Event was defined as death or permanent ventilation defined as tracheostomy or 16 or more hours of ventilatory support per day for more than 21 days in the absence of acute reversible event by an independent end point adjudication committee. The median time to an event was not reached in the nusinersen arm compared to 22.6 weeks results in the sham-controlled arm. (15) In the FDA label, 40% of the nusinersen group and 0% of the sham-controlled group achieved the primary endpoint responder definition of achieving motor milestones. Similarly, 63% of patients who received nusinersen met the 4- or-more point improvement in CHOP-INTEND scores; whereas only 3% of sham-controlled group met this secondary endpoint. It is notable, however, that a majority of nusinersen treated subjects did not achieve the primary endpoint motor milestone response. Given the limited data on durability of response, long-term safety, and lack of efficacy in substantial number of patients, continued risk-benefit assessment of long-term treatment with nusinersen is necessary.

Table 2. Summary of Results of Pivotal ENDEAR Trial

Characteristics and Outcomes	**FDA (12)**		**Sponsor (14)**	
	Nusinersen	Sham-Controlled	Nusinersen	Sham-Controlled
N	52	30	51	27
Dead	≈23%[a]	≈43%[a]	11 (22%)	10 (37%)
Withdrawn	Not reported	Not reported	1 (2%)	1 (4%)

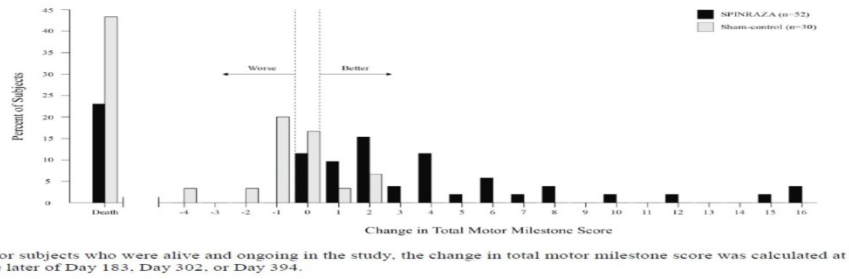
Included in interim analysis	52	30	51	27
Primary end point				
% motor milestone response (HINE section 2)	21 (40%)	0 (0%)	21 (41%)	0(0%)
Secondary end point				
≥4-point improvement in CHOP-INTEND	33 (63%)	1 (3%)	Not reported	Not reported
≥4-point worsening in CHOP-INTEND	2 (4%)	12 (40%)	Not reported	Not reported

Statistical testing not available with interim analysis. Values are percent or n (%) or as otherwise indicated.

CHOP-INTEND: Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders; FDA: Food and Drug Administration; HINE: Hammersmith Infant Neurologic Exam.

[a] Values estimated from graph in the prescribing.

Figure 1. Net Change From Baseline in Total Motor Milestone Score by Percentage of Patients in the Interim Efficacy Set[a]



Source: Food and Drug Administration label. (12)

At the final analysis, a significantly greater percentage of patients achieved a motor milestone response in the nusinersen group (51%) compared with the control group (0%). Sixteen of 73 patients (22%) in the nusinersen group achieved full head control, 6 of 73 patients (8%) achieved independent sitting, and 1 of 73 (1%) achieved standing. None of the patients in the control group achieved any of these milestones. Additionally, a 62.8% reduction in the risk of death, and a 34% reduction in the risk of or permanent ventilation was seen in the treatment group compared with the control. The percentage of patients who achieved a CHOP INTEND response was also significantly greater in the nusinersen group (71%) versus the control group (%). Several of nusinersen-treated infants had improvements of 10 or more points, but only 1 patient in the control group showed improvement. All other patients in the control group showed no change or worsened, many by more than 10 points. (17)

Subsection Summary: Symptomatic Infantile-Onset or Type I Spinal Muscular Atrophy

The evidence for use of nusinersen for symptomatic infantile-onset or type I spinal muscular atrophy consists of 2 double-blind RCTs (results not yet reported for one) and 1 single arm study. The largest RCT showed clinically meaningful improvement in motor milestones that exceeded those seen in the control group. Further, nusinersen increased event-

free survival compared to control arm. The findings of the open-labelled studies also support the findings of the larger phase 3 confirmatory ENDEAR trial.

Presymptomatic Patients

In a multi-center, single-arm open-label trial (NURTURE NCT02386553), 25 infants deemed most likely to develop SMA received nusinersen. The infant's age ranged from 8 days to 42 days at the time of first dose. Patients were documented to have 5q SMA homozygous gene deletion, homozygous variant or compound heterozygote and 2 or 3 copies of SMN2. The trial is ongoing and the study has not been published. Results of a planned interim analysis reported here were sourced from the AMCP dossier supplied by Biogen. (14) The primary endpoint was time to death or respiratory intervention (invasive or non- invasive ventilation for >6 hours/day continuously over for 7 or more days or tracheostomy). Multiple secondary endpoints related to motor improvement, growth, survival, need for ventilation and electrophysiology were also assessed. No formal sample size calculations done for this study.

The interim analysis was done when 17 of the 25 patients were enrolled and 13 patients reached day 64 of the study. None of the patients reached the primary endpoint. Although this was a single arm study, indirect comparison presymptomatic nusinersen treated patients in the NURTURE study with symptomatic nusinersen and sham-treated patients from the ENDEAR study show separation of Kaplan Meir curves (data not shown) for time to death or ventilation. (14, 15) Improvement in HINE scores was observed in 92% (12 of 13) at 2 months, 100% (10 of 10) at 6 months and 100% (5 of 5) at 10 months of follow-up. About 54% (7 of 13) of patients showed ≥ 4-point improvement in HINE section 2 scores. While FDA did not report these results in the label, they agreed with the sponsor findings that the open-labelled uncontrolled trials such as NURTURE were consistent with the results of pivotal RCT and support the efficacy of nusinersen in infantile SMA including when given to presymptomatic patients. The prescribing Label (12) states, "some patients achieved milestones such as ability to sit unassisted, stand, or walk when they would otherwise be unexpected to do so, maintained milestones at ages when they would be expected to be lost, and survived to ages unexpected considering the number of SMN2 gene copies of patients enrolled in the studies."

At a third interim analysis, only 1 patient received ventilation for ≥ 6 hours/day continuously for ≥1 day (4 to 6 hours for 9 continuous days) to treat a significant adverse event of respiratory distress. Additionally, motor milestone (as assessed by the HINE and WHO scales) were achieved by most patients treated with nusinersen. At days 183, 302, and 365, more than 50% of patients achieved the expected motor milestones based on age in the categories of head control (88%, 91%, and 100% respectively), rolling (81%, 82%, and 78% respectively), and sitting (63%, 73%, and 67% respectively). At day 365, all 9 patients with a day 365 visit had achieved the expected motor milestones based on age in the categories of ability to kick and head control, and more than 50% of patients achieved the expected motor milestones based on age in the categories of rolling (78%), sitting (67%), crawling (56%), and walking (56%). (17)

Subsection Summary: Presymptomatic Infantile-Onset or Type I Spinal Muscular Atrophy

The evidence for use of nusinersen for presymptomatic infantile-onset or type I SMA consists of 1 single-arm study. This study showed support for the efficacy as well as early initiation of nusinersen in infantile SMA patients as these patients achieved larger improvement in motor milestones when compared indirectly with the results of ENDEAR trial in symptomatic patients.

TYPE II OR III SPINAL MUSCULAR ATROPHY

The evidence base for patients with type II or III SMA is summarized in Table 3.

Table 3. Summary of Key Trial Characteristics in Type II and III SMA Patients

Author	Study	Design	Dates	(N)	Outcomes	Results
Chiriboga (2016) (16)	CS1	1 arm	Nov 2011	28	Safety and tolerability	Available
Chiriboga (2016) (16)	CS10	1 arm	Jan 2013	18	Safety and tolerability	Available
Unpublished	CS2	1 arm	Oct 2012	34	Safety and tolerability	Available
Unpublished	CS12	1 arm	Jan 2014	52	Safety and tolerability	Available
Unpublished	CHERISH	RCT	July 2014	126	Efficacy and safety	Available

RCT: randomized controlled trial; SMA: spinal muscular atrophy.

The evidence base of patients with type II and III SMA is limited to 4 early-phase open-labeled studies and one double-blind phase 3 RCT. Of these, results of 2 early-phase 1 studies (NCT01494701, NCT01780246) have been published but are not reviewed here because they were early dose-finding and proof of concept studies. The remaining studies- CS2 (NCT01703988), CS12 (NCT02052791), and CHERISH (NCT02292537) have not been published yet but data was sourced from the AMCP dossier supplied by Biogen. (14, 17)

The confirmatory phase 3 CHERISH (NCT02292537) trial was expected to be completed in May 2017 but was closed early as the results of a pre-planned interim analysis met the primary endpoint of efficacy. (14) Similar to ENDEAR, CHERISH trial was also designed as a multicenter, randomized, double-blind trial in which 126 nonambulatory patients with the onset of signs and symptoms at greater than 6 months and an age of 2 to 12 years at screening were randomized 2:1 to nusinersen (n=84) or sham-control (n=42). The primary end point was change in Hammersmith Functional Motor Scale Expanded (HFMSE) scale compared to baseline. Patients who received nusinersen (n=84) showed a statistically significant improvement in HFMSE scored as compared with patients in the control group (n=42) at 15 months. The results showed an improvement in HFMSE scores from baseline to month 15 in the nusinersen group of a lease squares mean change of 4.0 (95% CI, 2.9-5.1) and a decline in the control group of -1.9 (95% CI, -3.8 to 0.0), with a difference of 5.9 (95% CI, 3.7-8.1; P=0.0000002). While there were patients in the control group who lost motor milestones at 15 months (4 of 19, or 21%), there were no motor milestones lost in the nusinersen group. (17)

CS2 is phase 1/2, single-arm study that was completed in January 2015. (14) It included 34 patients between the ages of 2 and 15 with documented genetic diagnosis of 5q SMA and clinical signs and symptoms attributed to SMA. Patients received various doses of nusinersen ranging from 3 to 12 mg with an average 8-month follow-up. The primary endpoint was safety and secondary end point was pharmacokinetic parameters. Multiple exploratory end points related to motor function were assessed including change in HFMSE. CS12 was a long-term extension study that included patients from CS2 as well other studies. In the 6 patients with SMA type II the mean change after 1050 days of treatment was 12.3±5.46. In the 7 patients with SMA type III, the mean change after 1050 days of treatment was 1.6±3.91.

Section Summary: Type II or III Spinal Muscular Atrophy

The evidence for use of nusinersen for patients with type II or III SMA consists of 4 single-arm studies and 1 double-blind RCT. The confirmatory phase 3 CHERISH trial showed clinically meaningful improvement and retention of motor milestones that exceeded those seen in the control group.

TYPE 0 OR IV SPINAL MUSCULAR ATROPHY

There are currently no studies assessing efficacy and safety of nusinersen in patients with type 0 or IV spinal muscular atrophy.

HARMS

As per the prescribing label, thrombocytopenia including acute severe thrombocytopenia and renal toxicity including potentially fatal glomerulonephritis has been observed with antisense oligonucleotides. (12) In the controlled ENDEAR trial, the most common adverse reactions that occurred in at least 20% of nusinersen-treated patients and occurred at least 5% more frequently than sham-controlled patients were lower respiratory infection, upper respiratory infection, and constipation. Serious adverse reactions of atelectasis were more frequent in nusinersen-treated patients (14%) versus sham-control (5%). Adverse reactions that are reported verbally were not assessable in the sham-controlled trial because patients were infants. In the open labelled studies in patients with type II or III SMA, the most common adverse events were headache (50%), back pain (41%), and post lumbar puncture syndrome (41%), which occurred within 5 days of lumbar puncture. Other adverse events in these patients were consistent with adverse reactions observed in the controlled study. In addition, one case of severe hyponatremia in an infant that required salt supplementation for 14 months and 2 cases of rash were reported. Both patients with rash continued to receive nusinersen and had spontaneous resolution of the rash.

Development of anti-nusinersen antibodies were assessed in 126 patients of whom 5 (4%) developed treatment-emergent antidrug antibodies, of which 3 were transient and 2 were persistent. There are insufficient data to evaluate an effect of antidrug antibodies on clinical response, adverse events, or the pharmacokinetic profile of nusinersen. (12)

SUMMARY OF EVIDENCE

Infantile-Onset or Type I SMA

For individuals who have infantile-onset or type I SMA (symptomatic or presymptomatic) who receive nusinersen, the evidence includes 2 randomized, double-blind, controlled trial (results not yet reported for one) and 1 single-arm open-labelled study. Relevant outcomes are disease-specific survival, change in disease status, morbid events, functional outcomes, health status measures, quality of life, and treatment-related mortality and morbidity. Trial results in symptomatic patients showed clinically meaningful improvement in motor milestones as well as event-free survival that exceeded those seen in the control group with an acceptable safety profile. Given the limited data on durability of response, long-term safety, and lack of efficacy in substantial number of patients, continued risk-benefit assessment of long-term treatment with nusinersen is necessary. The open-label uncontrolled trial in presymptomatic infantile-onset SMA patients found a benefit of early treatment with nusinersen. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Type II and III SMA

For individuals who have type I or II SMA who receive nusinersen, the evidence includes 4 single arm studies and 1 double-blind RCT. Relevant outcomes are change in disease status, morbid events, functional outcomes, health status measures, quality of life, treatment-related mortality and treatment- related morbidity. Efficacy from single arm studies is difficult to interpret because these trials used a wide range of nusinersen dose, included both type II and III and lacked a control arm. However, results of the confirmatory phase III CHERISH trial showed clinically meaningful improvement and retention of motor milestones that exceeded those seen in the control group. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Type 0 and IV SMA

For individuals who have type 0 or IV SMA who receive nusinersen, no studies were identified. Relevant outcomes are change in disease status, morbid events, functional outcomes, health status measures, quality of life, treatment-related mortality and treatment-related morbidity. The evidence is insufficient to determine the effects of technology on health outcomes.

ONGOING AND UNPUBLISHED CLINICAL TRIALS

Some currently unpublished trials that might influence this review are listed in Table 4. Further, complete results of both pivotal trials (ENDEAR and CHERISH) have not been published.

Table 4. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT02594124[a]	An Open-Label Study (SHINE) for Patients With Spinal Muscular Atrophy (SMA) Who Participated in Studies With IONIS-SMNRx	271	Feb 2020

NCT: national clinical trial.

[a] Denotes industry-sponsored or cosponsored trial.

Contract:

Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Coding:

CODING:

Disclaimer for coding information on Medical Policies

Procedure and diagnosis codes on Medical Policy documents are included only as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, device or diagnosis codes in a Medical Policy document has **no** relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a medical policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT/HCPCS/ICD-9/ICD-10 Codes
The following codes may be applicable to this Medical policy and may not be all inclusive.

CPT Codes
96450

HCPCS Codes
J3490

ICD-9 Diagnosis Codes
Refer to the ICD-9-CM manual

ICD-9 Procedure Codes
Refer to the ICD-9-CM manual

ICD-10 Diagnosis Codes
Refer to the ICD-10-CM manual

ICD-10 Procedure Codes
Refer to the ICD-10-CM manual

Medicare Coverage:

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <http://www.cms.hhs.gov>.

References:

1. Wang CH, Finkel RS, Bertini ES, et al. Consensus statement for standard of care in spinal muscular atrophy. J Child Neurol. Aug 2007; 22(8):1027-1049. PMID 17761659

2. Lorson CL, Hahnen E, Androphy EJ, et al. A single nucleotide in the SMN gene regulates splicing and is responsible for spinal muscular atrophy. Proc Natl Acad Sci U S A. May 25 1999; 96(11):6307-6311. PMID 10339583

3. Lefebvre S, Burlet P, Liu Q, et al. Correlation between severity and SMN protein level in spinal muscular atrophy. Nat Genet. Jul 1997; 16(3):265-269. PMID 9207792

4. Muscular Dystrophy Association. Spinal Muscular Atrophy. Available at <https://www.mda.org> (accessed January 18, 2017).

5. National Organization for Rare Disorders, Russman B. Spinal Muscular Atrophy. 2012. Available at <https://rarediseases.org> (accessed January 18, 2017).

6. Zerres K, Rudnik-Schoneborn S. Natural history in proximal spinal muscular atrophy. Clinical analysis of 445 patients and suggestions for a modification of existing classifications. Arch Neurol. May 1995; 52(5):518-523. PMID 7733848

7. Finkel RS, McDermott MP, Kaufmann P, et al. Observational study of spinal muscular atrophy type I and implications for clinical trials. Neurology. Aug 26 2014; 83(9):810-817. PMID 25080519

8. Rudnik-Schoneborn S, Hausmanowa-Petrusewicz I, Borkowska J, et al. The predictive value of achieved motor milestones assessed in 441 patients with infantile spinal muscular atrophy types II and III. Eur Neurol. 2001; 45(3):174-181. PMID 11306862

9. Prior TW. Perspectives and diagnostic considerations in spinal muscular atrophy. Genet Med. Mar 2010; 12(3):145-152. PMID 20057317

10. 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. Jan 2012; 20(1):27-32. PMID 21811307

11. Prior TW, Snyder PJ, Rink BD, et al. Newborn and carrier screening for spinal muscular atrophy. Am J Med Genet A. Jul 2010; 152A(7):1608-1616. PMID 20578137

12. SPINRAZA (nusinersen) injection, for intrathecal use: Prescribing label. Biogen Inc. Available at <https://www.spinraza.com> (accessed January 18, 2017).

13. 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. Dec 17 2017; 388(10063):3017-3026. PMID 27939059

14. Biogen, RTI Health Solutions. Formulary Submission Dossier: Spinraza (Nusinersen) for Spinal Muscular Atrophy (NS-US-0199). Cambridge, MA 2016 December.

15. Finkel RS, Kuntz N, Mercuri E, et al. Primary Efficacy and Safety Results From the Phase 3 ENDEAR Study of Nusinersen in Infants Diagnosed With Spinal Muscular Atrophy (SMA). Paper presented at: 43rd Annual Congress of the British Paediatric Neurology Association; January 11-13 2017; Cambridge, UK.

16. 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. Mar 08 2016; 86(10):890-897. PMID 26865511

17. Biogen, RTI Health Solutions. Formulary Submission Dossier: Spinraza (Nusinersen) for Spinal Muscular Atrophy (NS-US-0199). Cambridge, MA 2017 April.

18. Nusinersen for Spinal Muscular Atrophy. Chicago, Illinois: Blue Cross Blue Shield Association. (February 2017) Prescription Drugs 5.01.28.

Policy History:

Date	Reason

6/15/2017	New medical document. The use of nusinersen (Spinraza™) may be considered medically necessary for patients with Type I, II, or III spinal muscular atrophy (SMA) with a documented genetic diagnosis of SMA when meeting specific criteria. Nusinersen (Spinraza™) is considered not medically necessary for SMA patients not meeting criteria. Nusinersen (Spinraza™) is considered experimental, investigational, and/or unproven for all other indications.