MEDICAL COVERAGE POLICY	
SERVICE:	**Risdiplam (Evrysdi)**
Policy Number:	**274**
Effective Date:	**11/01/2020**
Last Review:	**09/24/2020**
Next Review Date:	**09/24/2021**

Important note:
Unless otherwise indicated, this policy will apply to all lines of business.
Even though this policy may indicate that a particular service or supply may be considered medically necessary and thus covered, this conclusion is not based upon the terms of your particular benefit plan. Each benefit plan contains its own specific provisions for coverage and exclusions. Not all benefits that are determined to be medically necessary will be covered benefits under the terms of your benefit plan. You need to consult the Evidence of Coverage (EOC) or Summary Plan Description (SPD) to determine if there are any exclusions or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and your plan of benefits, the provisions of your benefits plan will govern. However, applicable state mandates will take precedence with respect to fully insured plans and self-funded non-ERISA (e.g., government, school boards, church) plans. Unless otherwise specifically excluded, Federal mandates will apply to all plans. With respect to Medicare-linked plan members, this policy will apply unless there are Medicare policies that provide differing coverage rules, in which case Medicare coverage rules supersede guidelines in this policy. Medicare-linked plan policies will only apply to benefits paid for under Medicare rules, and not to any other health benefit plan benefits. CMS's Coverage Issues Manual can be found on the CMS website. Similarly, for Medicaid-linked plans, the Texas Medicaid Provider Procedures Manual (TMPPM) supersedes coverage guidelines in this policy where applicable.

SERVICE: Risdiplam (Evrysdi)

PRIOR AUTHORIZATION: Required.

POLICY: Risdiplam (Evrysdi) for the treatment of spinal muscular atrophy (SMA) is considered not medically necessary as a clinical benefit has not been established in published, well-designed, controlled, clinical trials.

Risdiplam (Evrysdi) for the treatment of all other indications is considered experimental, investigational and/or unproven.

OVERVIEW:

Spinal muscular atrophy (SMA) is a severe, progressive, neuromuscular disease caused by deletions and/or loss-of function mutations in the survival of motor neuron 1 (SMN1) gene characterized by the muscle atrophy and, depending on the type of SMA, loss of physical strength and the ability to walk, eat or breathe.

SMN2 is a closely related gene to SMN1 and can compensate for SMN1 deficiency and modify the SMA phenotype. Thus, the phenotype of spinal muscular atrophy (type I, II, III, or IV) is largely related to the number of SMN2 gene copies present.

The incidence of SMA is approximately 4-10 per 100,000 live births with an estimated carrier frequency of 1 in 50. Usual care for SMA is supportive therapy which includes nutrition, physical therapy, and respiratory assistance.

Risdiplam (Evrysdi) 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. Risdiplam leads to an increase in SMN protein.

Risdiplam (Evrysdi) was approved by the FDA based on two unpublished clinical studies, Study 1 (NCT02913482) and Study 2 (NCT02908685). Study 1 was an open-label, 2-part study to investigate the safety and efficacy of risdiplam in patients with Type 1 SMA. Study 2 investigated the safety and efficacy of risdiplam in patients diagnosed with SMA Type 2 or Type 3.

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Risdiplam (Evrysdi) demonstrated tolerability in a phase I dose escalation study of pharmacokinetics and pharmacodynamics. It has no published, phase 2 or 3 peer-reviewed studies evaluating it as treatment of spinal muscular atrophy (SMA).

Classification:

- SMA Type 1 (infantile onset SMA or Werdnig-Hoffmann disease): symptoms are present at birth or by the age of 6 months
- SMA Type 2: onset between the ages of 7 and 18.
- SMA Type 3: onset after 18 months; children can stand and walk independently, although they may require aids.
- SMA Type 4 (adult-onset SMA or Kugelberg-Welander disease): onset in adulthood; are able to walk during their adult years.

MANDATES:

CODES:

Important note:
CODES: Due to the wide range of applicable diagnosis codes and potential changes to codes, an inclusive list may not be presented, but the following codes may apply. Inclusion of a code in this section does not guarantee that it will be reimbursed, and patient must meet the criteria set forth in the policy language.

CPT Codes:	
ICD10 codes:	G12.0 Infantile spinal muscular atrophy, type I [Werdnig-Hoffmann] G12.1 Other inherited spinal muscular atrophy G12.8 Other spinal muscular atrophies and related syndromes G12.9 Spinal muscular atrophy, unspecified
ICD10 Not covered:	
HCPCS Codes	J8499 – Prescription drug, oral, nonchemotherapeutic, NOS [Risdiplam (Evrysdi)]

CMS:

POLICY HISTORY:

Status	Date	Action
New	09/24/2020	New policy

REFERENCES:

The following scientific references were utilized in the formulation of this medical policy. SWHP will continue to review clinical evidence related to this policy and may modify it at a later date based upon the evolution of the published clinical evidence. Should additional scientific studies become available and they are not included in the list, please forward the reference(s) to SWHP so the information can be reviewed by the Medical Coverage Policy Committee (MCPC) and the Quality Improvement Committee (QIC) to determine if a modification of the policy is in order.

1. Evrysdi (risdiplam) [prescribing information]. San Francisco, CA: Genentech, Inc. August 2020.
2. Sturm S, Gunther A, Jaber B, et al. A phase 1 healthy male volunteer single escalating dose study of the pharmacokinetics and pharmacodynamics of risdiplam (RG7916, RO7034067), a SMN2 splicing modifier. Br J Clin Pharmacol (2019) 85 181–193.