Treatment for Spinal Muscular Atrophy

Medicare Advantage Medical Policy #MA-062
Original Effective Date: 02/01/2025
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Applies to all products administered or underwritten by the Health Plan, unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Blue Advantage does not cover investigational or experimental services, including any drug, device, procedure, or service provided under the investigational arm of a clinical trial or study unless mandated by the Centers for Medicare and Medicaid Services. Coverage is limited to routine services for Category A IDE studies and to devices and related services for Category B IDE studies when not supplied by the trial sponsor. Approved IDE studies are posted on www.cms.gov/medicare/coverage/evidence.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

nusinersen (Spinraza™)

Based on review of available data, the Health Plan may consider nusinersen (Spinraza™)‡ for the treatment of spinal muscular atrophy (SMA) to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for nusinersen (Spinraza) will be considered when the following criteria are met:

Initial (6 months)

- Patient has a diagnosis of types I, II, or III spinal muscular atrophy established by, or in consultation with a neuromuscular specialist or neurologist and confirmed by either:
  - SMA diagnostic test results confirming 0 copies of *SMN1*; OR
  - Bi-allelic mutations in the *SMN1* gene; AND
- Documentation of genetic testing confirming 2-4 copies of *SMN2*; AND
- Patient is not currently enrolled in a clinical trial for any experimental therapy for SMA; AND
- If the patient has previously received treatment with onasemnogene abeparvovec-xioi (Zolgensma™)‡, documentation is provided showing a decline of minimally clinically important difference from the highest score achieved on one of the following exams (based on member age and motor ability) after treatment with Zolgensma;
  - Hammersmith Infant Neurological Examination- Section 2 (HINE-2): decline of at least 2 points on kicking and 1 point on any other milestone (excluding voluntary grasp); OR
  - Hammersmith Functional Motor Scale- Expanded (HFMSE): decline of at least 3 points; OR

  - Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND): decline of at least 4 points; AND
- Spinraza will not be used in combination with risdiplam (Evrysdi™)‡; AND
- Patient does NOT have advanced SMA (e.g., complete paralysis of limbs, permanent ventilator dependence, or tracheostomy); AND
- The medication will be administered by or under the direction of a healthcare professional experienced in performing lumbar punctures; AND
- The requested dose is consistent with one of the Food and Drug Administration (FDA)-approved dosing regimens:
  - Low dose regimen: 12 milligrams (mg) administered with 4 loading doses; the first 3 loading doses should be administered at 14 day intervals. The 4th loading dose should be administered 30 days after the 3rd dose. A maintenance dose should be administered once every 4 months thereafter.
  - High dose regimen: two loading doses of 50 mg each administered at day 0 and day 14. Then 28 mg once every 4 months starting 4 months after the last loading dose.

Continuation (12 months)

- The "initial" criteria are met; AND
- There is documentation of clinically significant improvement in SMA-associated symptoms (for example, progression of motor function, stabilization of motor function, or decreased decline in motor function) compared to the predicted natural history trajectory of disease; AND
- Dosing will be in accordance with FDA-approved labeling: either 12 mg or 28 mg every 4 months starting 4 months after the last loading dose.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Health Plan considers the use of nusinersen (Spinraza) when the number of copies of *SMN2* criteria are not met, patient has advanced SMA, patient has types 0 or IV SMA, patient has previously received treatment with Zolgensma and has not experienced a clinical decline, or the patient is enrolled in a clinical trial to be **not medically necessary.****

Based on review of available data, the Health Plan considers the continued use of nusinersen (Spinraza) when there is NO documentation of clinically significant improvement in spinal muscular atrophy-associated symptoms (for example, progression of motor function, stabilization of motor function, or decreased decline in motor function) compared to the predicted natural history trajectory of disease to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Health Plan considers the use of nusinersen (Spinraza) when the patient selection criteria are not met (except those denoted as **not medically necessary****) to be **investigational.***

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

onasemnogene abeparvovec-xioi (Zolgensma)

Based on review of available data, the Health Plan may consider onasemnogene abeparvovec-xioi (Zolgensma) for the treatment of spinal muscular atrophy (SMA) to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for onasemnogene abeparvovec-xioi (Zolgensma) will be considered when the following criteria are met:

- Patient has a diagnosis of spinal muscular atrophy established by, or in consultation with a neuromuscular specialist or neurologist and confirmed by either:
  - SMA diagnostic test results confirming 0 copies of *SMN1*; OR
  - Bi-allelic mutations in the survival motor neuron 1 (*SMN1*) gene; AND
- Patient is younger than 2 years of age (and will still be younger than 2 years of age at the time of infusion); AND
- Patient has less than or equal to 4 copies of *SMN2*; AND
- Patient does NOT have advanced SMA (e.g., complete paralysis of limbs, permanent ventilator dependence, or tracheostomy); AND
- Patient has documentation of a test confirming anti-adeno-associated virus serotype 9 antibody titer less than or equal to 1:50; AND
- Patient weight is less than or equal to 21 kg; AND
- Patient does not have a contraindication or intolerance to corticosteroids; AND
- Patient has not received prior treatment with Zolgensma or any other gene therapy for SMA and is not currently enrolled in a clinical trial for any experimental therapy for SMA; AND
- If the patient has previously received Spinraza or Evrysdi, it will be discontinued prior to administration of Zolgensma (NOTE: member's medical record will be reviewed and any current authorizations for Spinraza or Evrysdi will be terminated upon Zolgensma approval); AND

- The requested one-time dose is consistent with the Food and Drug Administration (FDA)-approved dosing of $1.1x10^{14}$ vector genomes per kg of body weight.

Note: Authorization will be for no longer than 12 weeks from approval, or until 2 years of age, whichever is first.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Health Plan considers the use of onasemnogene abeparvovec-xioi (Zolgensma) when the patient has more than 4 copies of the *SMN2* gene, weighs more than 21 kg, has received prior treatment with Zolgensma or any other gene therapy, is currently enrolled in a clinical trial for an experimental therapy for SMA, or will be continuing treatment with Spinraza or Evrysdi to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Health Plan considers the use of onasemnogene abeparvovec-xioi (Zolgensma) when the patient selection criteria are not met (except those denoted as **not medically necessary****) to be **investigational.***

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

onasemnogene abeparvovec-brve (Itvisma®)

Based on review of available data, the Health Plan may consider onasemnogene abeparvovec-brve (Itvisma®)‡ for the treatment of spinal muscular atrophy (SMA) to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for onasemnogene abeparvovec-brve (Itvisma) will be considered when the following criteria are met:

- Patient has a diagnosis of spinal muscular atrophy (SMA) established by, or in consultation with a neuromuscular specialist or neurologist and confirmed by either:
    - SMA diagnostic test results confirming 0 copies of the survival motor neuron (*SMN1*) gene; OR
    - Bi-allelic mutations in the *SMN1* gene; AND

- Patient is greater than or equal to 2 years of age and less than or equal to 18 years of age; AND
- Patient is able to sit independently and has never achieved independent ambulation; AND
- Patient has documentation of genetic testing confirming 2-3 copies of *SMN2*; AND
- Patient has documentation of a test confirming anti-adeno-associated virus serotype 9 (AAV9) antibody titer less than or equal to 1:50; AND
- Patient does NOT have any of the following:
    - Hepatic dysfunction (i.e.. ALT, GGT, or GLDH greater than the upper limit of normal); OR
    - Requirement for invasive ventilation, awake noninvasive ventilation for greater than 6 hours during a 24-hour period, noninvasive ventilation for greater than 12 hours during a 24-hour period, or requiring tracheostomy; OR
    - Infectious process (for example, viral or bacterial) or febrile illness within 30 days prior to administration of Itvisma; OR
    - Contraindication or intolerance to corticosteroids; OR
    - Prior treatment with Zolgensma, Itvisma, or any other gene therapy for SMA or current enrollment in a clinical trial for any experimental therapy for SMA; AND
- If the patient previously received Spinraza or Evrysdi, it will be discontinued prior to administration of Itvisma (NOTE: Member's medical record will be reviewed and any current authorizations for Spinraza or Evrysdi will be terminated upon Itvisma approval); AND
- The requested one-time dose is consistent with the Food and Drug Administration (FDA)-approved dosing of 1.2×10^{14} vector genomes (vg) administered intrathecally.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Health Plan considers the use of onasemnogene abeparvovec-brve (Itvisma) when the patient is greater than 18 years of age, is not able to sit independently, has ever achieved independent ambulation, does not have 2 or 3 copies of the *SMN2* gene, meets above requirements for invasive ventilation, or will use Spinraza or Evrysdi after treatment with Itvisma to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Health Plan considers the use of onasemnogene abeparvovec-brve (Itvisma) when patient selection criteria are not met (except those noted above to be **not medically necessary****) to be **investigational.***

Background/Overview

Spinraza is a *SMN2*-directed antisense oligonucleotide indicated for the treatment of SMA in pediatric and adult patients. Spinraza is administered intrathecally by, or under the direction of, a healthcare professional experienced in performing lumbar punctures. There are two dosing regimen options. The low dose options includes four 12 mg loading doses. The first three loading doses should be administered at 14 day intervals. The fourth loading dose should be administered 30 days after the 3rd dose; a maintenance dose of 12 mg should be given once every 4 months thereafter. The high dose regimen includes two 50 mg loading doses given 14 days apart followed by a maintenance dose of 28 mg given every 4 months starting 4 months after the last loading dose.

Onasemnogene abeparvovec is a one-time gene replacement therapy designed to address the underlying genetic cause of spinal muscular atrophy (SMA). Two products are available with different routes of administration and indicated populations. Zolgensma is administered as a one-time intravenous infusion and is indicated for patients younger than 2 years of age with SMA. Itvisma is administered as a one-time intrathecal infusion and is indicated for patients 2 years of age and older with SMA. Both products utilize an adeno-associated viral (AAV) vector to deliver a functional copy of the human survival motor neuron 1 (*SMN1*) gene to target cells. The transgene does not integrate into the host genome, yet enables continuous production of SMN protein. Because motor neurons are largely nondividing cells, sustained expression of the SMN protein may be maintained over time following a single administration, supporting the potential for long-term therapeutic benefit.

Spinal Muscular Atrophy (SMA)

SMA is an inherited disorder (autosomal recessive) that occurs due to homozygous deletions or variants in the *SMN1* gene. As a consequence of absent or low levels of the SMN protein, the motor neurons in the spinal cord degenerate resulting in atrophy of the voluntary muscles of the limbs and trunk. *SMN2* is a nearly identical modifying gene capable of producing nearly identical compensatory SMN protein. However, 70% to 90% of the transcripts produced from the *SMN2* gene produce a truncated protein that is defective and unstable due to lack of exon 7. Further, humans exhibit variability (range, 0-6) in the number of copies of the *SMN2* gene, and copy number is inversely proportional to severity of disease. Spinraza is a synthetic genetic material that is designed to bind to a specific sequence in exon 7 of the *SMN2* transcript causing the inclusion of exon 7 in the *SMN2* transcript leading to production of full length functional SMN protein. In contrast, Zolgensma and Itvisma contains a transgene that encodes for the SMN protein, allowing neurons to continuously produce the protein.

Despite being a rare disease, SMA is the most common genetic cause of death in infants. The incidence of spinal muscular atrophy is estimated to be 1 per 6,000 to 10,000 live births and is estimated to impact as many as 10,000 to 25,000 children and adults in the United States. The carrier frequency is 1 in 40 to 1 in 60, equating to approximately 6,000,000 carriers in the United States. SMA is classified into 5 main categories (Types 0-IV) based on the age at onset of symptoms. Generally, early onset of disease directly correlates to severity of symptoms and rate of disease

progression. There is no exact marker to classify these categories, and they are not well-distinguished by ICD-10-CM code. Type I SMA is the most common form of SMA and is categorized by SMA symptom onset at or before 6 months of age.

- 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: Onset within 6 months after birth and symptoms progress rapidly, with most infants dying before 1 year of age from respiratory failure. About 60% of patients with SMA constitute this phenotype.
- Type II: Onset is within 6 to 18 months with 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: Onset is after 18 months of age. Lifespan is not affected, with wide-ranging reductions in muscle strength with a chronic course. The outcome depends primarily on the severity of muscle weakness at presentation rather than age of onset, but earlier onset tends to correlate with greater weakness.
- Type IV: Onset usually presents in the third decade of life and is otherwise similar to type III SMA.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Spinraza is FDA approved for the treatment of spinal muscular atrophy (SMA) in pediatric and adult patients.

Zolgensma is FDA approved for the treatment of pediatric patients less than 2 years of age with spinal muscular atrophy (SMA) with bi-allelic mutations in the *survival motor neuron 1 (SMN1*) gene.

Itvisma is FDA approved for the treatment of spinal muscular atrophy in adult and pediatric patients 2 years of age and older with confirmed mutation in the *survival motor neuron 1 (SMN1*) gene.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Spinraza
Spinraza was studied in the phase III ENDEAR trial, a multicenter, randomized, double-blind, sham-procedure controlled study in 121 symptomatic infants (symptom onset before 6 months of age). Patients had 2 copies of *SMN2*. Patients were randomized to either receive Spinraza or a sham procedure. The primary endpoint assessed at the interim analysis was the proportion of responders: patients with an improvement in motor milestones according to section 2 of the Hammersmith Infant Neurologic Exam (HINE). A greater percentage of patients who received Spinraza achieved a motor milestone response compared with those that received the sham procedure (40% vs. 0%, $p < 0.0001$).

Evidence for use of Spinraza in later-onset (Type II or III) SMA includes several open-label studies and the phase III CHERISH trial. The single-arm studies included small numbers of patients and used multiple doses of Spinraza, but the results of those trials did not stratify by dose or type of SMA. CHERISH was a randomized, double-blind, sham-procedure controlled trial in 126 non-ambulatory patients with genetic documentation 5q SMA with the onset of signs and symptoms at more than 6 months and between ages 2 and 12 years at screening. Patients were required to be able to sit independently, have no history of the ability to walk independently, and have a baseline Hammersmith Functional Motor Scale—Expanded (HFMSE) score between 10 and 54. Children were excluded if they had a severe contracture, evidence of severe scoliosis on radiography, respiratory insufficiency, or a gastric tube placed to provide adequate nutrition. Participants were randomized 2:1 to receive either Spinraza or a sham injection. The primary end point was change in HFMSE score compared with baseline. HFMSE scores range from 0 to 66, with higher scores indicating better motor function. A higher percentage of children in the nusinersen group (57%) than in the control group (26%; $p < 0.001$) had an increase from baseline to month 15 in the HFMSE score of at least 3 points, which was considered meaningful.

The results of the sham-controlled trial in infantile-onset and later-onset SMA patients were supported by the open-label NURTURE trial conducted in presymptomatic SMA patients ($n = 25$), who ranged in age from 3 days to 42 days at the time of first dose and had a minimum of 2 but less than 4 copies of *SMN2*. Patients received 12 mg Spinraza as a series of loading doses administered intrathecally followed by maintenance doses administered every 4 months. Interim results from this study demonstrated that 100% of patients were alive, 100% achieved sitting without support, 88% achieved walking with assistance, and 68% achieved walking alone after 27 months of median follow-up. Early treatment resulted in the achievement of motor milestones among patients who were not likely to attain them without treatment.

Additional evidence evaluating the use of Spinraza following prior gene therapy is available from the phase IV RESPOND study, an open-label, single-arm trial in pediatric patients with SMA who had previously received Zolgensma and were determined by investigators to have suboptimal clinical status. Interim results included 37 symptomatic patients aged $\leq$ 36 months, the majority of whom (92%) had 2 copies of *SMN2*. Patients initiated Spinraza a median of approximately 6 months after gene therapy. At baseline, participants demonstrated evidence of ongoing disease activity, including low compound muscle action potential (CMAP) amplitudes and elevated neurofilament light chain (NfL) levels, consistent with active neurodegeneration. Improvements from baseline

were observed across multiple clinical and biomarker endpoints at Day 302, including motor function (HINE-2 and CHOP-INTEND scores), achievement of motor milestones such as independent sitting, increases in CMAP amplitudes, and reductions in NfL levels. Among patients with 2 *SMN2* copies, mean HINE-2 scores increased by approximately 8 points and 52% of patients who were unable to sit at baseline achieved independent sitting during follow-up. Treatment was generally well tolerated, and no new safety concerns were identified. However, interpretation of results is limited by the open-label, single-arm design and lack of a comparator group. These findings suggest that Spinraza may provide additional clinical benefit in patients with residual disease following gene therapy, although further controlled studies are needed.

There are currently no studies assessing the safety and efficacy of Spinraza in patients with Type 0 or IV SMA. Therefore, the criteria for coverage presented in this medical policy represent coverage for types I, II, and III SMA only. More information is needed to assess the safety and clinical utility of Spinraza in broader patient populations of SMA.

Evidence evaluating a higher-dose regimen of Spinraza is available from the phase II/III DEVOTE study, a multicenter trial assessing the safety, pharmacokinetics, and clinical efficacy of increased nusinersen dosing in patients with spinal muscular atrophy. The study included both treatment-naïve patients and those previously treated with nusinersen. Early-phase results demonstrated that higher-dose nusinersen regimens resulted in increased cerebrospinal fluid (CSF) drug exposure compared with the standard 12 mg dosing regimen. Across study cohorts, improvements in motor function outcomes were observed, including increases in HFMSE and CHOP-INTEND scores. The safety profile of higher-dose nusinersen was consistent with that observed with the approved dosing regimen, with no new safety signals identified. These findings support the use of an increased dosing regimen to enhance drug exposure and potentially improve clinical outcomes, although long-term comparative data are limited.

Zolgensma
Zolgensma was approved based on a phase 1 study as well as preliminary data from the ongoing STRIVE-US phase 3 study. In the phase 1 study, 12 of 15 infants with 2 copies of the *SMN2* gene received the proposed dose while 3 received a minimally effective dose. At the end of the 2-year follow-up, all 15 infants survived and none of the 12 patients who received the proposed therapeutic dose required permanent ventilation. All 12 patients also achieved at least 1 motor milestone, with 92% of those achieving CHOP INTEND scores greater than 40. The observed treatment effect on survival, event-free survival, and achievement of motor functions is beyond what is typical based on the known natural history of patients with SMA type 1 with two copies of *SMN2*. The available published data support a durable treatment effect through 2 years.

For individuals who are presymptomatic with a genetic diagnosis of SMA and less than 3 copies of *SMN2* who receive Zolgensma, the evidence includes a prospective cohort with a planned enrollment of 44 patients and a planned follow-up of 18-24 months. This single prospective cohort study (SPRINT) is currently ongoing. At the March 2019 update, 18 patients had been treated with a median follow up of 2.9 months. All 18 children were alive and “event free.” Among 8 patients with

2 copies of *SMN2*, all reportedly achieved age-appropriate motor milestones including 4 who could sit without support and 1 who could stand with assistance. Data was much more limited for patients with 3 copies of *SMN2*. However, early increases in mean Bayley-III Gross Motor score were observed.

Itvisma
The efficacy of Itvisma was evaluated in a randomized, double-blind, sham-controlled study that included patients with spinal muscular atrophy (SMA) who were treatment-naïve and able to sit but never able to walk independently. Patients with elevated (> 1:50) baseline serum anti-AAV9 antibody titer were excluded. A total of 136 patients were randomized in a 3:2 ratio to receive either Itvisma at a dost of 1.2×10^{14} vg by single lumbar intrathecal injection or sham procedure. Randomization was stratified by age and pre-treatment Hammersmith Functional Motor Scale-Expanded (HFMSE) score at screening. A total of 126 patients received the assigned treatment and were included in the efficacy evaluation. The mean age of patients was 6 years (range: 2 to 17 years).

The primary endpoint was the change from baseline in HFMSE total score at the end of follow-up, defined as the average of the Week 48 and Week 52 assessment, in Itvisma compared to sham. The HFMSE evaluates motor function in patients with SMA who have limited ambulation, comprising of 33 graded items that assess various motor skills ranging from sitting to using the stairs. Each item is scored from 0-2, with a maximum total score of 66. Higher scores indicate better motor function. In the Itvisma group (n = 75), the mean change from baseline in HFMSE total score (SEM) was 2.39 (0.439). In the sham procedure group (n = 51), the mean change from baseline was 0.51 (0.532). This corresponds to a treatment difference of 1.88 (95% CI 0.51-3.25) (p = 0.0074).

References

1. Spinraza [package insert]. Biogen, Inc. Cambridge, Massachusetts. Updated March 2026.
2. Spinraza [dossier]. Biogen, Inc. Cambridge, Massachusetts. Updated December 2016.
3. Spinraza. Express Scripts Drug Evaluation. Updated January 2017.
4. 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 USA.* May 25 1999;96(11):6307-6311.
5. Lefebvre S, Burlet P, Liu Z, et al. Correlation between severity and SMN protein level in spinal muscular atrophy. *Nat Genet.* Jul 1997;16(3):265-269.
6. Zolgensma [package insert]. Novartis Gene Therapies, Inc. Bannockburn, IL. Updated June 2026.
7. Zolgensma Drug Evaluation. Express Scripts. Updated May 2019.
8. De Vivo DC, Bertini E, Hwu WL, et al. Nusinersen in Infants Who Initiate Treatment in a Presymptomatic Stage of Spinal Muscular Atrophy (SMA): Interim Efficacy and Safety Results from the Phase 2 NURTURE Study. Paper presented at: 23rd International Annual congress of the World Muscle Society. 2018; October 2-6; Mendoza, Argentina.
9. Mercuri E, Darras BT, Chiriboga CA, et al. Nusinersen versus sham control in later-onset spinal muscular atrophy. N Engl J Med. Feb 15 2018;378(7):635-635.

10. Mendell JR, Al-Zaidy S, Shell R, et al. Single-dose gene-replacement therapy for spinal muscular atrophy. N Engl J Med. Nov 2 2017;377(18):1713-1722.
11. Day JW, Feltner DE, Ogrinc F, et al. AVXS-101, Gene-Replacement Therapy for Spinal Muscular Atrophy Type 1 (SMA1): Pivotal Study (STR1VE) Update (P.181). the 23rd International Annual congress of the World Muscle Society; October 2-6, 2018; Mendoza, Argentina.
12. Itvisma [package insert]. Novartis Gene Therapies, Inc. Bannockburn, IL. Updated June 2026.
13. Itvisma New Drug Review. IPD Analytics. Updated December 2025.
14. Proud CM, Finkel RS, Parsons JA, et al; RESPOND Study Group. Open-label phase IV trial evaluating nusinersen after onasemnogene abeparvovec in children with spinal muscular atrophy. *J Clin Invest*. 2025;135(22):e193956.
15. Finkel, R. S., Mercuri, E., Darras, B. T., et al. (2023). DEVOTE study exploring higher dose of nusinersen in spinal muscular atrophy: Study design and part A results. Journal of Neuromuscular Diseases, 10(5), 813–823.

Policy History

Original Effective Date: 02/01/2025
Current Effective Date: 11/01/2026

11/19/2024	UM Committee review and approval. New policy.
09/16/2025	UM Committee review and approval. Added language to clarify approval timeframe for Spinraza initial and continuation.
08/18/2026	UM Committee review and approval. Updated Spinraza criteria to reflect new high dose regimen. Added new drug, Itvisma, to policy with relevant criteria and background information.

Next Scheduled Review Date: 08/2027

Coding

The five character codes included in the Health Plan Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2025 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	J2326, J3399 Add code effective 11/01/2026: J3405
ICD-10 Diagnosis	All Related Diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and 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 that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the Health Plan definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Health Plan recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

NOTICE: All codes listed on the Medical Policy require prior authorization. This ensures appropriate utilization and alignment with current clinical guidelines.

NOTICE: If an authorization for an ongoing course of treatment has been provided to a member and the member changes from one health plan to another health plan (e.g., a member moves from carrier A to Blue Advantage), Blue Advantage may honor the previous health plan's authorization for the same service under the same type of in-network benefit for a 90-day transition period. Documentation of the authorization for the ongoing course of treatment from the previous health plan must be provided to us by the member or their provider and the services provided for the course of treatment must otherwise be a covered service under the Blue Advantage health plan.

Medicare Advantage Members

Established coverage criteria for Medicare Advantage members can be found in Medicare coverage guidelines in statutes, regulations, National Coverage Determinations (NCD)s, and Local Coverage Determinations (LCD)s. To determine if a National or Local Coverage Determination addresses coverage for a specific service, refer to the Medicare Coverage Database at the following link: https://www.cms.gov/medicare-coverage-database/search.aspx. You may wish to review the Guide to the MCD Search here: https://www.cms.gov/medicare-coverage-database/help/mcd-bene-help.aspx.

When coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs, internal coverage criteria may be developed. This policy is to serve as the summary of evidence, a list of resources and an explanation of the rationale that supports the adoption of this internal coverage criteria.