Washington State Health Care Authority

Spinal Muscular Atrophy Agents – Evrysdi (risdiplam)

Medical policy no. 74.70.65 Effective Date: TBD

Related medical policies:

- **74.70.00 - Spinal Muscular Atrophy Agents - Spinraza**

Note: *New-to-market drugs included in this class based on the Apple Health Preferred Drug List are non-preferred and subject to this prior authorization (PA) criteria. Non-preferred agents in this class require an inadequate response or documented intolerance due to severe adverse reaction or contraindication to at least TWO preferred agents. If there is only one preferred agent in the class documentation of inadequate response to ONE preferred agent is needed. If a drug within this policy receives a new indication approved by the Food and Drug Administration (FDA), medical necessity for the new indication will be determined on a case-by-case basis following FDA labeling.*

To see the list of the current Apple Health Preferred Drug List (AHPDL), please visit: https://www.hca.wa.gov/assets/billers-and-providers/apple-health-preferred-drug-list.xlsx

Background:

Spinal muscular atrophy (SMA) is a rare autosomal recessive disease characterized by loss of motor neurons in the spinal cord and lower brain stem resulting from the compound deletion or mutation of the survival motor neuron 1 (SMN1) gene. This results in severe and progressive muscular atrophy, hypotonia, diffuse symmetric weakness, and restrictive lung disease. Patients with the most severe types of SMA may be paralyzed, not able to sit or walk, and have difficulty breathing and swallowing due to bulbar muscle weakness (requiring mechanical ventilation, gastrostomy tube enteral feeding, and nursing care). Risdiplam (Evrysdi) was approved by the Food and Drug Administration (FDA) in August 2020, and is the first orally administered medication for the treatment of SMA. In the absence of a functioning SMN1 gene, risdiplam upregulates a similar gene (SMN2), resulting in improved maintenance of motor neurons.

Medical necessity

Drug	Medical Necessity
Evrysdi (risdiplam)	EVRYSDI may be considered medically necessary when used for the treatment of: • Spinal muscular atrophy (SMA)

Clinical policy:

Clinical Criteria	
Spinal Muscular Atropy (SMA) Evrysdi (risdiplam)	Evrysdi (risdiplam) may be approved if ALL of the following criteria are met: 1. Confirmed diagnosis of spinal muscular atrophy (SMA) defined as **ONE** of the following genetic tests of 5q13 demonstrating: a. Homozygous SMN1 gene deletion; **OR** b. Homozygous SMN1 gene mutation; **OR** c. Compound heterozygous SMN1 gene mutation; **AND** 2. Patient is symptomatic with a phenotype of SMA I, SMA II, or SMA III; **AND**

3. Patient is two months of age or older; **AND**
4. Not used simultaneously with Spinraza (nusinersen); **AND**
5. Patient has not been treated with Zolgensma; **AND**
6. Completion of **ONE** or more of the following functional scales that is appropriate for patient age and motor function within the last 90 days:
    a. Six-Minute Walk Test (6MWT); **OR**
    b. Hammersmith Functional Motor Scale Expanded (HFMSE); **OR**
    c. Revised Upper Limb Module (RULM) Test; **OR**
    d. Motor Function Measure 32 (MFM32); **OR**
    e. Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND); **OR**
    f. Hammersmith Infant Neurological Exam (HINE) – infant and early childhood; **AND**
7. Baseline documentation of ALL of the following:
    a. Neurologic examination; **AND**
    b. Manual Muscle Test (MMT); **AND**
    c. Pulmonary Function Test (PFTs), if able; **AND**
8. Does not require tracheostomy or invasive ventilation; **AND**
9. Prescribed by a provider specializing in the treatment of SMA.

If all the above criteria are met Evrysdi may be approved for **6 months**.

If all criteria are not met, but there are documented medically necessary or situational circumstances, based on the professional judgement of the clinical reviewer, requests may be approved on a case-by-case basis up to the initial authorization duration.

Criteria (Reauthorization)

Evrysdi may be reauthorized if all the following criteria are met:

1. Documentation of ONE of the following:
    a. Disease **improvement** or **stability** as demonstrated by at least one of the functional scales or motor milestones listed above evaluated in the previous 90 days; **OR**
    b. Disease progression is slower than what would otherwise be expected

If all the above criteria are met Evrysdi may be approved for **6 months.**

If all criteria are not met, but there are documented medically necessary or situational circumstances, based on the professional judgement of the clinical reviewer, requests may be approved on a case-by-case basis up to the reauthorization duration.

Dosage and quantity limits

Population	Dose	Quantity Limit
2 months to less than 2 years	0.2 mg/kg orally once daily	

2 years or older (less than 20kg)	0.25 mg/kg orally once daily	160mL (2 bottles, 120 mg) per 24 days
2 years or older (20kg or greater), including adults	5 mg orally once daily	

Expiration date after constitution: 64 days in refrigerator

Definitions:

Definition	
Improvement	• **HFMSE*:** At least 3 points increase in score from pretreatment baseline • **HINE***: More motor milestones have improved than have worsened. Improvement is defined as a 2 point increase in ability to kick OR at least 1 point ability increase in motor milestones of head control, rolling, sitting, crawling, standing or walking. • **CHOP-INTEND*:** At least a 4-point increase in score from the pretreatment baseline • **MFM32*:** At least 3-point increase in score from pretreatment baseline • **6MWT (ambulatory):** At least a 30-meter increase from pretreatment baseline • **RULM (non-ambulatory):** At least a 2-point increase in score from the pretreatment baseline
Stability	• The functional scale score did not worsen from baseline

*Improvement is based on minimal clinically important difference in Evyrsdi and/or Sprinraza clinical trials

Risdiplam (Evrysdi) was evaluated in infant-onset SMA (Type I) in a two-part clinical trial. In part one, 21 infants with a median age and disease onset of 6.7 and 2 months, respectively, were administered up to 2.2 mg/kg/day of risdiplam. After 12 months, 41% could sit upright without assistance for greater than 5 seconds. Further, 90% of patients were alive and did not require permanent ventilation at 12 months, and 81% at 23 months. Of note, it has been observed that approximately 25% of patients who do not obtain treatment survive without permanent ventilation through 14 months of age. In both parts of the trial, upper respiratory tract infection, pneumonia, constipation, and vomiting were the most frequently reports adverse reactions, occurring is greater than 10% of participants. Neither part of this trial has been published.

Risdiplam was also studied in a randomized, double-blind, placebo-controlled trial among patients 2 to 25 years old with SMA type II or III (n=180). Change from baseline in the Motor Function Measure 32 score (MFM32), a daily function assessment expressed as a percentage (0%-100%), was the primary outcome. Participants who received risdiplam experienced a 1.36 percentage increase in MFM32 compared to a 0.19 percentage decrease in those taking a placebo, achieving statistical significance (95% CI - 1.55 [0.3-2.81]). A greater proportion of participants using risdiplam also achieved a clinically meaningful improvement in MFM32 from baseline (defined as 3% or greater) relative to placebo (38.3% vs 23.7%, p 0.0469). Finally, a statistically significant increase from baseline in the Revised Upper Limb Module Test (RULM) was observed in those taking risdiplam compared with placebo. Notably, diarrhea, rash, mouth ulcers, arthralgia, and urinary tract infections were recorded more in the treatment group.

References

1. Evrysdi [Prescribing Information]. Genentech, Inc: San Francisco, CA. August 2020.

2. Mercuri E, Finkel RS, Muntoni F et al. Diagnosis and management of spinal muscular atrophy – Part 1: Recommendations for diagnosis, rehabilitation, orthopedic and nutritional care. Neuromuscular Disorders 2018:103-115. Available from: https://www.nmd-journal.com/article/S0960-8966(17)31284-1/pdf
3. Finkel RS, Mercuri E, Meyer OH et al. Diagnosis and management of spinal muscular atrophy – Part 2: Pulmonary and acute care; medications, supplements and immunizations; other organ systems; and ethics. Neuromuscular Disorders 2018:197-207. Available from: https://www.nmd-journal.com/article/S0960-8966(17)31290-7/pdf
4. Food and Drug Administration (FDA). FDA Approves Oral Treatment for Spinal Muscular Atrophy. August 7, 2020. Available at: FDA Approves Oral Treatment for Spinal Muscular Atrophy | FDA
5. Hoffmann-La Roche. A Two Part Seamless, Open-Label, Multicenter Study to Investigate the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics and Efficacy of Ro7034067 in Infants with Type 1 Spinal Muscular Atrophy. Available from: https://clinicaltrials.gov/ct2/show/NCT02913482. NLM Identifier: NCT02913482. Accessed March 5, 2021.
6. Hoffmann-La Roche. A Study to Investigate the Safety, Tolerability, Pharmacodynamics and Efficacy of Risdiplam (RO7034067) in Type 2 and 3 Spinal Muscular Atrophy (SMA) Participants (SUNFISH). Available from: https://clinicaltrials.gov/ct2/show/NCT02908685. NLM Identifier: NCT02908685. Accessed March 5, 2021.
7. Biogen. A Phase 3, Randomized, Double-Blind, Sham-Procedure Controlled Study to Assess the Clinical Efficacy and Safety of Isis 396443 Administered Intrathecally in Patients with Infantile-Onset Spinal Muscular Atrophy. Available at: https://clinicaltrials.gov/ct2/show/NCT02193074.NLM Identifier: NCT02193074. Accessed March 5, 2021.
8. Biogen. A Phase 3, Randomized, Double-Blind, Sham-Procedure Controlled Study to Assess the Clinical Efficacy and Safety of Isis 396443 Administered Intrathecally in Patients with Later-Onset Spinal Muscular Atrophy. Available at: https://clinicaltrials.gov/ct2/show/NCT02292537. NLM Identifier: NCT02292537. Accessed March 5, 2021.

History

Date	Action and Summary of Changes
1/20/21	New Policy

Washington State Health Care Authority

Spinal Muscular Atrophy Agents

Please provide the information below, please print your answer, attach supporting documentation, sign, date, and return to our office as soon as possible to expedite this request. Without this information, we may deny the request in seven (7) working days.

Date of request:	Reference #:	MAS:	
Patient	Date of birth	ProviderOne ID	
Pharmacy name	Pharmacy NPI	Telephone number	Fax number
Prescriber	Prescriber NPI	Telephone number	Fax number
Medication and strength	Directions for use	Qty/Days supply	

1. Is this request for a continuation of existing therapy? ☐ Yes ☐ No
   If yes, is there documentation of disease improvement or stability demonstrated by one of the following?
   - ☐ At least one of the functional scales or motor milestones evaluated in the previous 90 days
   - ☐ Disease progression is slower than what would otherwise be expected
   - ☐ None of the above

2. Indicate patient's diagnosis:
   - ☐ Spinal muscular atrophy (SMA)
   - ☐ Other. Specify: _____

3. Does the patient have a diagnosis of Spinal muscular atrophy (SMA) and genetic test 5q13 that demonstrates one of the following?
   - ☐ Homozygous SMN1 gene deletion
   - ☐ Homozygous SMN1 gene mutation
   - ☐ Compound heterozygous SMN1 gene mutation
   - ☐ None of the above

4. Is patient symptomatic with a phenotype of SMA I, SMA II OR SMA III? ☐ Yes ☐ No

5. Will this medication be used in combination with other Spinal Muscular Atrophy Agents (i.e Evrysdi, Spinraza)?
   - ☐ Yes. Specify: _____
   - ☐ No

6. Has the patient previously been treated with Zolgensma (onasemnogene abeparvovec-xioi)? ☐ Yes ☐ No

7. Indicate which of the following functional scales were used to document baseline and current (within the last 90 days) motor function?
   - ☐ Six-minute walk test (6MWT)
     Baseline: Date taken: Current: Date taken:
   - ☐ Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND)
     Baseline: Date taken: Current: Date taken:
   - ☐ Hammersmith Infant Neurological Exam (HINE) infant and early childhood
     Baseline: Date taken: Current: Date taken:
   - ☐ Hammersmith Functional Motor Scale Expanded (HFMSE)
     Baseline: Date taken: Current: Date taken:
   - ☐ Motor function measure (MFM32)
     Baseline: Date taken: Current: Date taken:

☐ Revised upper Limb Module (RULM) Test (non-ambulatory)
Baseline: Date taken: Current: Date taken:
☐ Other. Specify:

8. Does the patient have baseline documentation of all the following (check all that apply)?
   ☐ Neurologic examination.
   Baseline: Date taken: Current: Date taken:
   ☐ Manual Muscle Test (MMT).
   Baseline: Date taken: Current: Date taken:
   ☐ Pulmonary Function Test (PFT).
   Baseline: Date taken: Current: Date taken:
   ☐ Other. Specify:

9. Is the patient ambulatory?
   ☐ Yes
   ☐ No. When did the patient lose the ability to walk?

10. Does the patient require a tracheostomy or invasive ventilation? ☐ Yes ☐ No

11. Indicate for the patient:
    Weight (kg): Date taken:

12. Is the medication prescribed by a provider specializing in the treatment of SMA? ☐ Yes ☐ No

Required with this request:

- **Neurologic examination**
- **Manual Muscle Test (MMT)**
- **Pulmunary Function Test (PFT)**
- **All motor function tests**
- **Chart notes**

Prescriber signature	Prescriber specialty	Date