

## Pharmacy Policy Bulletin

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**Title:** Risdiplam (Evrysdi™)  
**Policy #:** Rx.01.243

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**Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, quantity, or formulary restrictions (ie limits on non-preferred drugs). Individual member benefits must be verified.**

**This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.**

**Members are advised to use participating pharmacies in order to receive the highest level of benefits.**

**Intent:**

The intent of this policy is to communicate the medical necessity criteria for **Risdiplam (Evrysdi®)** as provided under the member's prescription drug benefit.

**Description:**

Spinal muscular atrophy (SMA) is characterized by degeneration of the anterior horn cells in the spinal cord and motor nuclei in the lower brainstem, which results in progressive muscle weakness and atrophy. The diagnosis of SMA should be suspected for any infant with unexplained weakness or hypotonia. Additional clues suggesting the diagnosis in infants, children, or adults include a history of motor difficulties, loss of motor skills, proximal muscle weakness, hyporeflexia or areflexia, tongue fasciculations, and signs of lower motor neuron disease on examination. These diseases classified as types 0 through 4, depending upon the age of onset and clinical course.

Risdiplam is a survival of motor neuron 2 (SMN2) splicing modifier designed to treat patients with spinal muscular atrophy (SMA) caused by mutations in chromosome 5q that lead to SMN protein deficiency. Using in vitro assays and studies in transgenic 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.

Evrysdi is indicated for the treatment of spinal muscular atrophy (SMA) in pediatric and adult patients.

**Policy:**

**INITIAL CRITERIA:** Risdiplam (Evrysdi™) is approved when ALL of the following are met:

1. Diagnosis of spinal muscular atrophy (SMA) type 1, 2 or 3; and
2. BOTH of the following:
  - a. The mutation or deletion of genes in chromosome 5q resulting in one of the following:
    - i. Homozygous gene deletion or mutation (e.g., homozygous deletion of exon 7 at locus 5q13); or
    - ii. Compound heterozygous mutation (e.g., deletion of SMN1 exon 7 [allele 1] and mutation of SMN1 [allele 2]); and
3. Member has at least 2 copies of SMN2; and Prescribed by or in consultation with a neurologist or a psychiatrist with subspecialty certification in neuromuscular medicine; and
4. Member is not to receive concomitant chronic survival motor neuron (SMN) modifying therapy for the treatment of SMA (e.g., Spinraza)

Initial authorization duration: 12 months

**REAUTHORIZATION CRITERIA:** Risdiplam (Evrysdi™) is re-approved when ALL of the following are met:

1. Documentation of positive clinical response to therapy from pretreatment baseline status; and
2. Prescribed by or in consultation with a neurologist or a psychiatrist with subspecialty certification in neuromuscular medicine; and
3. Member is not to receive concomitant chronic survivor motor neuron (SMN) modifying therapy for the treatment of SMA (e.g., Spinraza)

Reauthorization duration: 2 years

**Black Box Warning as shown in the drug Prescribing Information:**

N/A

**Guidelines:**

Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

**BENEFIT APPLICATION**

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the prescription drug benefits of the Company's products when the medical necessity criteria listed in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

**References:**

Evrysdi™ (risdiplam) [prescribing information]. San Francisco, CA: Genentech, Inc; March 2023. Available from: [https://www.gene.com/download/pdf/evrysdi\\_prescribing.pdf](https://www.gene.com/download/pdf/evrysdi_prescribing.pdf). Accessed April 19, 2023.

Bodamer, OA. Spinal muscular atrophy. In: UpToDate. April 2023. Available from: [www.uptodate.com](http://www.uptodate.com). Accessed April 19, 2023.

Day JW, Anoussamy M, Baranello G, et al. SUNFISH Part 2: 24-month efficacy outcomes of risdiplam (RG7916) treatment in patients with Type 2 or 3 spinal muscular atrophy (SMA). Presented at the 2020 Virtual SMA Research & Clinical Care Meeting.

Servais L, Baranello G, Masson R, et al. FIREFISH Part 2: Efficacy and safety of risdiplam (RG7916) in infants with Type 1 spinal muscular atrophy (SMA). Presented at the 2020 Virtual SMA Research & Clinical Care Meeting.

Markowitz JA, Sing P, Darras BT. Spinal muscular atrophy: a clinical and research update. *Pediatr Neurol.* 2012;46(1):1-12.

Wang CH, Finkel RS, Bertini ES, et al. Consensus statement for standard of care in spinal muscular atrophy. *J Child Neurol.* 2007;22(8):1027-1049.

Bertini E DJ, Muhaizea A, et al. RAINBOWFISH: A Study of Risdiplam (RG7916) in Newborns with Presymptomatic Spinal Muscular Atrophy. Presented at: World Muscle Society; October 1–5, 2019; Copenhagen, Denmark.

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. *J Neuromuscul Dis.* 2018;28(2):103-115. Page 723

Stolte B, Bois JM, Kizina K, et al. Minimal clinically important differences in functional motor scores in adults with spinal muscular atrophy. *Eur. J. Neurol.* 2020; 0:1-9.

Pera, M., Coratti, G., Mazzone, E., et al. (2019). Revised upper limb module for spinal muscular atrophy: 12 month changes. *Muscle Nerve.* Apr;59(4):426-430.

Kirschner J, Butoianu N, Goemans N, et al. European ad-hoc consensus statement on gene replacement therapy for spinal muscular atrophy. *Eur J Paediatr Neurol.* 2020. <https://doi.org/10.1016/j.ejpn.2020.07.001>

**Applicable Drugs:**

Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

Brand Name	Generic Name
Evrysdi™	Risdiplam

**Cross References:**

Rx.01.33 Off Label Use

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<b>Policy Version Number:</b>	4.00
<b>P&amp;T Approval Date:</b>	March 16, 2023
<b>Policy Effective Date:</b>	July 01, 2023
<b>Next Required Review Date:</b>	March 16, 2024

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The Policy Bulletins on this web site were developed to assist the Company in administering the provisions of the respective benefit programs, and do not constitute a contract. If you have coverage through the Company, please refer to your specific benefit program for the terms, conditions, limitations and exclusions of your coverage. Company does not provide health care services, medical advice or treatment, or guarantee the outcome or results of any medical services/treatments. The facility and professional providers are responsible for providing medical advice and treatment. Facility and professional providers are independent contractors and are not employees or agents of the Company. If you have a specific medical condition, please consult with your doctor. The Company reserves the right at any time to change or update its Policy Bulletins.

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