

Clinical Policy: Risdiplam (Evrysdi)

Reference Number: PA.CP.PHAR.477

Effective Date: 08/2020

Last Review Date: 04/2026

Description

Risdiplam (Evrysdi[™]) is a survival motor neuron 2 (SMN2) gene pre-mRNA splicing modifier.

FDA Approved Indication(s)

Evrysdi is indicated for the treatment of spinal muscular atrophy (SMA) in patients 2 months of age and older.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness[®] that Evrysdi is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Spinal Muscular Atrophy (must meet all):

1. Diagnosis of SMA;
2. Genetic testing confirms the presence of one of the following (a, b, or c):
 - a. Homozygous deletions of SMN1 gene (e.g., absence of the SMN1 gene);
 - b. Homozygous mutation in the SMN1 gene (e.g., biallelic mutations of exon 7);
 - c. Compound heterozygous mutation in the SMN1 gene [e.g., deletion of SMN1 exon 7 (allele 1) and mutation of SMN1 (allele 2)];
3. Prescribed by or in consultation with a neurologist;
4. If request is for tablet formulation, both of the following (a and b):
 - a. Age $\geq$ 2 years;
 - b. Weight $\geq$ 20 kg;
5. Documentation of one of the following baseline scores (*see Appendix D*) (a or b):
 - a. For age $<$ 2 years: Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorder (CHOP-INTEND) score or Hammersmith Infant Neurological Examination (HINE) Section 2 motor milestone score;
 - b. For age $\geq$ 2 years: Hammersmith functional motor scale expanded (HFMSE) score, Revised Hammersmith Scale (RHS), Upper Limb Module (ULM), Revised Upper Limb Module (RULM), or 6-Minute Walk Test (6MWT);
6. Evrysdi is not prescribed concurrently with Spinraza[®], Itivisma[®] or Zolgensma[®];
7. If the member is currently on Spinraza, documentation of prescriber attestation of Spinraza discontinuation upon initiation of Evrysdi;
8. If the member has a history of treatment with Zolgensma or Itivisma, must meet both of the following (a and b):
 - a. Provider must submit evidence of poor response to Zolgensma or Itivisma (e.g., sustained decrease in CHOP-INTEND or HFMSE score over a period of at least 6 months);

- b. Documentation of prescriber attestation of clinical deterioration;
- 9. Dose does not exceed of the following (a, b or c):
 - a. Age < 2 months: 0.15 mg/kg per day;
 - b. Age 2 months to < 2 years: 0.2 mg/kg per day;
 - c. Age ≥ 2 years (i or ii):
 - i. Weight < 20 kg: 0.25 mg/kg per day;
 - ii. Weight ≥ 20 kg: 5 mg per day.

Approval duration: 6 months

B. Other diagnoses/indications

- 1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. Spinal Muscular Atrophy (must meet all):

- 1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
- 2. Evrysdi is not initiated concurrently with Spinraza and/or Zolgensma;
- 3. Provider submits documentation of the number of categories of improvement and decline in motor milestones based on the CHOP-INTEND, HINE, or HFMSE score (based on member's age) since the most recent approval (*see Appendix D*);
- 4. Based on the prescriber's assessment, continues to benefit from Evrysdi (risdiplam);
- 5. Evrysdi is not prescribed concurrently with Spinraza, Ivisma or Zolgensma;
- 6. If request is for a dose increase, dose does not exceed any of the following (a, b or c):
 - a. Age < 2 months: 0.15 mg/kg per day;
 - b. Age 2 months to < 2 years: 0.2 mg/kg per day;
 - c. Age ≥ 2 years (i or ii):
 - i. Weight < 20 kg: 0.25 mg/kg per day;
 - ii. Weight ≥ 20 kg: 5 mg per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2):

- 1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.
Approval duration: Duration of request or 6 months (whichever is less); or
- 2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CHOP-INTEND: Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorder
FDA: Food and Drug Administration
HFMSE: Hammersmith functional motor scale expanded
HINE: Hammersmith infant neurological examination

MPLA: multiplex ligation-dependent probe amplification
RHS: Revised Hammersmith scale
RULM: Revised upper limb module
SMA: spinal muscular atrophy
SMN: survival motor neuron
ULM: upper limb module
6MWT: 6-minute walk test

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: General Information

- SMA is an autosomal recessive genetic disorder. It is caused by mutations in the SMN1 (survival motor neuron) gene that is found on chromosome 5 (hence the name 5q-SMA). To develop SMA, an individual must inherit two faulty (deletion or mutation) SMN1 genes, one from each parent.
- SMN-related SMA is classified as type 1 through 4 depending on time of onset. The age of disease onset of symptoms correlates with disease severity: the earlier the age of onset, the greater the impact on motor function. Children who display symptoms at birth or in infancy typically have the lowest level of functioning (type 1). SMA onset in children (types 2 and 3), teens or adults (type 4) generally correlates with increasingly higher levels of motor function.
- SMN2 gene copy and SMA types
 - SMN2 gene copy numbers are variable in individuals with spinal muscular atrophy. Higher numbers typically correlate with less severe disease.
 - More than 95% of individuals with spinal muscular atrophy retain at least 1 copy of the SMN2 gene
 - About 80% of individuals with Type I spinal muscular atrophy have 1 or 2 copies of the SMN2 gene
 - About 82% of individuals with Type II spinal muscular atrophy have 3 copies of the SMN2 gene
 - About 96% of individuals with Type III spinal muscular atrophy have 3 or 4 copies of the SMN2 gene
- The CHOP-INTEND score is a validated 16-item, 64-point scale shown to be reliable and sensitive to change over time for SMA Type 1. In a prospective cohort study of SMA type I patients (n = 34), the mean rate of decline in the CHOP-INTEND score was 1.27 points/year (95% CI 0.21-2.33, p = 0.02). A CHOP-INTEND score greater than 40 is considered a clinically meaningful change.
- The HINE Section 2 motor milestone exam is an easily performed and relatively brief standardized clinical neurological examination that is optimal for infants aged between 2 and 24 months with good inter-observer reliability. This endpoint evaluates seven

different areas of motor milestone development, with a maximum score between 2-4 points for each, depending on the milestone, and a total maximum score of 26 points.

- The HFSME score combines the Hammersmith Functional Motor Scale with a 13-item expansion module for ability to distinguish motor skills among individuals who may be older or with SMA types II and III. Each item is graded from 0 to 3, with 0 signifying no response, with a total of 66 points. HFMSE has demonstrated reliability and validity in patients with SMA. An increase of greater than 2 points in total score is unlikely in untreated SMA.
- The RHS is an ordinal scale which consist of 33 items with grades of 0,1 and 2. For individuals who can achieve the task without any compensation it is given a score of 2. For those who only attempt the movement or finish it with some form of compensation is scored 1 and sore of 0 is given when patients are unable to perform any part of the item. The total maximum score is 69 points.
- The RULM is a set of 19 tasks that measure motor function in non-ambulatory SMA patients. Each task is assessed with a 3 point ordinal scale, with a total maximum score of 37 points. Meanwhile, the maximum score for ULM was 18.
- The 6MWT is a clinical outcome measure for ambulatory SMA that has been determined to be functionally meaningful and capable of capturing disease severity.
- Per the 2025 AAN SMA update, when considering a medication or treatment plan change, unless there is an URGENT indication, a medication and associated patient outcomes should be monitored for a minimum of 6–12 months before making a change (89% agreement)
 - URGENT indications to consider changing a treatment plan outside of a 6–12 months assessment period (100% agreement) include:
 - Significant side effects or intolerance to medication not acceptable to patient or HCP
 - Intolerance to medication administration route
 - Significant disease progression as determined by the health care provider and patient/caregiver
 - Loss of motor milestones (infancy and young child)

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
SMA	Weight-based dose PO QD: <i>Evrysdi for oral solution</i> • Less than 2 months of age: 0.15 mg/kg • 2 months to less than 2 years of age: 0.2 mg/kg • 2 years of age and older, weighing less than 20 kg: 0.25 mg/kg <i>Evrysdi for oral solution or Evrysdi tablet</i> • 2 years of age and older, weigh 20 kg or more: 5 mg	5 mg/day

VI. Product Availability

- For oral solution: 60 mg risdiplam as a powder for constitution to provide 0.75 mg/mL solution

- Tablet: 5 mg

VII. References

1. Evrysdi Prescribing Information. South San Francisco, CA: Genentech Inc.; February 2025. Available at: https://www.gene.com/download/pdf/evrysdi_prescribing.pdf. Accessed January 21, 2026.
2. Baranello G, Servais L, Day JW, et al. FIREFISH Part 1: 1-Year results on motor function in infants with Type 1 SMA receiving risdiplam (RG7916). Presented at the Annual Meeting of the American Academy of Neurology in Philadelphia, PA; May 4–10, 2019. AAN Oral Presentation.
3. Mercuri E, Baranello G, Kirschner J, et al. Update from SUNFISH Part 1: Safety, tolerability and PK/PD from the dose-finding study, including exploratory efficacy data in patients with Type 2 or 3 spinal muscular atrophy (SMA) treated with risdiplam (RG7916). Presented at the Annual Meeting of the American Academy of Neurology in Philadelphia, PA; May 4–10, 2019. AAN Oral Presentation.
4. Wang CH, Finkel RS, Bertini ES, et al. Consensus Statement for Standard of Care in Spinal Muscular Atrophy. *Journal of Child Neurology*. 2007; 22:1027-1049.
5. Cobben JM, de Visser M, Scheffer H, et al. Confirmation of clinical diagnosis in requests for prenatal prediction of SMA type I. *J Neurol Neurosurg Psychiatry*. 1993; 56: 319-21.
6. Maitre NL, Chorna O, Romeo DM, and Guzzetta A. Implementation of the Hammersmith Infant Neurological Examination in a High-Risk Infant Follow-Up Program. *Pediatric Neurology*. 2016; 65:31-38.
7. Dunaway Young S, Montes J, Kramer SS, et al. Six-minute walk test is reliable and valid in spinal muscular atrophy. *Muscle and Nerve*. 2016. 54: 836-842.
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11. 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. *Neuromuscul Disord*. 2018;28(2):103-115.
12. 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. *Neuromuscul Disord*. 2018;28(3):197-207.
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14. Schroth MK, Deans J, Bharucha Goebel DX, et al. Spinal Muscular Atrophy Update in Best Practices: Recommendations for Treatment Considerations. *Neurol Clin Pract*. 2025 Feb;15(1):e200374. doi: 10.1212/CPJ.0000000000200374.

Reviews, Revisions, and Approvals	Date
Policy created	08/2020
2Q 2021 annual review: no significant changes; references reviewed and updated.	04/2021
1Q 2022 annual review: added based on prescriber's assessment, continues to benefit from treatment from state's guidance; references reviewed and updated.	01/2022
1Q 2023 annual review: no significant changes; references reviewed and updated.	01/2023
1Q 2024 annual review: added "not concurrently receiving Spinraza and/or Zolgensma"; updated dosing; references reviewed and updated.	01/2024
1Q 2025 annual review: no significant changes; references reviewed and updated.	01/2025
2Q 2026 annual review: no significant changes; clarified "at least" 6 months of trial prior to treatment change per 2025 AAN SMA update; added Itvisma, a newly approved one-time intrathecal version of Zolgensma, as another example for no concurrent use; added HFMSE as an alternative option for demonstrating prior treatment response; RT4: added new tablet dosage formulation [5 mg] to criteria with requirement that member must be age ≥ 2 years and weight ≥ 20 kg; references reviewed and updated.	04/2026