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Section:	Prescription Drugs	**Effective Date:**	July 1, 2022
Subsection:	Neuromuscular Agents	**Original Policy Date:**	September 11, 2020
Subject:	Evrysdi	**Page:**	1 of 6

Last Review Date: June 16, 2022

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 with spinal muscular atrophy (SMA) and if the conditions indicated below are met.

Evrysdi may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 2 months to 25 years of age

Diagnosis

Patient must have the following:

Spinal Muscular Atrophy (SMA)

AND ALL of the following:

a. Diagnosis confirmed by genetic testing demonstrating bi-allelic mutations in the survival motor neuron 1 (SMN1) gene with **ONE** of the following:
   i. Deletion of both copies of the SMN1 gene **OR**

ii. Pathogenic variant(s) in both copies of the SMN1 gene

b. Patient has **ONE** of the following:
   i. Patient is symptomatic with documentation of a genetic test confirming 2 to 4 copies of the SMN2 gene
   ii. Patient is asymptomatic with documentation of a genetic test confirming 2 to 3 copies of the SMN2 gene
c. Patient is not on permanent ventilator dependence
d. 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)
e. Prescribed by a neurologist, neuromuscular specialist, or pediatrician with expertise in treating SMA
f. **NOT** used in combination with nusinersen
g. Patient has not previously received gene therapy for SMA (see Appendix 1)
h. Patient is not concurrently enrolled in a clinical trial for an experimental therapy for SMA

Prior – Approval *Renewal* Requirements

Age 2 months to 25 years of age

Diagnosis

Patient must have the following:

1. Spinal Muscular Atrophy (SMA)

AND ALL of the following:
   a. Clinically meaningful improvement or stabilization in motor milestones from baseline
   b. **NOT** used in combination with nusinersen

c. Patient has not previously received gene therapy for SMA (see Appendix 1)

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity 7 bottles (560 mL) per 84 days

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

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: Genentech, Inc.; April 2021.
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
March 2022	Annual review and reference update
April 2022	Per FEP: Changed age requirement from 2 months of age and older to 2 months to 25 years of age. Updated genetic testing requirement. Added requirement for prescriber needing to have expertise in treating SMA. Added requirement excluding patients enrolled in clinical trials for SMA. Removed contraception requirement. Removed continuation requirement for 2 or 1 point decrease in motor milestone score for type II and type III SMA. Added less specific continuation requirement for improvement and stabilization in motor milestones from baseline. Changed PA duration to 12 months.
June 2022	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 16, 2022 and is effective on July 1, 2022.

Appendix 1 - List of Gene Therapies for SMA

Generic Name	Brand Name
Onasemnogene abeparvovec-xioi	Zolgensma