Pharmacy Management Drug Policy

SUBJECT: Spinal Muscular Atrophy (SMA) **POLICY NUMBER: PHARMACY-68** **EFFECTIVE DATE: 03/02/2017** **LAST REVIEW DATE: 03/06/2025**
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.

Spinraza (nusinersen) is indicated for the treatment of SMA in pediatric and adult patients. It's 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 of with SMA with bi-allelic mutations 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.

POLICY:

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. Must be prescribed by or in consultation with a provider who specializes in the treatment of Spinal Muscular Atrophy (SMA) and/or neuromuscular disorders **AND**
2. Must have a diagnosis of Type I, II, or III Spinal Muscular Atrophy
    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) **AND**
3. Must have genetic testing confirming 1, 2, 3 or 4 copies of the SMN2 gene
    a. If genetic testing confirms 4 copies of the SMN2 gene, Evrysdi will only be approved if the patient is symptomatic **AND**
4. The patient must not have advanced disease (e.g., complete limb paralysis or permanent ventilator dependence) **AND**
5. Progress notes containing results of at least one of the following 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**
6. Dosing should not exceed 0.2mg/kg/day for patients aged 2 months to less than 2 years of age, 0.25mg/kg/day for 2 years of age and older weighing less than 20kg, and 5mg for 2 years of age and older weighting 20kg or more **AND**
7. Evrysdi will not be approved for use in patients that have previously been treated with Zolgensma and will not be approved in combination with Spinraza or any other experimental therapy for spinal muscular atrophy **AND**
8. Quantity Limits = 80 ml/30 day
9. Initial and continued approval will be at 12-month intervals for commercial, exchange, and Medicaid members. 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:
            1. Improvement or maintenance of previous improvement of at least 2 points (or maximal score) increase in ability to kick **OR**
            2. 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:
            1. Improvement or maintenance of previous improvement of at least a 3- point increase in score from pretreatment baseline **OR**

2. 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:
      1. Improvement or maintenance of previous improvement of at least a 2- point increase in score from pretreatment baseline **OR**
      2. 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:
      1. Improvement or maintenance of previous improvement of at least a 4- point increase in score from pretreatment baseline **OR**
      2. 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:
      1. Improvement or maintenance of previous improvement of at least a 3-point or greater change from pretreatment baseline **OR**
      2. 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

Commercial/Essential/ Child Health Plus:

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:

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 **AND**
2. Must have a diagnosis of Type I, II, or III Spinal Muscular Atrophy
   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) **AND**
3. Must have genetic testing confirming 1, 2, 3 or 4 copies of the SMN2 gene
   a. If genetic testing confirms 4 copies of the SMN2 gene, Spinraza will only be approved if the patient is symptomatic **AND**
4. The patient must not have advanced disease (e.g., complete limb paralysis or permanent ventilator dependence **AND**
5. Progress notes containing results of at least one of the following 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) **AND**
6. There must be a proven contraindication to Evrysdi **AND**
7. Dosing should not exceed12mg (5mL) per dose. Initiated with 4 loading doses; the first 3 loading doses should be administered at 14-day intervals; the 4th loading dose administered 30 days after the 3rd dose. A maintenance dose is then administered once every 4 months thereafter **AND**
8. Spinraza will not be approved for use in patients that have previously been treated with Zolgensma or in combination with Evrysdi or any other experimental therapy for spinal muscular atrophy **AND**
9. Initial approval will be for 6 months, and continued approval will be at 12-month intervals for commercial, exchange, and Medicaid members. 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:
         1. Improvement or maintenance of previous improvement of at least 2 points (or maximal score) increase in ability to kick **OR**
         2. 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:
         1. Improvement or maintenance of previous improvement of at least a 3- point increase in score from pretreatment baseline **OR**
         2. 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:
         1. Improvement or maintenance of previous improvement of at least a 2- point increase in score from pretreatment baseline **OR**
         2. 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:
         1. Improvement or maintenance of previous improvement of at least a 4- point increase in score from pretreatment baseline
         2. Patient has achieved and maintained any new motor milestone from pretreatment baseline when they would otherwise be unexpected to do so.

Medicaid/HARP 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 **AND**
2. Must have a diagnosis of Type I, II, or III Spinal Muscular Atrophy
   1. 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) **AND**

3. The patient must not have advanced disease (e.g., complete limb paralysis or permanent ventilator dependence **AND**
4. Progress notes containing results of at least one of the following baseline exams must be submitted to establish baseline motor ability:
    1. Hammersmith Infant Neurological Exam (HINE) **OR**
    2. Hammersmith Functional Motor Scale Expanded (HFMSE) **OR**
    3. Upper Limb Module (ULM) Test/Revised Upper Limb Module Test (RULM) **OR**
    4. Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP- INTEND) **AND**
5. Dosing should not exceed12mg (5mL) per dose. Initiated with 4 loading doses; the first 3 loading doses should be administered at 14-day intervals; the 4th loading dose administered 30 days after the 3rd dose. A maintenance dose is then administered once every 4 months thereafter **AND**
6. Spinraza will not be approved for use in patients that have previously been treated with Zolgensma or in combination with Evrysdi or any other experimental therapy for spinal muscular atrophy **AND**
7. Initial approval will be for 6 months, and continued approval will be at 12-month intervals for commercial, exchange, and Medicaid members. Subsequent approval will require documentation of positive response to therapy from pretreatment baseline status as evidenced by at least one of the following exams:
    1. HINE milestones:
        i. One of the following:
            1. Improvement or maintenance of previous improvement of at least 2 points (or maximal score) increase in ability to kick **OR**
            2. 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.)
    2. HFMSE:
        i. One of the following:
            1. Improvement or maintenance of previous improvement of at least a 3- point increase in score from pretreatment baseline **OR**
            2. Patient has achieved and maintained any new motor milestone from pretreatment baseline when they would otherwise be unexpected to do so
    3. ULM/RULM:
        i. One of the following:
            1. Improvement or maintenance of previous improvement of at least a 2- point increase in score from pretreatment baseline **OR**
            2. Patient has achieved and maintained any new motor milestone from pretreatment baseline when they would otherwise be unexpected to do so
    4. CHOP-INTEND
        i. One of the following:
            1. Improvement or maintenance of previous improvement of at least a 4- point increase in score from pretreatment baseline
            2. Patient has achieved and maintained any new motor milestone from pretreatment baseline when they would otherwise be unexpected to do so.

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 be prescribed by or in consultation with a provider who specializes in the treatment of Spinal Muscular Atrophy (SMA) and/or neuromuscular disorders **AND**
2. Must be less than 2 years of age at the time of treatment and weigh ≤ 21 kg
    a. For neonatal patients born prematurely, term gestational age (37 weeks) must be reached **AND**
3. Must have a diagnosis of Spinal Muscular Atrophy with bi-allelic mutations in the SMN1 gene
    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) **AND**
4. Must have genetic testing confirming 1, 2, 3 or 4 copies of the SMN2 gene **AND**
5. Must have baseline anti-AAV9 antibody titers of ≤ 1:50 (e.g., anti-AAV9 antibody titers of ≤ 1:25) **AND**
6. Must not have received previous Zolgensma treatment **AND**
7. Patients with advanced SMA (i.e., complete paralysis of limbs, permanent ventilator dependence) will be excluded from treatment due to lack of literature support
    a. Permanent ventilation defined as required invasive ventilation (tracheostomy), or invasive/noninvasive respiratory assistance for ≥ 16 hours daily for ≥ 14 days in the absence of an acute reversible illness and excluding perioperative ventilation **AND**
8. Zolgensma will not be approved for use in combination with Spinraza or Evrysdi or any other experimental therapy for spinal muscular atrophy **AND**
9. 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
10. 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

POLICY GUIDELINES:

1. Spinraza is administered intrathecally and Zolgensma is administered intravenously. Both products will be covered under the medical benefit. Evrysdi is administered orally and will be covered under the pharmacy benefit.
2. Unless otherwise stated above within the individual drug criteria, approval time periods are listed in the table below
    - Continued approval at time of recertification will require documentation that the drug is providing ongoing benefit to the patient in terms of improvement or stability in disease state or condition.
3. Clinical documentation must be submitted for each request (initial and recertification) unless otherwise specified (e.g., provider attestation required). Supporting documentation includes, but is not limited to, progress notes documenting previous treatments/treatment history, diagnostic testing, laboratory test results, genetic testing/biomarker results, imaging and other objective or subjective measures of benefit which support continued use of the requested product is medically necessary.

Also, ongoing use of the requested product must continue to reflect the current policy's preferred formulary. Recertification reviews may result in the requirement to try more cost-effective treatment alternatives as they become available (i.e., generics, biosimilars, or other guideline supported treatment options). Requested dosing must continue to be consistent with FDA-approved or off-label/guideline-supported dosing recommendations.

4. 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.
5. 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. 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.
6. 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).
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.

Approval time periods

Line of Business	Initial approval	Continued approval
Commercial, Exchange, and SafetyNet (Medicaid, HARP, CHP, Essential Plan)	All sites of service – 6 months	All sites of service – 6 months
Medicare	All sites of service – 6 months	All sites of service – 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
J3399 Zolgensma (Effective 07/01/2020)

UPDATES:

Date:	Revision:
03/06/2025	Revised
12/23/2024	Revised
11/21/2024	P&T Committee Review / Approval

09/13/2024	Revised
06/20/2024	Revised
1/11/2024	Revised
11/30/2023	P&T Committee Approval
7/1/2023	Revised
4/28/2023	Revised
3/20/2023	Revised
9/22/2022	P&T Committee Approval
9/16/2022	Revised
9/16/2021	Reviewed / P&T Committee Approval
02/01/2021	Revised
9/16/2020	P & T Approval
9/3/2020	Revised
02/26/2020	Revised
09/27/2019	Revised
08/24/2018	Revised
06/05/2017	Revised
03/02/2017	Initial Effective Date

REFERENCES:

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2. Finkel FS, Chiriboga CA, Vajsar J, et al. Treatment of infantile-onset spinal muscular atrophywith nusinersen: a phase 2, open-label, dose-escalation study. *Lancet.* 2016 Dec 6. [Epub ahead of print]
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4. Mecuri E, Darras B.T, Chiriboga C.A, et al. Neusinersen versus Sham Control in Later-Onset Spinal Muscular Atrophy. *NEJM*. 2018 Feb 15 ; 378:625-35
5. AveXis, Inc. Zolgensma Package Insert; May 2019
6. Glascock J, Sampson J, Haidet-Phillips A, et al. Treatment Algorithm for Infants Diagnosed with Spinal Muscular Atrophy through Newborn Screening. *Journal of Neuromuscular Diseases*. 2018; 5(2):145-158
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8. AveXis, Inc. Zolgensma Package Insert; May 2019
9. Genentech, Inc. Evrysdi Package Insert; September 2022