Protocol for Spinal Muscular Atrophy (SMA) Products
Updated April 2024

Updated and approved January 2023

Evrysdi (risdiplam)
Spinraza (nusinersen) – Protocol approved August 2017
Zolgensma (onasemnogene abeparvovec) – Protocol approved July 2019

Background:
Spinal muscular atrophy (SMA) is characterized by degeneration of the anterior horn cells in the spinal cord and motor nuclei in the lower brainstem, which results in progressive muscle weakness and atrophy.

***Evrysdi** is a small molecule SMN2 splicing modifier that binds two sites in SMN2 pre-messenger RNA, thereby correcting the splicing deficit of SMN2, leading to increased levels of full-length SMN protein.*
***Spinraza** is an antisense oligonucleotide (ASO) that modifies splicing of the SMN2 gene to increase production of normal, full-length survival motor neuron protein, which is deficient in SMA*
***Zolgensma** is a recombinant adeno-associated viral vector containing complementary DNA encoding the normal human survival motor neuron protein (SMN1).*

Criteria for Approval:

1. Patient has a diagnosis of spinal muscular atrophy (SMA)
2. Diagnosis is confirmed by one of the following:
    a. Molecular genetic testing showing homozygous deletions of exon 7 of SMN1;
    OR
    b. Compound heterozygous mutation of SMN1 gene
3. Prescribed by or in consultation with a pediatric/adult neurologist or a physician who is an expert in the treatment of SMA
4. Patient's weight will be monitored
5. Medication is prescribed in accordance with Food and Drug Administration (FDA) established indication and dosing regimens or in accordance with medically appropriate off-label indication and dosing according to American Hospital Formulary Service, Micromedex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs (Lexicomp), national guidelines, or other peer-reviewed evidence.

For Evrysdi:
1. Patient will not receive concomitant surviving motor neuron modifying therapy (e.g., Spinraza or Zolgensma)

For Spinraza:

1. Patient will not receive concomitant surviving motor neuron modifying therapy (e.g., Evrysdi or Zolgensma)
2. Lab testing of platelet count to be done at baseline and prior to each dose

For Zolgensma:

1. Patient is less than 2 years of age
2. Patient has bi-allelic mutations in the survival motor neuron (SMN1) gene
3. Patient does not have advanced SMA (e.g., complete paralysis of limbs, permanent ventilator dependence)
4. Baseline anti-AAV9 antibody testing is done, and titers is ≤ 1:50
5. Patient will not receive concomitant surviving motor neuron (SMN) modifying therapy (e.g., Spinraza or Evrysdi)
6. Patient will receive systemic corticosteroid equivalent to oral prednisolone 1mg/kg/day at least 1 day prior to Zolgensma infusion and will continue to receive corticosteroid therapy for at least a total of 30 days (*patient's weight information must be received/documented prior to treatment)*
7. Prescriber attests that patient has not received Zolgensma in their lifetime
8. One dose only will be approved for the treatment of SMA
9. Patient's liver function is assessed prior to administration of Zolgensma and for at least 3 months after infusion

Initial and Renewal Approval:

- **Spinraza:** 12 months
- **Evrysdi:** 12 months
- **Zolgensma:** 4 weeks

Quantity Level Limit:

- **Spinraza:** 12 mg (5 mL) every 4 months
- **Evrysdi:** 2 bottles (120 mg) per 24 days
- **Zolgensma:** one time infusion per lifetime

References:

1. Evrysdi [package insert]. Genentech Inc. South San Francisco, CA 94080; September 2022
2. Spinraza [package insert]. Biogen Inc. Cambridge, MA 02142; June 2020.
3. Zolgensma [package insert] Novartis Gene Therapies, Inc. Bannockburn, IL 60015; August 2022
4. Finkel RS, Kuntz N, Mercuri E, et al. Primary Efficacy and Safety Results from the Phase 3 ENDEAR Study of Nusinersen in Infants Diagnosed with Spinal Muscular Atrophy. Poster presented at: 43rd Annual Congress of the British Paediatric Neurology Association; 11-13 January, 2016; Cambridge, UK.

5. Clinical Pharmacology® Gold Standard Series [Internet database]. Tampa FL. Elsevier 2016. Updated periodically.
6. Bodamer OA. Spinal muscular atrophy. In: UpToDate, Dashe JF (Ed). UpToDate, Waltham, MA. (Accessed November 10, 2022)
7. Keinath MC, Prior DE, Prior TW. Spinal Muscular Atrophy: Mutations, Testing, and Clinical Relevance. Appl Clin Genet. 2021 Jan 25;14:11-25.
8. D'Amico, A., Mercuri, E., Tiziano, F.D. et al. Spinal muscular atrophy. Orphanet J Rare Dis 6, 71 (2011).