Evrysdi™ (risdiplam)
(Oral)

Document Number: IC-0560

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Dates Reviewed: 09/2020, 08/2021, 06/2022

I. Length of Authorization

Coverage will be provided annually and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Evrysdi 60 mg oral solution: 1 bottle every 12 days

B. Max Units (per dose and over time) [HCPCS Unit]:

- 5 mg per day

III. Initial Approval Criteria [1,6-9]

Coverage is provided in the following conditions:

Universal Criteria

- Patient must not have previously received treatment with SMA gene therapy (i.e., onasemnogene abeparvovec-xioi); **AND**
- Patient will not use in combination with other agents for SMA (e.g., onasemnogene abeparvovec, nusinersen, etc.); **AND**
- Patient must not have advanced disease (complete limb paralysis, permanent ventilation support, etc.); **AND**

Spinal Muscular Atrophy (SMA) † Φ [1-9]

- Patient retains meaningful voluntary motor function (e.g., manipulate objects using upper extremities, ambulate, etc.); **AND**
- Patient must have a diagnosis of 5q spinal muscular atrophy confirmed by either homozygous deletion of the *SMN1* gene or dysfunctional mutation of the *SMN1* gene; **AND**
- Patient must have a diagnosis of SMA phenotype I, II, or III; **AND**
    - Patient has ≤ 3 copies of the *SMN2* gene *(Note: Patients with >3 copies of the SMN2 gene will be reviewed on a case-by-case basis)*; **OR**

- Patient has symptomatic disease (i.e., impaired motor function and/or delayed motor milestones); **AND**

- Baseline documentation of one or more of the following:
  - Motor function/milestones, including but not limited to, the following validated scales: Hammersmith Infant Neurologic Exam (HINE), Hammersmith Functional Motor Scale Expanded (HFMSE), Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND), Bayley Scales of Infant and Toddler development Third Ed. (BSID-III), 6-minute walk test (6MWT), upper limb module (ULM), motor function measure 32 (MFM32), revised upper limb module (RULM), etc.
  - Respiratory function tests [e.g., forced vital capacity (FVC), etc.]
  - Exacerbations necessitating hospitalization and/or antibiotic therapy for respiratory infection in the preceding year/timeframe
  - Patient weight (for patients without a gastrostomy tube)

† FDA-labeled indication(s), ‡ Compendia recommended indication(s); Φ Orphan Drug

IV. Renewal Criteria [1-9]

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), etc. identified in section III; **AND**
- Absence of unacceptable toxicity which would preclude safe administration of the drug. Examples of unacceptable toxicity include the following: severe diarrhea, etc.; **AND**
- Patient has responded to therapy compared to pretreatment baseline in one or more of the following:
  - Stability or improvement in net motor function/milestones, including but not limited to, the following validated scales: Hammersmith Infant Neurologic Exam (HINE), Hammersmith Functional Motor Scale Expanded (HFMSE), Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND), Bayley Scales of Infant and Toddler development Third Ed. (BSID-III), 6-minute walk test (6MWT), upper limb module (ULM), motor function measure 32 (MFM32), revised upper limb module (RULM), etc.
  - Stability or improvement in respiratory function tests [e.g., forced vital capacity (FVC), etc.]
  - Reduction in exacerbations necessitating hospitalization and/or antibiotic therapy for respiratory infection in the preceding year/timeframe
  - Stable or increased patient weight (for patients without a gastrostomy tube)
  - Slowed rate of decline in the aforementioned measures

V. Dosage/Administration [1]

Indication	Dose
Spinal Muscular Atrophy	Evrysdi is administered orally once daily. The recommended dosage is determined by age and body weight, as follows: • < 2 months of age: 0.15 mg/kg • 2 months to < 2 years of age: 0.2 mg/kg • 2 years of age and older weighing < 20 kg: 0.25 mg/kg • 2 years of age and older weighing ≥ 20 kg: 5 mg
Evrysdi powder must be constituted to the oral solution by a pharmacist or other healthcare provider prior to dispensing to the patient. Store the constituted oral solution in the original amber bottle to protect from light. Store in a refrigerator at 2°C to 8°C (36°F to 46°F). Discard any unused portion after 64 days.	

VI. Billing Code/Availability Information

HCPCS code:

- J8499 – Prescription drug, oral, non chemotherapeutic, not otherwise specified

NDC:

- Evrysdi 0.75 mg/mL oral solution – 60 mg glass bottle: 50242-0175-xx

VII. References

1. Evrysdi [package insert]. South San Francisco, CA; Genentech, Inc.; May 2022. Accessed May 2022.
2. Wang CH, Finkel RS, Bertini ES, et al. Consensus statement for standard of care in spinal muscular atrophy. J Child Neurol. 2007 Aug;22(8):1027-49.
3. Prior TW, Leach ME, Finanger E. Spinal muscular atrophy. GeneReviews. www.ncbi.nlm.nih.gov/books/NBK1352/ Initial Posting: February 24, 2000; Last Revision: December 3, 2022. Accessed on May 31, 2022.
4. Kichula E, Duong T, Glanzman A, et al. Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND) Feasibility for Individuals with Severe Spinal Muscular Atrophy II (S46.004). Neurology Apr 2018, 90 (15 Supplement) S46.004
5. Hoffman-La Roche. A Study to Investigate the Safety, Tolerability, Pharmacokinetics, 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?term=NCT02908685&draw=2&rank=1. NLM identifier: NCT02908685. Accessed August 13, 2020.
6. Baranello G, Darras BT, Day JW, et al; FIREFISH Working Group. Risdiplam in Type 1 Spinal Muscular Atrophy. N Engl J Med. 2021 Mar 11;384(10):915-923. doi: 10.1056/NEJMoa2009965. Epub 2021 Feb 24.
7. Mercuri E, Deconinck N, Mazzone ES, et al; 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, randomised, placebo-controlled trial. Lancet Neurol. 2022 Jan;21(1):42-52. doi: 10.1016/S1474-4422(21)00367-7.

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9. Servais L, Bertini E, Al-Muhaizea, et al. SMA–THERAPY: P.274 RAINBOWFISH: A study of risdiplam (RG7916) in infants with presymptomatic spinal muscular atrophy (SMA). Neuromuscular Disorders 30 (2020): S127. DOI: https://doi.org/10.1016/j.nmd.2020.08.273.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
G12.0	Infantile spinal muscular atrophy, type I [Werdnig-Hoffmann]
G12.1	Other inherited spinal muscular atrophy
G12.25	Progressive spinal muscle atrophy
G12.8	Other spinal muscular atrophies and related syndromes
G12.9	Spinal muscular atrophy, unspecified

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto Government Benefit Administrators, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC