Drug Coverage Policy

Effective Date.....03/15/2026
Coverage Policy Number.....IP0063
Policy Title.....Evrysdi

Spinal Muscular Atrophy – Evrysdi

- Evrysdi® (risdiplam oral solution and tablets – Genentech/Roche)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview
Evrysdi, a survival motor neuron (SMN)2 splicing modifier, is indicated for the **treatment of spinal muscular atrophy** in pediatric patients and adults.[1]

Disease Overview
Spinal muscular atrophy is a genetic, autosomal recessive muscular disorder caused by deletion or loss of function mutation in the SMN1 gene.[2-5] The estimated incidence in the US is one in 11,000.[3] The reduced level of SMN protein causes degeneration of lower motor neurons.[2-5] The phenotypic expression of the disease is impacted by the SMN2 gene copy number. Data have shown that patients with a higher number of SMN2 copies generally have a more mild phenotypic disease expression. Gene deletion testing for spinal muscular atrophy can be performed at many diagnostic laboratories. Table 1 describes the disease types. Of note, various motor ability assessments are used in clinical practice to characterize functional impairment in spinal muscular atrophy. Different functional motor scales are utilized to evaluate patients. When motor neuron function is lost, it cannot be regained, which greatly impacts patients who have experienced progression (e.g., patients with complete paralysis of limbs or permanent ventilator dependence).

Table 1. Types of Spinal Muscular Atrophy.[4,5]

	Age at Onset	**Features/Clinical Presentation/Motor Milestones***	**Lifespan***	**SMN2 Gene Copy Number**
Type 0 (< 1% of patients)	Prenatal	Severe hypotonia and weakness with respiratory failure at birth. There is no achievement of motor milestones.	A few weeks to days [< 6 months]	1
Type 1 (50%)	< 6 months	Poor muscle tone and lack of movement. Respiratory assistance may be needed. Some head control. Patients are never able to sit without support.	< 2 years	1 to 2 for 80% of patients
Type 2 (30% of patients)	6 to 18 months	Patients are able to sit. However, patients are unable to walk or stand without assistance.	Close to normal	2 to 3 for over 90% of patients
Type 3 (10% to 20% of patients)	> 18 months	Walks independently but may lose this ability as the disease progresses. There is loss of motor skills.	Normal	3 to 5 for most patients
Type 4 (< 1% of patients)	> 18 years	Independent walking. Fatigue and proximal muscle weakness.	Normal	4 for 75% of patients; 5 or 6 for 25% of patients

* With supportive care only; SMN2 – Survival motor neuron 2.

Clinical Efficacy
The efficacy of Evrysdi for the treatment of patients with infantile-onset (Type 1), later-onset (Type 2 and 3), and pre-symptomatic spinal muscular atrophy was evaluated in three clinical studies.[1,6-8] **FIREFISH** involved patients with Type 1 spinal muscular atrophy who had symptom onset between 28 days and 3 months of age.[1,6,7] Genetic confirmation of homozygous deletion or

compound heterozygosity predictive of loss of function of the SMN1 gene was required for trial entry.[1] Patients had two SMN2 gene copies. Many patients gained improvements in the ability to sit for at least 5 seconds independently, and there was an increase in the percentages of patients who were alive without permanent ventilation. **SUNFISH** evaluated Evrysdi in patients with later-onset (Type 2 or Type 3) spinal muscular atrophy. Most patients (90%) had three SMN2 gene copie.[1,8] In Part 2 of the study, benefits of Evrysdi vs. placebo were noted at Month 12 in motor function as well as in upper limb motor performance.[1] **RAINBOWFISH** investigated Evrysdi in infants up to 6 weeks of age (at the first dose) who had been genetically diagnosed with spinal muscular atrophy but did not have symptoms. Eight patients had two SMN2 gene copies, 13 patients had three SMN2 gene copies, and five patients had four or more SMN2 gene copies. The median age at first dose was 25 days. The primary efficacy endpoint was the proportion of patients with the ability to sit without support for at least 5 seconds at Month 12, which was achieved by 87.5% of patients with two SMN2 copies (n = 7/8) and 96.2% of patients (n = 25/26) in the full treated population. All 26 patients were alive at 12 months without permanent ventilation.

Guidelines
Evrysdi is not addressed in guidelines. According to a treatment algorithm from the Spinal Muscular Atrophy Newborn Screening Multidisciplinary Working Group (2018), immediate treatment is recommended in patients with two or three SMN2 gene copies.[9] In 2020, the Working Group updated recommendations that infants diagnosed with spinal muscular atrophy via newborn screening with four SMN2 gene copies should receive immediate treatment.[10] Patients with five (or more) SMN2 gene copies should be observed and screened for symptoms.

Coverage Policy

POLICY STATEMENT
Prior Authorization is required for benefit coverage of Evrysdi. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Evrysdi as well as the monitoring required for adverse events and long-term efficacy, approval requires Evrysdi to be prescribed by a physician who has consulted with or who specializes in the condition. If claims history is available, verification is required for certain criteria as noted by **[verification in claims history required]**. All reviews will be forwarded to the Medical Director for evaluation.

Documentation: Documentation is required where noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory results, medical test results, claims records, prescription receipts, and/or other information. All documentation must include patient-specific identifying information.

Evrysdi is considered medically necessary when the following are met:

FDA-Approved Indication

1. **Spinal Muscular Atrophy – Treatment.** Approve if the patient meets ONE of the following (A or B):
   A) Initial Therapy. Approve for 4 months if the patient meets ALL of the following (i, ii, iii, iv, and v):
      i. Baseline motor ability assessment that suggests spinal muscular atrophy (based on age, motor ability, and development) has been performed from ONE of the following exams (a, b, c, d, e, f, or g) **[documentation required]**:

a) Bayley Scales of Infant and Toddler Development ; OR
b) Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND); OR
c) Hammersmith Functional Motor Scale Expanded (HFMSE); OR
d) Hammersmith Infant Neurological Exam Part 2 (HINE-2); OR
e) Motor Function Measure-32 Items (MFM-32); OR
f) Revised Upper Limb Module (RULM) test; OR
g) World Health Organization motor milestone scale; AND

ii. Patient has had a genetic test confirming the diagnosis of spinal muscular atrophy with bi-allelic pathogenic variants in the survival motor neuron 1 (SMN1) gene **[documentation required]**; AND
Note: Pathogenic variants may include homozygous deletion, compound heterozygous mutation, or a variety of other rare mutations.

iii. Patient meets ONE of the following (a or b):
a) Patient has two or three survival motor neuron 2 (SMN2) gene copies **[documentation required]**; OR
b) Patient meets BOTH of the following ([1] and [2]):
(1) Patient has four survival motor neuron 2 (SMN2) gene copies **[documentation required]**; AND
(2) Patient has objective signs consistent with spinal muscular atrophy Types 1, 2, or 3 **[documentation required]**; AND

iv. Patient has not received Zolgensma (onasemnogene abeparvovec-xioi intravenous infusion) or Itvisma (onasemnogene abeparvovec-brve intrathecal injection) in the past **[verification in claims history required]**; AND
Note: If no claim for Zolgensma or Itvisma is present (or if claims history is not available), the prescribing physician confirms that the patient has not previously received Zolgensma or Itvisma.

v. Medication is prescribed by a physician who has consulted with a specialist or who specializes in the management of patients with spinal muscular atrophy and/or neuromuscular disorders; OR

B) Patient Currently Receiving Evrysdi. Approve for 1 year if the patient meets ALL of the following (i, ii, iii, and iv):

i. Patient has had a genetic test confirming the diagnosis of spinal muscular atrophy with bi-allelic pathogenic variants in the survival motor neuron 1 (SMN1) gene; AND
Note: Pathogenic variants may include homozygous deletion, compound heterozygous mutation, or a variety of other rare mutations.

ii. Patient meets ONE of the following (a or b):
a) Patient has two or three survival motor neuron 2 (SMN2) gene copies; OR
b) Patient meets BOTH of the following [(1) and (2)]:
(1) Patient has four survival motor neuron 2 (SMN2) gene copies; AND
(2) Patient has objective signs consistent with spinal muscular atrophy Types 1, 2, or 3; AND

iii. The medication is prescribed by a physician who has consulted with a specialist or who specializes in the management of patients with spinal muscular atrophy and/or neuromuscular disorders; AND

iv. Patient must meet ONE of the following (a or b):
a) Patient must have had a positive clinical response (for example, improvement or stabilization) from pretreatment baseline status (i.e., within the past 4 months) with Evrysdi in ONE of the following exams [(1), (2), (3), (4), (5), (6), or (7)] **[documentation required]**:
(1) Bayley Scales of Infant and Toddler Development; OR
(2) Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND); OR

(3) Hammersmith Functional Motor Scale Expanded (HFMSE); OR
(4) Hammersmith Infant Neurological Exam Part 2 (HINE-2); OR
(5) Motor Function Measure-32 Items (MFM-32); OR
(6) Revised Upper Limb Module (RULM) test; OR
(7) World Health Organization motor milestone scale; OR

b) According to the prescribing physician, the patient has responded to Evrysdi and continues to benefit from ongoing Evrysdi therapy by the most recent (i.e., within the past 4 months) physician monitoring/assessment tools **[documentation required]**.
Note: Examples include pulmonary function tests showing improvement, bulbar function test results suggesting benefits, reduced need for respiratory support, decrease in the frequency of respiratory infections or complications, and/or prevention of permanent assisted ventilation.

Conditions Not Covered

Evrysdi for any other use is considered not medically necessary including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Patient has Complete Paralysis of All Limbs.** Data are needed to determine if this patient population with advanced spinal muscular atrophy would derive benefits from Evrysdi.

2. **Patient has Permanent Ventilator Dependence.** Data are needed to determine if this patient population with advanced spinal muscular atrophy would derive benefits from Evrysdi.

3. **Concurrent use with Spinraza (nusinersen intrathecal injection).** Further study is needed to determine if use of Evrysdi with Spinraza is efficacious and safe.

References

1. Evrysdi® oral solution and tablets [prescribing information]. South San Francisco, CA: Genentech/Roche; February 2025.
2. Schroth M, Deans J, Arya K, et al. Spinal muscular atrophy update in best practices. Recommendations for diagnosis considerations. *Neurology*. 2024;14:e200310.
3. Yeo CJJ, Tizzano EF, Darras BT. Challenges and opportunities in spinal muscular atrophy therapeutics. *Lancet Neurol*. 2024;23:205-218.
4. Ramdas S, Oskoui M, Servais L. Treatment options in spinal muscular atrophy: a pragmatic approach for clinicians. *Drugs*. 2024;84:747-762.
5. Prior TW, Leach ME, Finanger E. Spinal Muscular Atrophy. 2000 Feb 24 [Updated 2024 September 19]. In: Adam MP, Feldman J, Mirzaa GM, et al, editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024. Available at: https://www.ncbi.nlm.nih.gov/books/NBK1352/pdf/Bookshelf_NBK1352.pdf. Accessed on July 26, 2025.
6. Baranello G, Darras BT, Day JW, et al, for the FIREFISH Working Group. Risdiplam in type 1 spinal muscular atrophy. *N Engl J Med*. 2021;384(10):915-923.
7. Darras BT, Masson R, Mazurkiewicz-Beldzinska M, et al, for the FIREFISH Working Group. Risdiplam-treated infants with type 1 spinal muscular atrophy versus historical controls. *N Engl J Med*. 2021;385(5):427-435.
8. Mercuri E, Deconinck N, Mazzone ES, et al, on behalf of the SUNFISH Study Group. Safety and efficacy of once daily risdiplam in type 2 and non-ambulant type 3 spinal muscular atrophy

(SUNFISH part 2): a phase 3, double-blind, randomized, placebo-controlled trial. *Lancet Neurol*. 2022;21:42-52.
9. Glascock J, Sampson J, Haidet-Phillips A, et al. Treatment algorithm for infants diagnosed with spinal muscular atrophy through newborn screening. *J Neuromuscul Dis*. 2018;5:145-158.
10. Glascock J, Sampson J, Connolly AM, et al. Revised recommendations for the treatment of infants diagnosed with spinal muscular atrophy via newborn screening who have 4 copies of SMN2. *J Neuromuscul Dis*. 2020;7(2):97-100.

Revision Details

Summary of Changes	Review Date	Effective Date
No criteria changes.	10/17/2024	12/15/2024
Policy Title: Updated from "Risdiplam" to "Spinal Muscular Atrophy – Evrysdi". **Added** Evrysdi oral tablets to the policy. **Spinal Muscular Atrophy – Treatment:** **Updated** documentation requirements throughout the policy. For Initial Therapy - **Updated** the initial authorization duration from "6 months" to "4 months". **Removed** the 6 Minute Walk Test from the list of baseline motor ability assessment options. **Updated** the genetic testing language from "Bi-allelic mutation" to "bi-allelic pathogenic variants". **Added** "patient has not received Zolgensma" criteria. **Removed** follow-on Evrysdi criteria in those who were previously treated with Zolgensma. **Removed** "individual is of childbearing potential, individual is not currently pregnant and has been counseled to use effective contraception during treatment and up until 1 month after the last Evrysdi dose". **Removed** "individual does not have hepatic impairment" criterion. For Patient Currently Receiving - **Updated** authorization duration from "6 months" to "4 months". **Updated** criteria for a patient currently receiving Evrysdi. **Removed** the 6 Minute Walk Test from the list of baseline motor ability assessment options. **Conditions Not Covered: Updated** the conditions not covered statement. **Updated** "Concurrent use of Spinraza" statement.	7/31/2025	08/15/2025
Spinal Muscular Atrophy – Treatment: For initial therapy, Itvisma was added as a gene therapy that the patient should not have received in the past. The Note now	2/12/2026	3/15/2026

includes that if no claim for Itvisma is present (or if claims history is not available), the prescribing physician confirms that the patient has not previously received Itvisma. The note providing examples of pathogenic variants was updated from homozygous mutation to heterozygous mutation. For Patients Currently Receiving Evrysdi: Approval duration was updated to 1 year, previously it was four months.		

The policy effective date is in force until updated or retired.