Pharmacy Management Drug Policy

SUBJECT: Spinal Muscular Atrophy (SMA)
POLICY NUMBER: PHARMACY-68
EFFECTIVE DATE: 03/02/2017
LAST REVIEW DATE: 11/18/2026

If the member's subscriber contract excludes coverage for a specific service or prescription drug, it is not covered under that contract. In such cases, medical or drug policy criteria are not applied. This drug policy applies to the following line/s of business:

Policy Application

Category:	☒ Commercial Group (e.g., EPO, HMO, POS, PPO)	☒ Medicare Advantage
	☒ On Exchange Qualified Health Plans (QHP)	☐ Medicare Part D
	☒ Off Exchange Direct Pay	☒ Essential Plan (EP)
	☒ Medicaid & Health and Recovery Plans (MMC/HARP)	☒ Child Health Plus (CHP)
	☐ Federal Employee Program (FEP)	☐ Ancillary Services
	☒ Dual Eligible Special Needs Plan (D-SNP)	

DESCRIPTION:

Spinal Muscular Atrophy (SMA) is a rare genetic condition that causes increasing weakness in muscles. Patients have inadequate amounts of survival motor neuron protein 1 (SMN1). The disease can be classified into five types with infantile onset (Type 1) being the most common. Symptoms and rate of disease progression can vary based on the type of SMA. Approximately 450-500 infants are born with SMA in the US annually.

The survival motor neuron 2 (SMN2) gene also produces SMN protein; however, only a small portion of the protein produced is functional. The number of SMN2 copies is important in determining the severity of SMA; however, those without SMN1 have an insufficient level of SMN protein regardless of the SMN2 copies. Characteristics of the different types of SMA are described in the chart below.

SMA Type	Age at Onset of Symptoms	Peak Motor Function Achieved	Lifespan	Copies of SMN2
Type 0	Prenatal onset	None	< 6 months	1 copy
Type 1	< 6 months	Sitting with support	< 2 years	1–3 copies
Type 2	6–18 months	May sit independently	> 2 years	2–3 copies
Type 3	> 18 months	May walk independently	Into adulthood	3–4 copies
Type 4	Adult onset	Will walk independently through adulthood	Death as an adult	≥ 4 copies

Spinraza (nusinersen) is indicated for the treatment of SMA in pediatric and adult patients. Its mechanism of action involves an increase of full-length SMN protein by targeting the process through which it is produced by the SMN2 gene. It was the first drug approved to treat SMA.

Zolgensma (onasemnogene abeparvovex-xioi) is an adeno associated virus vector-based gene therapy indicated for the treatment of pediatric patients less than 2 years of age with SMA with bi-allelic mutations in the survival motor neuron 1 (SMN1) gene.

Itvisma (onasemnogene abeparvovec-brve) is an adeno-associated virus vector-based gene therapy indicated for the treatment of spinal muscular atrophy (SMA) in adult and pediatric patients 2 years of age and older with a confirmed mutation in the survival motor neuron 1 (SMN1) gene.
Evrysdi (risdiplam) is a survival of motor neuron 2 (SMN2) splicing modifier that is indicated for the

treatment of spinal muscular atrophy (SMA) in patients 2 months of age and older. It is the first oral therapy approved to treat SMA.

Isembyld (apitegromab-mstn) is a recombinant monoclonal antibody targeting proforms of myostatin, indicated for the treatment of spinal muscular atrophy (SMA) in adults and pediatric patients 2 years of age and older who are currently receiving a survival motor neuron 2 (SMN2)-targeted treatment.

POLICY:

	Spinraza (nusinersen) low dose	**Spinraza (nusinersen) high dose**	**Evrysdi (risdiplam)**	**Isembyld (apitegromab-mstn)**	**Zolgensma (onasemnogene abeparvovec-xioi)**	**Itvisma (onasemnogene abeparvovec-brve)**
Benefit	Medical	Medical	Rx	Medical	Medical	Medical
SMA Type	Type I, II, or III	Severe Type I (defined as symptom onset ≤ 6 months or ≤ 2 SMN2 copies) Types I, II, or III if already on low dose Spinraza	Type I, II, or III	Type II or III	Type I or II	Type II or non-ambulatory Type III
Number of copies of the SMN2 gene* *does not apply to Medicaid/ HARP	1, 2, 3, or 4 If genetic testing confirms 4 copies of the SMN2 gene, Spinraza will only be approved if the patient is symptomatic	≤2 copies OR 3 or 4 copies if already on low dose Spinraza	1, 2, 3, or 4 If genetic testing confirms 4 copies of the SMN2 gene, Evrysdi will only be approved if the patient is symptomatic	2, 3 or 4 If genetic testing confirms 4 copies of the SMN2 gene, Isembyld will only be approved if the patient is symptomatic	1, 2, 3, or 4	2, 3, or 4 copies
Age	Pediatric and adults	Pediatric and adults	Pediatric and adults	≥2 years of age	<2 years of age at time of treatment and weigh ≤ 21 kg For neonatal patients born prematurely, term gestational age (37 weeks) must be reached	Medicaid/HARP: ≥2 years of age Commercial/ Essential Plan/ Child Health Plus/Medicare Advantage: ≥2 years and <18 years of age

Universal criteria:

1. Must be prescribed by or in consultation with a provider who specializes in the treatment of Spinal Muscular Atrophy (SMA) and/or neuromuscular disorders
2. Must have a diagnosis of SMA Type as outlined in the above table
   a. Confirmed by targeted mutation analysis
      i. Homozygous deletions of SMN1 gene **OR**

ii. Homozygous mutation in the SMN1 gene (e.g., biallelic mutations of exon 7) **OR**
iii. Compound heterozygous mutation in the SMN1 gene (e.g., deletion of SMN1 exon 7 and mutation of SMN1)

3. The patient must not have advanced disease (e.g., complete limb paralysis or permanent ventilator dependence) due to lack of literature support
   a. Permanent ventilation defined as required invasive ventilation (tracheostomy), or invasive/non-invasive respiratory assistance for ≥ 16 hours daily for ≥ 14 days in the absence of an acute reversible illness and excluding perioperative ventilation
4. All except Spinraza high dose, Zolgensma, and Itvisma: Progress notes containing results of at least one of the following age-appropriate baseline exams must be submitted to establish baseline motor ability:
   a. Hammersmith Infant Neurological Exam (HINE) **OR**
   b. Hammersmith Functional Motor Scale Expanded (HFMSE) **OR**
   c. Upper Limb Module (ULM) Test/Revised Upper Limb Module Test (RULM) **OR**
   d. Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP- INTEND) **OR**
   e. Motor Function Measure 32 (MFM32) **OR**
   f. Bayley Scales of Infant and Toddler Development- Third Edition gross motor scale (BSID-III) (For Infantile-Onset disease only) **AND**
5. Therapy will not be approved for use in patients that have previously been treated with Zolgensma or Itvisma
6. Therapy will not be approved for use in combination with any other experimental therapy for spinal muscular atrophy

EVRYSDI

Based upon our assessment and review of the peer-reviewed literature, Evrysdi has been medically proven to be effective and, therefore, **medically appropriate** for the following:

1. Evrysdi will not be approved for use in combination with Spinraza **AND**
2. Approved Daily Dosing
   a. Less than 2 months of age: 0.15 mg/kg of Evrysdi Oral Solution
   b. 2 months to less than 2 years of age: 0.20 mg/kg of Evrysdi Oral Solution
   c. 2 years of age and older weighing less than 20 kg: 0.25 mg/kg of Evrysdi Oral Solution
   d. 2 years of age and older weighing 20 kg or more: 5 mg of Evrysdi Oral Solution or Evrysdi Tablet
3. Quantity Limit
   a. Oral Solution: 80 mL per 30 days
      i. The allowed quantity will be reviewed at each authorization request in accordance with the FDA-approved weight-based dosing regimen. Coverage will be limited to the minimum number of 80 mL (60 mg) bottles necessary to deliver the patient's prescribed daily dose for the approved supply period, accounting for the 64-day in-use expiration of the constituted oral solution.
      ii. To accommodate anticipated pediatric weight gain between reviews, a volume buffer may be applied to the calculated quantity based on the patient's age:
         a) Infants < 2 months: 25%
         b) Infants/Toddlers 2 months to < 2 years: 15%
         c) Children ≥ 2 years and < 20 kg: 10%
         d) Patients ≥ 20 kg: no volume buffer required due to fixed 5 mg/day dose
   b. Tablet: 30 tablets per 30 days
4. Initial and continued approval will be at 12-month intervals. Subsequent approval will require

documentation of positive response to therapy from pretreatment baseline status as evidenced by at least one of the following exams:

a. HINE milestones:
    i. One of the following:
        a) Improvement or maintenance of previous improvement of at least 2 points (or maximal score) increase in ability to kick **OR**
        b) Improvement or maintenance of previous improvement of at least 1-point increase in any other HINE milestone (e.g., head control, rolling, sitting, crawling, etc.)
b. HFMSE:
    i. One of the following:
        a) Improvement or maintenance of previous improvement of at least a 3- point increase in score from pretreatment baseline **OR**
        b) Patient has achieved and maintained any new motor milestone from pretreatment baseline when they would otherwise be unexpected to do so
c. ULM/RULM:
    i. One of the following:
        a) Improvement or maintenance of previous improvement of at least a 2- point increase in score from pretreatment baseline **OR**
        b) Patient has achieved and maintained any new motor milestone from pretreatment baseline when they would otherwise be unexpected to do so
d. CHOP-INTEND
    i. One of the following:
        a) Improvement or maintenance of previous improvement of at least a 4- point increase in score from pretreatment baseline **OR**
        b) Patient has achieved and maintained any new motor milestone from pretreatment baseline when they would otherwise be unexpected to do so
e. MFM32
    i. One of the following:
        a) Improvement or maintenance of previous improvement of at least a 3-point or greater change from pretreatment baseline **OR**
        b) Patient has achieved and maintained any new motor milestone from pretreatment baseline when they would otherwise be unexpected to do so
f. BSID-III
    i. Infantile-onset disease **AND** ability to sit without support for at least 5 seconds (BSID-III, Item 22)

SPINRAZA

Based upon our assessment and review of the peer-reviewed literature, Spinraza has been medically proven to be effective and, therefore, **medically appropriate** for the following:

Spinraza for Commercial/Essential Plan/ Child Health Plus/Medicare Advantage:

1. There must be a proven contraindication to Evrysdi
    a. This requirement does not apply to Medicare Advantage **AND**
2. Spinraza will not be approved for use in combination with Evrysdi **AND**
3. Administration and Dose
    a. Spinraza must be administered in accordance with the current FDA-approved prescribing information.
    b. Low-Dose Spinraza will be required for all patients unless they meet the coverage criteria

described in Spinraza High-Dose Criteria section below

c. Both Low-Dose (12 mg) and High-Dose (28 mg maintenance) regimens must follow the labeled dosing schedule and monitoring requirements **AND**

4. Approval Timeframe and Recertification Requirements
   a. Approval Timeframe: 12-months
   b. Recertification Requirements
      i. Initial (12-months from treatment initiation), there must be documentation of **ONE** of the following:
         1. Clinically meaningful response from pre-treatment baseline on at least one validated, age-appropriate SMA motor function scale:
            - CHOP-INTEND: ≥4-point improvement from baseline
            - HINE-2: Improvement in ≥1 motor milestone category without worsening in any category
            - HFMSE or MFM32: ≥3-point improvement from baseline
            - ULM/RULM: ≥2-point improvement from baseline
            - BSID-III: Infantile-onset disease **AND** ability to sit without support for at least 5 seconds (BSID-III, Item 22)
            - **OR**
         2. The patient has achieved or maintained a motor milestone not expected based on natural history (e.g., independent sitting, standing, ambulation, head control) **OR**
         3. For patients with advanced disease at baseline (HFMSE ≤10 or CHOP-INTEND ≤20), there must be documentation of stabilization of motor function **AND** at least ONE of the following: respiratory stabilization (no new requirement for permanent ventilation), bulbar stabilization (no new requirement for enteral feeding), or preservation of a functionally meaningful motor ability as attested by the treating specialist.

      ii. Continued (every 12-months after initial response has been established), there must be documentation of ongoing clinically meaningful therapeutic benefit, defined as meeting at least ONE of the following:
         1. No decline exceeding the minimal clinically important difference (MCID) threshold for clinically meaningful deterioration on the primary motor scale used for monitoring (HFMSE or MFM32: >3-point decline; CHOP-INTEND: >4-point decline; RULM: >2-point decline, BSID: ability to sit without support for at least 5 seconds), OR no loss of a previously achieved motor milestone.
         2. Further improvement on a validated motor scale from the most recent assessment.
         3. Documentation that the patient's disease course is meaningfully altered relative to the expected natural history for their SMA type, SMN2 copy number, and disease duration. This may include but is not limited to:
            - Preservation of respiratory function (stable ventilatory support requirements; no progression to permanent invasive ventilation)
            - Preservation of bulbar function (stable nutritional support requirements)
            - Maintenance of functional independence in activities of daily living
            - Slowed rate of motor decline relative to published natural history data

Spinraza for Medicaid/HARP:

1. Spinraza will not be approved for use in combination with Evrysdi **AND**
2. Administration and Dose
    a. Spinraza must be administered in accordance with the current FDA-approved prescribing information.
    b. Low-Dose Spinraza will be required for all patients unless they meet the coverage criteria described in Spinraza High-Dose Criteria section below
    c. Both Low-Dose (12 mg) and High-Dose (28 mg maintenance) regimens must follow the labeled dosing schedule and monitoring requirements **AND**
3. Approval Timeframe and Recertification Requirements
    a. Approval Timeframe: 12-months
    b. Recertification Requirements
        i. Initial (12-months from treatment initiation), there must be documentation of ONE of the following:
            1. Clinically meaningful response from pre-treatment baseline on at least one validated, age-appropriate SMA motor function scale:
                - CHOP-INTEND: ≥4-point improvement from baseline
                - HINE-2: Improvement in ≥1 motor milestone category without worsening in any category
                - HFMSE or MFM32: ≥3-point improvement from baseline
                - ULM/RULM: ≥2-point improvement from baseline
                - BSID-III: Retain ability to sit without support for at least 5 seconds (BSID-III, Item 22) **OR**
            2. The patient has achieved or maintained a motor milestone not expected based on natural history (e.g., independent sitting, standing, ambulation, head control) **OR**
            3. For patients with advanced disease at baseline (HFMSE ≤10 or CHOP-INTEND ≤20), there must be documentation of stabilization of motor function **AND** at least ONE of the following: respiratory stabilization (no new requirement for permanent ventilation), bulbar stabilization (no new requirement for enteral feeding), or preservation of a functionally meaningful motor ability as attested by the treating specialist.
        ii. Continued (every 12-months after initial response has been established), there must be documentation of ongoing clinically meaningful therapeutic benefit, defined as meeting at least ONE of the following:
            1. No decline exceeding the minimal clinically important difference (MCID) threshold for clinically meaningful deterioration on the primary motor scale used for monitoring (HFMSE: >3-point decline; CHOP-INTEND: >4-point decline; RULM: >2-point decline, BSID: ability to sit without support for at least 5 seconds), OR no loss of a previously achieved motor milestone.
            2. Further improvement on a validated motor scale from the most recent assessment.
            3. Documentation that the patient's disease course is meaningfully altered relative to the expected natural history for their SMA type, SMN2 copy number, and disease duration. This may include but is not limited to:
                - Preservation of respiratory function (stable ventilatory support requirements; no progression to permanent invasive ventilation)
                - Preservation of bulbar function (stable nutritional support requirements)
                - Maintenance of functional independence in activities of daily living
                - Slowed rate of motor decline relative to published natural history data

Spinraza High-Dose Criteria (Applies to all lines of business)

The patient must meet **ONE** of the following (1,2, or 3):

1. The patient must have severe Type 1 disease (defined as symptom onset ≤6 months or ≤2 SMN2 copies) **OR**
2. The patient is currently receiving the Low Dose Regimen for Spinraza for an adequate trial period (≥12 months) with documentation of plateau or declining function
    a. Plateau or declining function on the Low Dose Regimen is defined as any of the following:
        i. Failure to achieve meaningful improvement from pre-treatment baseline, defined as
            (1) < 4-point improvement on CHOP-INTEND
            (2) < 3-point improvement on HFMSE or MFM32
            (3) < 2-point improvement on ULM/RULM
        ii. Clinically meaningful decline exceeding expected natural disease progression assessed over a 12-month time period, defined as:
            (1) ≥ 4 points decline on CHOP-INTEND
            (2) ≥ 3 points on HFMSE or MFM32
            (3) ≥ 2 points on ULM/RULM
            (4) Loss of a previously achieved motor milestone (per HINE-2 criteria)
        iii. New requirement for respiratory support (BiPAP, CPAP, or mechanical ventilation) not present at treatment initiation
        iv. New requirement for nutritional support (G-tube or NG tube) not present at treatment initiation
3. For patients currently receiving the Low Dose Regimen for ≥ 12 months who are clinically stable (i.e., does not meet for coverage for plateau or declining function), coverage requires at least **ONE** of the following features considered high-risk for rapidly progressive disease:
    a. The patient has bulbar dysfunction as evidenced by dysphagia, weak suck/swallow, aspiration risk, feeding difficulty, or need for NG/G-tube nutritional support
    b. The patient has respiratory insufficiency as evidenced by need for BiPAP, CPAP, invasive ventilation, cough-assist dependence, recurrent respiratory decompensation, or clinically significant decline in pulmonary status attributable to SMA
4. The following patients do not qualify for coverage of the High Dose Regimen:
    a. Patients that are clinically stable on Low Dose Regimen for >12 months **AND** do not have a high-risk feature for rapidly progressive disease
5. Spinraza will not be approved for use in combination with Evrysdi
6. Approval Timeframe and Recertification Requirements
    a. For patients initiating treatment directly on the High-Dose Regimen (e.g., treatment naïve severe Type I disease) should follow the Approval Timeframe and Recertification Requirements described in the Spinraza Coverage Criteria section.
    b. For patients transitioning from the Low-Dose Regimen to the High-Dose Regimen after prior Spinraza exposure, recertification following the first 12 months of High-Dose therapy requires documentation of at least ONE of the following:
        i. Improvement on a validated motor function scale relative to status at High-Dose initiation
        ii. Stabilization of previously declining motor function relative to the period immediately preceding High-Dose initiation
        iii. Preservation of previously achieved motor milestones
        iv. Preservation or stabilization of respiratory function (e.g., no progression in ventilatory support requirements)
        v. Preservation or stabilization of bulbar function (e.g., no progression in nutritional support requirements)

vi. Documentation from the treating specialist that the patient's disease trajectory has been meaningfully altered relative to the clinical course observed prior to High-Dose initiation
vii. Following establishment of response to the High-Dose Regimen, patients should meet the Continued Recertification Requirements described in the Spinraza Coverage Criteria section.

Isembyld (apitegromab-mstn) for Commercial/Exchange/Essential Plan/Child Health Plus:
Based on a review of the available peer-reviewed evidence, Isembyld (apitegromab-mstn) is considered not medically necessary for the treatment of Spinal Muscular Atrophy (SMA).

Apitegromab was studied in the multicenter phase 2 (NCT03921528) TOPAZ trial in patients with Type 2 or 3 SMA on nusinersen or no SMA therapy. This trial demonstrated the lack of efficacy in ambulatory patients and older non-ambulatory patients aged 5-21 based on the mean change from baseline in the Revised Hammersmith Scale (RHS) of -0.3 points in the ambulatory cohort (±2 points representing minimal detectable change) and Hammersmith Functional Motor Scale Expanded of 0.6 points in the older non-ambulatory cohort (approximately 3-4 point change represents clinically meaningful change).

The Phase 3, 52-week double-blind, placebo-controlled SAPPHIRE trial (NCT05156320) studied apitegromab at 10 mg/kg and 20 mg/kg dosing in non-ambulatory patients age 2-21 with types 2 or 3 SMA on background nusinersen or risdiplam therapy. At 12 months, the primary endpoint least squares mean difference in HFMSE change from baseline was 1.8 (95% CI 0.30 to 3.32, p=0.019) points for participants aged 2-12 years receiving apitegromab versus placebo (least squares mean 0·6 vs -1.2). This does not meet the 3-4 point range that represents a clinically meaningful change. The secondary endpoint of least squares mean difference in HFMSE change from baseline in the 10 mg/kg group was 2.2 (95% CI 0.49 to 3.95); however, subgroup analyses had mixed results depending on nusinersen vs. risdiplam use, age, and region.

Spinal Muscular Atrophy is a rare, progressive neuromuscular disorder with both pharmacologic as well as gene therapies available. Therefore, disease rarity, unique mechanism, and unmet needs were not considered sufficient to resolve the uncertainty regarding the clinical meaningfulness of the demonstrated incremental benefit.

Reconsiderations of Medical Necessity
This determination will be reevaluated when new evidence materially addresses the uncertainty regarding the clinical meaningfulness of apitegromab's treatment-attributable benefit. Evidence that may support reconsideration includes:

- Replication or confirmation of clinically meaningful responder benefit in an additional adequately designed study
- Demonstration of sustained benefit beyond the currently established 52-week controlled treatment period
- Comparative or add-on evidence demonstrating clinically meaningful incremental benefit relative to established therapies

Isembyld (apitegromab-mstn) for Medicare Advantage/Medicaid Managed Care (MMC)/Health and Recovery Plans (HARP):

1. Must be non-ambulatory (Non-ambulatory patients must be able to sit independently (sits up straight with head erect for at least 10 seconds; does not use arms or hands to balance body or support position) per World Health Organization (WHO) motor milestones definition)
2. Must be on one background therapy for SMA (i.e., either nusinersen or risdiplam)
    a. If on Spinraza (nusinersen), patient must be currently receiving Spinraza for an adequate trial period (≥ 12 months)
        i. If patient was escalated to high dose Spinraza (nusinersen), patient must be currently receiving high dose Spinraza for an adequate trial period (≥ 12 months)
    b. If on Evrysdi (risdiplam), patient must be currently receiving Evrysdi for an adequate trial period (≥ 12 months)
3. Isembyld must be administered in accordance with the current FDA-approved prescribing information at a dose of 10 mg/kg.
4. Isembyld will not be authorized for any non-FDA approved indication
5. Approval Timeframe and Recertification Requirements
    a. Approval Timeframe: 12-months
    b. Recertification Requirements
        i. Initial (12-months from treatment initiation), there must be documentation of ONE of the following:
            1. Clinically meaningful response from pre-treatment baseline on at least one validated, age-appropriate SMA motor function scale:
                a. CHOP-INTEND: ≥ 4-point improvement from baseline
                b. HINE-2: Improvement in ≥ 1 motor milestone category without worsening in any category
                c. HFMSE or MFM32: ≥ 3-point improvement from baseline
                d. ULM/RULM: ≥ 2-point improvement from baseline
            2. The patient has achieved or maintained a motor milestone not expected based on natural history (e.g., independent sitting, standing, ambulation, head control) OR
            3. For patients with advanced disease at baseline (HFMSE ≤ 10 or CHOP-INTEND ≤ 20), there must be documentation of stabilization of motor function AND at least ONE of the following: respiratory stabilization (no new requirement for permanent ventilation), bulbar stabilization (no new requirement for enteral feeding), or preservation of a functionally meaningful motor ability as attested by the treating specialist.
        ii. Continued (every 12-months after initial response has been established), there must be documentation of ongoing clinically meaningful therapeutic benefit, defined as meeting at least ONE of the following:
            1. No decline exceeding the minimal clinically important difference (MCID) threshold for clinically meaningful deterioration on the primary motor scale used for monitoring (HFMSE or MFM32: > 3-point decline; CHOP-INTEND: > 4-point decline; RULM: > 2-point decline), OR no loss of a previously achieved motor milestone.
            2. Further improvement on a validated motor scale from the most recent assessment.
            3. Documentation that the patient's disease course is meaningfully altered relative to the expected natural history for their SMA type, SMN2 copy number, and disease duration. This may include but is not limited to:

a. Preservation of respiratory function (stable ventilatory support requirements; no progression to permanent invasive ventilation)
b. Preservation of bulbar function (stable nutritional support requirements)
c. Maintenance of functional independence in activities of daily living
d. Slowed rate of motor decline relative to published natural history data

ZOLGENSMA

Based upon our assessment and review of the peer-reviewed literature, Zolgensma has been medically proven to be effective and, therefore, **medically appropriate** for the following:

1. Must have baseline anti-AAV9 antibody titers of ≤ 1:50 (e.g., anti-AAV9 antibody titers of ≤ 1:25) **AND**
2. Zolgensma will not be approved for use in combination with Spinraza, Evrysdi, Isembyld or any other experimental therapy for spinal muscular atrophy **AND**
3. Must not have previously received any gene therapy, including either formulation of onasemnogene abeparvovec or any other AAV9- or SMN1-directed gene-replacement therapy (including investigational treatments). This exclusion applies regardless of route of administration of prior therapy as antibody response is systemic AND
4. Retreatment with Zolgensma has not been proven to be safe and effective and will be considered experiment/investigational. This includes patients who received a partial or incomplete dose of Zolgensma.
5. Dosage should not exceed 1.1×10^{14} vector genomes (vg) per kg of body weight administered as an IV infusion over 60 minutes. Systemic corticosteroids (equivalent to oral prednisolone at 1mg/kg of body weight) must be administered starting one day prior to Zolgensma infusion and continuing for a total of 30 days
    a. Refer to the prescribing information for the determination of the appropriate dose volume that corresponds to the patient's weight. Coverage will be limited to one customized Zolgensma kit that meets these dosage requirements
6. Approval timeframe will be for 3 months to allow for the administration of the one-time treatment or until 2 years of age, whichever occurs first

ITVISMA

Based upon our assessment and review of the peer-reviewed literature, Itvisma has been medically proven to be effective and, therefore, **medically appropriate** for the following:

Itvisma for Commercial/Essential Plan/ Child Health Plus/Medicare Advantage

1. Must have a clinical presentation consistent with SMA Type 2 or non-ambulatory SMA Type 3, characterized by:
   a. Absence of sustained independent ambulation at the time of the request **OR** documented loss of independent ambulation within the prior 12 months **AND**
   b. Evidence of preserved motor neuron reserve, demonstrated by:
      i. Ability to sit independently without external support (e.g., without a caregiver assisting, without positioning devices) **OR**
      ii. Preserved antigravity upper-limb function on clinical examination or standardized assessment (e.g., RULM) AND
   c. Must have objective evidence of disease progression, demonstrated by documentation of
      i. A decline in standardized motor function assessments, (e.g., HFMS-E, RULM, or equivalent) within the prior 12 -months **OR**
      ii. A loss of motor milestones within the prior 12-months
2. Must have a current (within 30 days prior to treatment) anti-AAV9 neutralizing antibody titer at or below the laboratory's validated cutoff (typically ≤1:50; some validated assays use ≤1:25)
   a. Laboratory report must specify assay type, date, and threshold **AND**
3. Vaccination and Infection Precautions
   a. Must have no active infection at the time of treatment; patient must be clinically stable
   b. Must have no live-attenuated vaccine (e.g., MMR, varicella, zoster) within 30 days before or 2 months after treatment
   c. Must have documentation of varicella immunity (IgG positive or prior vaccination) must be submitted **AND**
4. Documentation must confirm that the patient does not have any contraindication to lumbar puncture, including:
   a. Increased intracranial pressure due to mass lesion or hydrocephalus;
   b. Coagulopathy (INR > 1.4 or platelets < 100,000/μL) or current anticoagulant use;
   c. Local infection at the puncture site or systemic sepsis;
   d. Severe spinal deformity, fusion, or hardware precluding safe LP access; **AND**
5. The provider must attest to completing a baseline laboratory assessment within 7 days of treatment
   a. AST, ALT, total bilirubin, PT/INR
   b. CBC with platelets
   c. BUN/creatinine
   d. LDH and haptoglobin
   e. Blood pressure
   f. Varicella IgG
6. Exclusion Criteria - Coverage will not be approved if any of the following apply:
   a. Significant hepatic impairment (AST/ALT > 5× ULN or bilirubin > 2× ULN);
   b. Active infection or febrile illness within 30 days;
   c. Uncorrected coagulopathy or thrombocytopenia;
   d. Contraindication to lumbar puncture (see Section 6);
   e. Ventilator dependence or end-stage SMA (complete paralysis of limbs, permanent ventilator use);

   f. Recent major surgery or pulmonary decompensation (< 2 months);
   g. Active varicella or herpes zoster infection;
   h. Prior treatment with any AAV-based or other viral-vector gene therapy.
7. For SMA treatment experienced patients:
   a. If previously treated with nusinersen (Spinraza), the patient must have received their last dose of nusinersen ≥ 4 months
   b. If previously treated with risdiplam (Evrysdi), the patient must have received their last dose of risdiplam ≥ 15 days prior
8. Itvisma will not be approved for use in combination with Spinraza, Evrysdi, Isembyld, or any other experimental therapy for spinal muscular atrophy
9. Must not have previously received any gene therapy, including either formulation of onasemnogene abeparvovec or any other AAV9- or SMN1-directed gene-replacement therapy (including investigational treatments). This exclusion applies regardless of route of administration of prior therapy as antibody response is systemic.
10. Retreatment with Itvisma has not been proven to be safe and effective and will be considered experiment/investigational. This includes patients who received a partial or incomplete dose of Itvisma.
11. Itvisma must be dosed and administered per the FDA-approved prescribing information which includes:
    a. Single-dose intrathecal injection of 1.2×10^{14} vector genomes (vg) via lumbar puncture
    b. Required corticosteroid regimen (prednisolone 1 mg/kg/day beginning one day prior to injection, continued for 30 days, followed by gradual taper)
    c. Post-treatment monitoring of liver function and platelet counts as specified in the prescribing information
12. Approval timeframe will be for 3 months to allow for the administration of the one-time treatment

POLICY GUIDELINES:

1. Spinraza and Itvisma are administered intrathecally. Zolgensma and Isembyld are administered intravenously. These products will be covered under the medical benefit. Evrysdi is administered orally and will be covered under the pharmacy benefit.
2. Utilization Management are contract dependent. Refer to specific contract/benefit language for exclusions.
   a. Coverage criteria may be dependent on the contract renewal date.
   b. Coverage of drugs listed in this policy are contract dependent.
   c. Not all contracts/benefits allow coverage of healthcare professional administered drugs as part of their pharmacy benefit
   d. Not all contracts/benefits cover all medical infusible drugs
   e. Not all policy criteria may apply if treatment of specific disease states or conditions is not a covered benefit.
3. This policy is applicable to drugs that are included on a specific drug formulary (Pharmacy benefit only). If a drug referenced in this policy is non-formulary, please reference the Non-Formulary Medication Exception Review Policy for review guidelines.
4. Clinical documentation must be submitted for each request (initial and recertification [if applicable]) unless otherwise specified (e.g., provider attestation required). Supporting documentation includes, but is not limited to, progress notes documenting previous treatments and treatment history, diagnostic testing, laboratory test results, genetic testing or biomarker results, imaging, and other objective or subjective measures of clinical benefit. For recertification, continued approval requires documentation demonstrating that the requested product is providing ongoing benefit to the patient, evidenced by improvement or stability in the disease state or

condition, and that continued use remains medically necessary. Ongoing use of the requested product must continue to align with the current policy's preferred formulary. Recertification reviews may result in a requirement to trial more cost-effective treatment alternatives as they become available (e.g., generics, biosimilars, or other guideline-supported treatment options). Requested dosing must remain consistent with FDA-approved or off-label/guideline-supported dosing recommendations.

5. This policy does not apply to Medicare Part D and D-SNP pharmacy benefits. The drugs in this policy may apply to all other lines of business including Medicare Advantage.
6. For members with Medicare Advantage, medications with a National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) will be covered pursuant to the criteria outlined by the NCD and/or LCD. NCDs/LCDs for applicable medications can be found on the CMS website at https://www.cms.gov/medicare-coverage-database/search.aspx. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS permits a Medicare Advantage Organization (MAO) to establish its own coverage determinations in accordance with 42 CFR § 422.101(b)(6). Indications that have not been addressed by the applicable medication's LCD/NCD will be covered in accordance with criteria determined by the Health Plan (which may include review per the Health Plan's Off-Label Use of FDA Approved Drugs policy). Step therapy requirements may be imposed in addition to LCD/NCD requirements.
7. All utilization management requirements outlined in this policy are compliant with applicable New York State insurance laws and regulations. Policies will be reviewed and updated as necessary to ensure ongoing compliance with all state and federally mandated coverage requirements.
8. All requests will be reviewed to ensure they are being used for an appropriate indication and may be subject to an off-label review in accordance with our Off-Label Use of FDA Approved Drugs Policy (Pharmacy-32).
9. Dose and frequency should be in accordance with the FDA label or recognized compendia (for off-label uses). When services are performed in excess of established parameters, they may be subject to review for medical necessity.
10. Manufacturers may either discontinue participation in, or may not participate in, the Medicaid Drug Rebate Program (MDRP). Under New York State Medicaid requirements, physician-administered drugs must be produced by manufacturers that participate in the MDRP. Products made by manufacturers that do not participate in the MDRP will not be covered under Medicaid Managed Care/HARP lines of business. Drug coverage will not be available for any product from a non-participating manufacturer. For a complete list of New/Reinstated & Terminated Labelers please visit: https://www.medicaid.gov/medicaid/prescriptiondrugs/medicaid-drug-rebate-program/newreinstated-terminated-labeler-information/index.html
11. This policy is based on available evidence as of the last review date. Coverage determinations are subject to applicable plan documents, state and federal regulations, and individual patient circumstances. This policy does not constitute medical advice.
12. For commercial contracts, medical necessity determinations align with the Certificate of Coverage issued by the Health Plan, which states that covered services must be clinically appropriate and not primarily for the convenience of the member, the member's family, or the provider.
13. This policy is subject to ongoing revision. Newly marketed drugs and existing drugs with new indications may require prior authorization until formal coverage criteria are established. Inclusion of a drug in this policy does not guarantee its current availability on the market, as some agents may be discontinued, withdrawn, or otherwise unavailable. As product status changes, drugs may be removed from the policy.
14. The requested site of care may impact approval timeframe and is subject to review.

15. Approval timeframes may be extended to align authorization periods for drugs administered as part of a multidrug regimen, including when regimen components are administered across different benefits. This provision does not apply when the approval timeframe reflects a drug-specific limitation on duration of therapy.
16. The following applies to all gene and cellular therapies unless otherwise specified within the drug-specific coverage criteria:
    a. Administration, Retreatment, and Treatment with Additional or Other Gene/Cellular Therapies
        i. One-Time Administration
            1. Most gene and cellular therapies, whether autologous, allogeneic ("off-the-shelf"), or in vivo gene-transfer therapies, are designed and studied as one-time treatments.
            2. Repeat dosing, reinfusion, or sequential therapy with other gene or cellular products has not been established as safe, effective, or clinically appropriate.
        ii. Retreatment/Repeat Administration
            1. Retreatment with the same gene or cellular therapy product is considered experimental and investigational because:
                a. Clinical trials evaluated these therapies as single-administration interventions
                b. Safety, efficacy, and durability of a second administration have not been established
                c. Risks of immune activation, insertional mutagenesis, or vector immunity may be increased with repeat dosing
        iii. Treatment with an Additional or Other Gene/Cellular Therapy
            1. Treatment with an additional or different gene or cellular therapy after prior exposure to any gene or cellular therapy is currently considered experimental and investigational as there is lack of evidence demonstrating the following (a-c):
                a. Anticipated clinical benefit beyond available standard therapies
                b. Safety of sequential administration
                c. Justification for selecting a second gene/cellular intervention after a prior one
            2. This includes, but is not limited to:
                a. Switching between CAR-T products (e.g., CD19 → CD19 or CD19 → BCMA)
                b. Switching between autologous and allogeneic cellular therapies
                c. Sequential use of CAR-T, TCR-T, NK-cell therapies, or other genetically engineered cell therapies
                d. Receiving a gene therapy after previous gene or cellular therapy exposure
                e. Receiving an in vivo gene therapy following any prior vector-based therapy
        iv. Prior Gene/Cell Therapy Exposure
            1. An individual is generally not eligible for additional gene or cellular therapy if they have previously received:
                a. Any autologous cellular therapy (e.g., CAR-T, TCR-T, TIL)
                b. Any in vivo gene therapy (e.g., AAV, lentiviral vector)
                c. Any ex vivo gene-modified cell product
                d. Are being considered for any other gene or cellular therapy without documented evidence supporting safety and anticipated benefit.

Approval time periods:

Unless otherwise stated within the individual drug criteria, approval time periods are listed in the table below:

Line of Business	Initial approval	Continued approval
Commercial, Exchange, and SafetyNet (Medicaid, HARP, CHP, Essential Plan)	6 months	6 months

Medicare	6 months	6 months

CODES:

Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract. Codes may not be covered under all circumstances. Please read the policy and guidelines statements carefully.

Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy update.

HCPCS:

J2326 **Spinraza** (Effective 01/01/2018)
J3399 **Zolgensma** (Effective 07/01/2020)
J3405 **Itvisma** (Effective 7/1/2026)
J3590 **Isembyld** (unspecified code)

UPDATES:

Date:	Revision:
11/18/2026	Revised. P&T Committee Review & Approval.
11/12/2026	Reviewed / P&T Committee Approval
06/12/2026	Revised
06/01/2026	Revised
04/01/2026	Revised
11/19/2025	Revised
11/13/2025	P&T Committee Review & Approval
03/06/2025	Revised
12/23/2024	Revised
11/21/2024	P&T Committee Review & Approval
09/13/2024	Revised
06/20/2024	Revised
01/11/2024	Revised
11/30/2023	P&T Committee Review & Approval
07/01/2023	Revised
04/28/2023	Revised
03/20/2023	Revised
09/22/2022	P&T Committee Review & Approval
09/16/2022	Revised
09/16/2021	P&T Committee Review & Approval
02/01/2021	Revised
09/16/2020	P&T Committee Review & Approval
09/03/2020	Revised
02/26/2020	Revised
09/27/2019	Revised
08/24/2018	Revised
06/05/2017	Revised
03/02/2017	Initial Effective Date

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