

## PHARMACY COVERAGE GUIDELINE

### EVRYSDI™ (risdiplam) oral Generic Equivalent (if available)

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#### **This Pharmacy Coverage Guideline (PCG):**

- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively “Service”) is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider’s judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member’s benefit plan; and
- Is subject to change as new information becomes available.

#### **Scope**

- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

#### **Instructions & Guidance**

- To determine whether a member is eligible for the Service, read the entire PCG.
  - This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
  - Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
  - The “Criteria” section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member’s benefit plan.
  - The “Description” section describes the Service.
  - The “Definition” section defines certain words, terms or items within the policy and may include tables and charts.
  - The “Resources” section lists the information and materials we considered in developing this PCG
  - **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
  - Information about medications that require prior authorization is available at [www.azblue.com/pharmacy](http://www.azblue.com/pharmacy). You must fully complete the [request form](#) and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to [Pharmacyprecert@azblue.com](mailto:Pharmacyprecert@azblue.com).
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#### **Criteria:**

- **Criteria for initial therapy:** Evrysdi (risdiplam) and/or generic equivalent (if available) is considered **medically necessary** and will be approved when **ALL** the following criteria are met:
  1. Prescriber is a physician specializing in the patient’s diagnosis or is in consultation with a Neurologist or Pediatric Neurologist
  2. Individual has a confirmed diagnosis of **ONE** of the following:
    - a. Infantile-onset Type 1 SMA with onset of symptoms occurring before 3 months of age
    - b. Later-onset Type 2 or Type 3 SMA with onset of symptoms occurring before 25 years of age
    - c. Infant with genetically determined pre-symptomatic SMA (asymptomatic)

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3. Genetic testing demonstrating bi-allelic mutations or deletions in chromosome 5q in the survival motor neuron 1 (*SMN1*) gene is **ONE** of the following:
  - a. Deletion of both copies of the *SMN1* gene (exon 7 at locus 5q13)
  - b. Compound heterozygous of the *SMN1* gene (exon 7 at locus 5q13) is **ONE** of the following:
    - i. Pathogenic variant(s) in both copies of the *SMN1* gene
    - ii. Pathogenic variant in one copy and deletion of the second copy of the *SMN1* gene
4. **ONE** of the following:
  - a. Patient is symptomatic and genetic test confirms 2, 3 or 4 copies of the *SMN2* gene
  - b. Patient is asymptomatic and genetic test confirms minimum of 2 but less than 4 copies of the *SMN2* gene
5. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] ([see Definitions section](#))
6. Individual has completed **ALL** the following **baseline tests** before initiation of treatment and will have continued monitoring as clinically appropriate:
  - a. Negative pregnancy test in a woman of childbearing potential
  - b. Motor function and milestone assessed via an age-appropriate validated exam scale (e.g., Bayley Scales of Infant and Toddler Development Third Edition (BSID-III), Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND), Hammersmith Functional Motor Scale Expanded (HFSME), Hammersmith Infant Neurologic Exam (HINE-2), Revised Upper Limb Module (RULM), 6-Minute Walk Test (6MWT))
7. There are **NONE** of the following:
  - a. For infants and very young children (age <2 years) with SMA who are ventilator-dependent
  - b. Advanced SMA (e.g., complete paralysis of limbs, permanent ventilator dependence (i.e., invasive ventilation (tracheostomy), or respiratory assistance for 16 or more hours per day (including noninvasive ventilatory support) continuously for 14 or more days in absence of an acute reversible illness, excluding perioperative ventilation)
  - c. Previous use, concurrent use, or after administration of virus vector-based gene therapy, e.g., Zolgensma (onasemnogene abeparvovec-xioi)
  - d. Previous use or concurrent use of SMN2-targeting antisense oligonucleotide, e.g., Spinraza (nusinersin)
  - e. Concomitant or previous administration of another SMN2 therapy
  - f. The patient is concurrently enrolled in a clinical trial for any experimental therapy for SMA
  - g. SMA without chromosome 5q mutations or deletions
  - h. Severe hepatic impairment (Child-Pugh Class C)

**Initial approval duration:** 6 months

- **Criteria for continuation of coverage (renewal request):** Evrysdi (risdiplam) and/or generic equivalent (if available) is considered **medically necessary** and will be approved when **ALL** the following criteria are met (**samples are not considered for continuation of therapy**):

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1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Neurologist or Pediatric Neurologist
2. Individual is **ONE** of the following:
  - a. Individual was  $\leq 25$  years of age when Evrysdi therapy was started and had onset of symptoms before 25 years of age (before 3 months of age for Type 1 SMA)
  - b. If the individual is  $\geq 26$  years of age, with documentation initiation of Evrysdi therapy was started  $\leq 25$  years of age and had onset of symptoms before 25 years of age (before 3 months of age for Type 1 SMA)
  - c. Individual has genetically determined pre-symptomatic SMA (asymptomatic)
3. Individual has documentation of positive clinical response to therapy defined as **TWO** of the following:
  - a. Documentation of efficacy and disease stability by use of age-appropriate evaluation tool such as CHOP-INTEND, Bayley-III Scale (motor part), HFMSE, RULM, 6-MWT, etc. of **TWO** of the following:
    - i. Must demonstrate improvement or maintenance of previous scores from baseline
    - ii. Must demonstrate improvement in at least one more motor milestone category over baseline rather than worsening
    - iii. Must demonstrate improvement in more motor milestone categories than worsening over baseline
    - iv. Must demonstrate achieved additional motor milestone(s) over baseline
    - v. No evidence of disease progression defined as a decline in motor function test score(s)
  - b. Reduced need for respiratory support
  - c. Prevention of permanent assisted ventilation
4. Individual has been adherent with the medication
5. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] ([see Definitions section](#))
6. There are **NONE** of the following:
  - a. For infants and very young children (age  $<2$  years) with SMA who are ventilator-dependent
  - b. Advanced SMA (e.g., complete paralysis of limbs, permanent ventilator dependence (i.e., invasive ventilation (tracheostomy), or respiratory assistance for 16 or more hours per day (including noninvasive ventilatory support) continuously for 14 or more days in absence of an acute reversible illness, excluding perioperative ventilation)
  - c. Previous use, concurrent use, or after administration of virus vector-based gene therapy, e.g., Zolgensma (onasemnogene abeparvovec-xioi)
  - d. Previous use or concurrent use of SMN2-targeting antisense oligonucleotide, e.g., Spinraza (nusinersin)
  - e. Concomitant or previous administration of another SMN2 therapy
  - f. The patient is concurrently enrolled in a clinical trial for any experimental therapy for SMA
  - g. SMA without chromosome 5q mutations or deletions
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**Renewal duration:** 12 months

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➤ Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**
  2. **Off-Label Use of Cancer Medications**
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#### **Description:**

Evrysdi (risdiplam) is a survival motor neuron 2 (SMN2) directed RNA splicing modifier indicated for the treatment of spinal muscular atrophy (SMA) in pediatric and adult patients.

Risdiplam is a survival motor neuron 2 (SMN2) splicing modifier designed to treat patients with SMA caused by mutations in chromosome 5q that lead to SMN protein deficiency. Using animal models of SMA, risdiplam was shown to increase exon 7 inclusion in SMN2 messenger ribonucleic acid (mRNA) transcripts and production of full-length SMN protein in the brain. *In vitro* and *in vivo* data indicate that risdiplam may cause alternative splicing of additional genes, including FOXM1 and MADD. FOXM1 and MADD are thought to be involved in cell cycle regulation and apoptosis, respectively, and have been identified as possible contributors to adverse effects seen in animals.

In clinical trials, Evrysdi led to an increase in SMN protein with a greater than 2-fold median change from baseline within 4 weeks of treatment initiation. The increase was sustained throughout the treatment period (of at least 12 months) across all SMA types.

Safety and effectiveness in pediatric patients below the age of 16 days of age have not been established.

SMA encompasses a spectrum of phenotypes ranging from severe forms with early onset to milder forms with later onset. The natural history of SMA according to phenotype is summarized as follows: SMA type 0 (prenatal onset) is associated with early death from respiratory failure, usually within weeks after birth; SMA type 1 (onset between birth and age six months) leads to death from respiratory failure before the age of two years; SMA type 2 (onset between 3 and 15 months of age) is notable for inability to achieve independent walking or standing but is compatible with survival into adulthood, most individuals live to age 25 years; SMA type 3 (onset between age 18 months and adulthood) is characterized by slowly progressive proximal weakness, which may lead to loss of independent ambulation, but is associated with a normal lifespan; SMA type 4 (adult onset) is otherwise similar to SMA type 3 and is associated with a normal lifespan.

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#### **Definitions:**

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting  
[MedWatch Forms for FDA Safety Reporting | FDA](#)

#### **Clinical features spinal muscular atrophy (SMA):**

The diagnosis of SMA should be suspected of any infant with unexplained weakness or hypotonia. Additional suspicions suggesting the diagnosis in infants, children, or adults include a history of motor difficulties, loss of

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motor skills, proximal muscle weakness, hyporeflexia or areflexia, tongue fasciculations, and signs of lower motor neuron disease on examination.

All forms of SMA have diffuse symmetric proximal muscle weakness that is greater in the lower than upper limbs and absent or markedly decreased deep tendon reflexes. In addition, SMA is associated with a restrictive, progressive respiratory insufficiency, particularly SMA type 0 and type 1.

#### **Clinical classification spinal muscular atrophy (SMA):**

Type	Age of Onset	Requires respiratory support at birth	Able to sit	Able to stand	Able to walk	Life expectancy	Predicted SMN2 copy number
0	Prenatal	Yes	No	No	No	< 6 months	1
1	< 6 months	No	No	No	No	< 2 years	2
2	6-18 months	No	Yes	No	No	10-40 years	3
3	> 18 months	No	Yes	Yes	Assisted	Adult	3 or 4
4	> 5 years	No	Yes	Yes	Yes	Adult	> 4

*Butchbach ME. Copy Number Variations in the Survival Motor Neuron Genes: Implications for Spinal Muscular Atrophy and Other Neurodegenerative Diseases. Front Mol Biosci 2016; 3:7.*

#### **Genetic testing confirms the presence of one of the following (a, b, or c):**

- Homozygous deletions of SMN1 gene (e.g., absence of the SMN1 gene)
- Homozygous mutation in the SMN1 gene (e.g., biallelic mutations of exon 7)
- Compound heterozygous mutation in the SMN1 gene [e.g., deletion of SMN1 exon 7 (allele 1) and mutation of SMN1 (allele 2)]

#### **SMA evaluation tools:**

##### **CHOP INTEND (Children’s Hospital of Philadelphia Infant Test of Neuromuscular Disorders)**

- Measures motor function via 16 different items, which capture neck, trunk, proximal, and distal limb strength
- Scored from 0 (least function) to 4 (most function) for each of the 16 items
- Validated as part of a multicenter natural-history study and was found to reflect measures of disease severity such as number of SMN2 copies and respiratory support needed
- A validated 64-point scale shown to be reliable and sensitive to change over time for SMA Type 1
- Maintenance scores of > 40 points is considered to be clinically meaningful in SMA

##### **HINE (Hammersmith Infant Neurological Examination)**

- Measures functional ability and achievement of motor milestones
- Consists of three sections:
  - Neurological exam (postures, cranial nerve function, reflexes, tone, and movements)
  - Development of motor function (head control, sitting, voluntary grasping, rolling, crawling, and walking)
  - State of behavior (consciousness, social orientation, and emotional state)
- The overall score ranges from 0 to 78
- At 9 or 12 months, the scores  $\geq 73$  are regarded as optimal
- Healthy-term infants should have a median score  $\geq 67$  at 3 months and  $\geq 70$  at 6 months

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- HFMSE (Hammersmith Functional Motor Scale Expanded)
- Expanded version of the original 20-item Hammersmith Functional Motor Scale that incorporates 13 items from the Gross Motor Function Measure assessment
- Consists of 33 items investigating the child's ability to perform various activities
  - Each activity (item) is scored on a 3-point system, with a score of 2 for "performs without modification," 1 for "performs with modification/adaptation," and 0 for "unable to perform."
- The total score can range from 0 (if all the activities failed) to 66 (if all the activities are achieved)
- A clinically meaningful change was estimated to be a 3-point change in the modified HFMS at 6 months in a multicenter phase 2 trial of L-carnitine and valproic acid in patients with SMA Type II or III

#### 6MWT (6-Minute Walking Test)

- An objective evaluation of functional exercise capacity that measures the maximum distance a person can walk in 6 minutes over a 25-meter linear course
- Detects physiological fatigue in ambulatory patients with SMA as demonstrated by a 17% decrease in gait velocity from the first minute to the last
- Has been used in assessment of function and has been accepted by regulatory agencies as a clinically meaningful endpoint in other neurologic disorders
- Has been found to be reliable in other pediatric disorders and in healthy children. Demonstrates good test-retest reliability and is sensitive to change

#### Revised Hammersmith scale (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 score of 0 is given when patients are unable to perform any part of the item
- The total maximum score is 69 points

#### Revised upper limb module (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

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### **Resources:**

Evrysdi (risdiplam) product information, revised by manufacturer Genentec, Inc. 02-2025. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed June 27, 2025.

Bodamer OA. Spinal muscular atrophy. In: UpToDate, Nordli DR, Firth HV, Martin R, Dashe JF (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at <http://uptodate.com>. Literature current through August 2025. Topic last updated September 25, 2025. Accessed September 26, 2025.

Mercuri E, Deconinck N, Mazzone ES, et al. 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. Re-evaluated September 26, 2025.