Spinal Muscular Atrophy (SMA)
Evrysdi™, Spinraza™

FDA INDICATIONS AND USAGE[1,2]

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. Spinraza™ is a survival motor neuron-2 (SMN2)-directed antisense oligonucleotide indicated for the treatment of spinal muscular atrophy (SMA) in pediatric and adult patients. SMA is a genetic disorder characterized by weakness and wasting (atrophy) in muscles used for movement (skeletal muscles). It is caused by a loss of specialized nerve cells, called motor neurons that control muscle movement.

APPROVAL CRITERIA[1,2,3,4,5,6,7]

1. Patient's age is to FDA label **AND**;
2. Prescribed by or in consultation with a neurologist that specializes in SMA **AND**;
3. Patient has the diagnosis of SMA confirmed by genetic testing for one of the following:
    a. Homozygous gene deletion or mutation (I.E., homozygous deletion of exon 7 at locus 5q13) **OR;**
    b. Compound heterozygous mutation (I.E., deletion of SMN1 exon 7 [allele 1] and mutation of SMN1 [allele 2]) **AND**;
4. Documented baseline motor ability assessment that suggests SMA in at least one of the following:
    a. If the infant is less than one month of age and the prescriber agrees to provide baseline assessments at 1 month of age **OR;**
    b. Hammersmith Infant Neurological Exam Part 2 (HINE-2)1,8,12 (infant to early childhood) **OR;**
    c. Hammersmith Functional Motor Scale Expanded (HFMSE) **OR;**
    d. Bayley Scales of Infant and Toddler Development, Third Edition (BSID-III) [Item 22] **OR;**
    e. Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND)
    f. Revised Upper Limb Module (RULM) test **OR;**
    g. Motor Function Measure-32 Items (MFM-32) **AND**;
5. For Spinraza™, thrombocytopenia and coagulation abnormalities testing and quantitative spot urine protein testing will be performed at baseline and prior to each dose. **AND**;
6. Female patients of reproductive potential only: patient will be advised to use effective contraception during treatment and for at least 1 month after the last dose.

DENIAL CRITERIA [1,2,8]

1. Failure to meet approval criteria **OR;**
2. Concomitant use of Evrysdi™ and Spinraza™ together **OR;**
3. Patient has previously received gene replacement therapy for the treatment of SMA.

CAUTIONS[1,2]

- See package inserts.
  - https://www.gene.com/download/pdf/evrysdi_prescribing.pdf
  - https://www.spinraza.com/content/dam/commercial/spinraza/caregiver/en_us/pdf/spinraza-prescribing-information.pdf

DURATION OF APPROVAL

- Initial Approval: up to 6 months
- Reauthorization Approval: up to 12 months if the prescriber documents that the patient has shown improvement or is stable from baseline

QUANTITY LIMIT

- Evrysdi™
  - 0.2 mg/kg once daily if the individual is < 2 years of age
  - 0.25 mg/kg once daily if the individual is ≥ 2 years of age and weighs < 20 kg
  - 5 mg once daily if the individual is ≥ 2 years of age and weighs ≥ 20 kg
- Spinraza™
  - The recommended dosage is 12 mg (5 mL) per administration
  - Initiate SPINRAZA treatment with 4 loading doses. The first three loading doses should be administered at 14-day intervals. The 4th loading dose should be administered 30 days after the 3rd dose. A maintenance dose should be administered once every 4 months thereafter.
  - HCPCS – J2326

REFERENCES / FOOTNOTES:

1. Evrysdi™ oral solution [prescribing information]. South San Francisco, CA; Genentech/Roche; April 2021.
2. Spinraza™ intrathecal injection [prescribing information]. Cambridge, MA: Biogen; June 2020.
3. Glascock J, Sampson J, Connolly AM, et al. Revised recommendations for the treatment of infants diagnosed with spinal muscular atrophy via newborn screening who

have 4 copies of SMN2. J Neuromuscul Dis. 2020;7(2):97-100.
4. Haataja L, Mercuri E, Regev R, et al. Optimality score for the neurologic examination of the infant at 12 and 18 months of age. J Pediatr. 1999 Aug;135(2 Pt 1):153-61.
5. Glanzman AM, O'Hagen JM, McDermott MP, et al. Validation of the Expanded Hammersmith Functional Motor Scale in spinal muscular atrophy type II and III. J Child Neurol. 2011;26(12):1499-507.
6. O'Hagen JM, Glanzman AM, McDermott MP, et al. An expanded version of the Hammersmith Functional Motor Scale for SMA II and III patients. Neuromuscular disorders : NMD. 2007;17(9-10):693-7.
7. 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. Neuromuscul Disord. 2018;28(2):103-115.
8. Zolgensma® intravenous infusion [prescribing information]. Bannockburn, IL: AveXis; March 2021.