Blue Cross Blue Shield Blue Care Network of Michigan

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Effective Date: 08/08/2024

Spinraza® (nusinersen)

HCPCS: J2326

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. Types 1, 2, or 3 Spinal Muscular Atrophy (SMA) confirmed by genetic testing
   b. FDA approved age
   c. Prescribed by or in consultation with a neurologist specializing in pediatric neuromuscular disorders
   d. Patient is not fully ventilator dependent
   e. Patient is not concurrently taking SMN2-targeting antisense oligonucleotide or SMN2 splicing modifier or gene therapy AND patient has not received prior treatment with any gene therapy for SMA (such as Zolgensma)
   f. Submission of a baseline, age appropriate exam to establish baseline motor function and ability. Examples of baseline motor ability assessments include:
      i. Hammersmith Infant Neurological Exam (HINE)
      ii. Hammersmith Functional Motor Scale Expanded (HFMSE)
      iii. Upper Limb Module (ULM) Test (nonambulatory patients)
      iv. Six-Minute Walk Test (6MWT) (ambulatory patients only)
      v. Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND)
   g. The requesting physician attests to providing clinical outcome information within the appropriate provider portal as requested by BCBSM
   h. Trial and failure, contraindication, or intolerance to the preferred drugs as listed in BCBSM/BCN's prior authorization and step therapy documents

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limit: Align with FDA recommended dosing
   b. Authorization Period: 6 months at a time
   c. Renewal Criteria: Continuation of coverage requires submission of repeat motor ability assessment and documentation of response to therapy defined as a clinically significant improvement in SMA-associated motor milestones and motor function (for example, progression, stabilization, or decreased functional motor decline) compared to predicted natural history and progression

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- SMA is a severe, inherited progressive neuromuscular disease that causes devastating muscle atrophy and disease-related complications in approximately 4 to 10 per 100,000 live births. SMA is caused by a mutation in the survival motor neuron 1 (SMN1) gene that results in a deficiency of SMN protein. People have a "backup" copy of this gene called SMN2 that produces low levels of SMN protein. SMA varies in severity with four different types that inversely correlates to the number of SMN2 copies a person has. The type of SMA a person has is based on function and age of onset. Type 1 is the most severe type of SMA and the most common. It affects 6 out of every 10 children with SMA. Those with Type 1 have the fewest number of SMN2 copies (usually 2 or fewer). Type 1 patients have an age of onset usually between 0-6 months, and as the natural history of those with Type 1 SMA progresses the children will never be able to sit unsupported. Life expectancy of untreated Type 1 patients is less than 2 years old. Type 2 patients usually present around 7-18 months of age and will have the ability to sit, but never stand. The majority of SMA Type 2 patients have 3 copies of SMN2. Type 3 SMA patients present after 18 months of age and usually are able to stand and walk. About 51% of the patients with SMA Type 3 have 3 copies of SMN2 while 46% have 4 copies of SMN2. Although there is an inverse correlation between severity of disease and number of SMN2 copies, diagnoses of type is not solely based on number of SMN2 copies.

- Spinraza is an antisense oligonucleotide that alters splicing of SMN2, increasing full-length, SMN (survival motor neuron) mRNA protein production. This is thought to improve motor function and achievement of motor milestones in patients and delays the progression in presymptomatic patients. Thus, early treatment is thought to result in the greatest potential benefit.

- Although approved to treat all SMA patients regardless of type and age:

    - Spinraza has only been studied in patients with SMA types 1-3 which make up approximately 95% of all SMA cases. SMA type 4 is usually later onset (often after age 30) and patients are able to achieve motor milestones and maintain mobility throughout life.

    - There is a lack of clinical data supporting the benefits of Spinraza on fully ventilator dependent patients.

    - Therefore, the safety and efficacy of Spinraza has not been confirmed outside of the above patient population.

- SMA patients' motor function and ability are monitored in a variety of ways, including but not limited to Bayley Scales of Infant and Toddler development (BSID), Motor Function Measure 32 (MFM-32), Hammersmith Infant Neurological Exam (HINE), Hammersmith Functional Motor Scale Expanded (HFMSE), Revised Upper Limb Module (RULM) Test (non-ambulatory patients), Six-Minute Walk Test (6MWT) (ambulatory patients only) and Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND).

- There is currently no data supporting co-administration of Spinraza with other SMA therapies, in those who have received gene therapy for SMA, and in patients requiring invasive ventilation. The pivotal clinical studies did not include this patient population, therefore the safety and efficacy of Spinraza is unknown in this patient population at this time.

- Bridging therapy with either Evrysdi or Spinraza prior to the use of Zolgensma can be appropriate in young patients with elevated anti-AAV9 antibodies. Elevated titers are not common (~13%) in SMA patients. Those that do have titers can get it from the placenta at birth from mothers who have acquired them. Just like other maternal antibodies passed on to children, these antibodies diminish over time. Bridging therapy allows patients to start therapy without delay, and waits for the titers to naturally diminish. Scientists have stressed the importance of treating SMA as early as possible, and suggested that patients with elevated antibodies be given disease-modifying therapies that work through different mechanisms — Spinraza (nusinersen) or Evrysdi (risdiplam) — as "bridge treatments" until able to receive Zolgensma.

- Provider portals are used to capture clinical outcome information for patients on select high-cost treatments, such as gene and cellular therapies. If a patient meets medical necessity as defined by this policy and is approved for treatment, the requesting physician must attest to providing clinical outcome information within the appropriate provider portal at the requested cadence.

References:

1. SPINRAZA [Prescribing Information]. Cambridge, MA:Biogen; June 2020.
2. Wang CH, Finkel RS, Bertini ES, Schroth M, Simonds A, Wong B, Aloysius A, Morrison L, Main M, Crawford TO, Trela A; Participants of the International Conference on SMA Standard of Care.. Consensus statement for standard of care in spinal muscular atrophy. J Child Neurol. 2007 Aug;22(8):1027-49.
3. Finkel, Richard S et al. Treatment of infantile-onset spinal muscular atrophy with nusinersen: a phase 2, open-label, dose-escalation study. The Lancet , Volume 388 , Issue 10063 , 3017 – 3026.
4. Chiriboga CA, Swoboda KJ, Darras BT, Iannaccone ST, Montes J, De Vivo DC, Norris DA, Bennett CF, Bishop KM. Results from a phase 1 study of nusinersen (ISIS-SMN(Rx)) in children with spinal muscular atrophy. Neurology. 2016 Mar 8;86(10):890-7.
5. Daras BT, et al. Nusinersen in Treatment Naïve-Patients with Later-Onset SMA: Efficacy Results from a Phase 1b/2a Multicentre Study (CS2) and its Open-label Extension (CS12). October 4-8, 2016. Granada, Spain.
6. Bertini E, et al. Nusinersen in Pre-symptomatic Infant with SMA: Interim Efficacy and Safety Results from the Phase 2 NURTURE Study. October 4-8, 2016. Granada, Spain.
7. Finkel RS, Chiriboga CA, Vajsar J, Day JW, Montes J, De Vivo DC, Yamashita M, Rigo F, Hung G, Schneider E, Norris DA, Xia S, Bennett CF, Bishop KM. Treatment of infantile-onset spinal muscular atrophy with nusinersen: a phase 2, open-label, dose-escalation study. Lancet. 2016 Dec 17; 388(10063):3017-3026.
8. SMA Overview. SMA Foundation. http://www.smafoundation.org/wp-content/uploads/2012/03/SMA-Overview.pdf Accessed September 4, 2020.
9. Ferrante, L., Melendez-Zaidi, A., Lindsey, W. and Lotze, T. (2022), Novel use of nusinersen as a therapeutic bridge to onasemnogene abeparvovec-xioi in a premature neonate with type 1 spinal muscular atrophy. Muscle & Nerve, 66: E8-E10. https://doi.org/10.1002/mus.27648
10. Meglio M. NeurologyLive. Despite limited literature, combination therapy occurring in spinal muscular atrophy. Despite Limited Literature, Combination Therapy Occurring in Spinal Muscular Atrophy (neurologylive.com) accessed June 2024

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<tr><th colspan="3">Policy History</th></tr>
<tr><th>#</th><th>Date</th><th>Change Description</th></tr>
<tr><td>2.4</td><td>Effective Date: 08/08/2024</td><td>Updated to prevent concurrent use with other SMA therapies including gene therapy, but to allow the use of Spinraza prior to Zolgensma with regard to bridging therapy</td></tr>
<tr><td>2.3</td><td>Effective Date: 04/11/2024</td><td>Annual Review of Medical Policy</td></tr>
<tr><td>2.2</td><td>Effective Date: 04/06/2023</td><td>Annual review of criteria was performed, no changes were made</td></tr>
<tr><td>2.1</td><td>Effective Date: 04/14/2022</td><td>Update to include Audaire Health™ requirements</td></tr>
<tr><td>2.0</td><td>Effective Date: 06/10/2021</td><td>Removed upper age limit criteria. Added not to be used in combination with other SMA therapies</td></tr>
<tr><td>1.9</td><td>Effective Date: 08/13/2020</td><td>Annual review of criteria was performed, no changes were made</td></tr>
<tr><td>1.8</td><td>Effective Date: 08/15/2019</td><td>Added must not be used in combination with Zolgensma</td></tr>
<tr><td>1.7</td><td>Effective Date: 10/01/2018</td><td>UM medical management system update for BCNA
<table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>Yes</td></tr><tr><td>BCNA</td><td>Yes</td></tr></table></td></tr>
<tr><td>1.6</td><td>Effective Date: 08/09/2018</td><td>Annual review of criteria was performed, no changes were made.</td></tr>
<tr><td>1.5</td><td>Effective Date: 02/12/2018</td><td>UM medical management system update for MAPPO
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<tr><td>1.4</td><td>Effective Date: 08/10/2017</td><td>Specified initial authorization</td></tr>
<tr><td>1.3</td><td>Effective Date: 06/02/2017</td><td>UM medical management system update for BCN
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<tr><td>1.2</td><td>Effective Date: 03/23/2017</td><td>Preliminary Criteria updated</td></tr>
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<tr><td>1.1</td><td>Effective Date: 03/01/2017</td><td>UM medical management system update for BCBS
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<tr><td>1.0</td><td>Effective Date: 02/09/2017</td><td>New Drug Criteria</td></tr>
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** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*