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Section:	Prescription Drugs	**Effective Date:**	April 1, 2021
Subsection:	Neuromuscular Agents	**Original Policy Date:**	September 11, 2020
Subject:	Evrysdi	**Page:**	1 of 6

Last Review Date: March 12, 2021

Evrysdi

Description

Evrysdi (risdiplam) for oral solution

Background
Evrysdi (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. Evrysdi was shown to increase exon 7 inclusion in SMN2 messenger ribonucleic acid (mRNA) transcripts and production of full-length SMN protein in the brain (1).

Regulatory Status
FDA-approved indication: Evrysdi is a survival of motor neuron 2 (SMN2) splicing modifier indicated for the treatment of spinal muscular atrophy (SMA) in patients 2 months of age and older (1).

In the clinical studies done for Evrysdi, the patients in these studies had Type I, II, or III SMA. The clinical studies did not include Types 0 and IV (1).

Evrysdi powder must be constituted to the oral solution by a pharmacist prior to dispensing to the patient. The constituted oral solution must be kept in the original amber bottle to protect from light and stored in a refrigerator. Any unused portion should be discarded 64 days after constitution (1).

Evrysdi may cause embryofetal harm when administered to a pregnant woman. Female patients of reproductive potential should be advised to use effective contraception during treatment with Evrysdi and for at least 1 month after the last dose (1).

Multiple tools have been developed in order to determine a baseline motor milestone score for patients with SMA. These assessments can also be utilized to measure improvement, and include: Hammersmith Infant Neurologic Exam (HINE), Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND), Upper Limb Module (ULM), and the Hammersmith Functional Motor Scale (HFMS) / Hammersmith Functional Motor Scale - Expanded (HFMSE) (2-3).

The safety and effectiveness of Evrysdi in pediatric patients below the age of 2 months have not been established (1).

Related policies
Spinraza, Zolgensma

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Evrysdi may be considered **medically necessary** in patients 2 months of age and older with spinal muscular atrophy (SMA) and if the conditions indicated below are met.

Evrysdi may be considered **investigational** in patients less than 2 months of age and for all other indications.

Prior-Approval Requirements

Age 2 months of age and older

Diagnosis

Patient must have the following:

Spinal Muscular Atrophy (SMA)

AND ALL of the following:

a. Diagnosis confirmed by genetic testing showing 5q SMA of **ONE** of the following:

i. Homozygous gene deletion or mutation (e.g., homozygous deletion of exon 7 at locus 5q13)
ii. Compound heterozygous mutation (e.g., deletion of SMN1 exon 7 [allele 1] and mutation of SMN1 [allele 2])

b. Type I, II, or III SMA
c. Obtain a baseline motor milestone score from **ONE** the following assessments:
    i. Hammersmith Infant Neurologic Exam (HINE)
    ii. Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND)
    iii. Upper Limb Module (ULM)
    iv. Hammersmith Functional Motor Scale (HFMS) / Hammersmith Functional Motor Scale - Expanded (HFMSE)
    v. Motor Function Measure 32 (MFM32)
    vi. Revised Upper Limb Module (RULM)
d. **NOT** used in combination with nusinersen
e. Patient has not previously received gene therapy for SMA (see Appendix 1)
f. Female patients of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Evrysdi and for 1 month after the last dose

Prior – Approval *Renewal* Requirements

Age 2 months of age and older

Diagnosis

Patient must have the following:

1. Spinal Muscular Atrophy (SMA) with **ONE** of the following:
    a. Type I SMA
        i. Improvement in motor milestone score from baseline
    b. Type II or III SMA
        ii. Improvement in motor milestone score of **ONE** of the following:
            i. 2 points from baseline for HINE, CHOP-INTEND, ULM, or HFMS/HFMSE
            ii. 1 point from baseline for MFM32 or RULM

AND ALL of the following:

a. **NOT** used in combination with nusinersen
b. Patient has not previously received gene therapy for SMA (see Appendix 1)
c. Female patients of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Evrysdi and for 1 month after the last dose

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity	7 bottles (560 mL) per 84 days
Duration	6 months

Prior – Approval *Renewal* Limits

Quantity	7 bottles (560 mL) per 84 days
Duration	12 months

Rationale

Summary

Evrysdi (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. Evrysdi was shown to increase exon 7 inclusion in SMN2 messenger ribonucleic acid (mRNA) transcripts and production of full-length SMN protein in the brain. The safety and effectiveness of Evrysdi in pediatric patients below the age of 2 months have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate and cost-effective use of Evrysdi while maintaining optimal therapeutic outcomes.

References

1. Evrysdi [package insert]. South San Francisco, CA: Genetech, Inc.; August 2020.
2. Mazzone E, Bianco F, et al. Assessing upper limb function in nonambulant SMA patients: Development of a new module. *Neuromuscular Disorders* 21 (2011) pg: 406-412.
3. De Sanctis, Roberto, et. al. Developmental milestones in type I spinal muscular atrophy. *Neuromuscular Disorders* 26 (2016) pg: 754-759.

Policy History

Date	Action
September 2020	Addition to PA
December 2020	Annual review
March 2021	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 12, 2021 and is effective on April 1, 2021.

Appendix 1 - List of Gene Therapies for SMA

Generic Name	Brand Name
Onasemnogene abeparvovec-xioi	Zolgensma