

Proposed Addendum to Protocol for Spinal Muscular Atrophy (SMA) Products April 2026

Evrysdi® (risdiplam)

Spinraza® (nusinersen)

Zolgensma® (onasemnogene abeparvovec-xioi)

Itvisma® (onasemnogene abeparvovec-brve)

Protocol applies to FDA approved biosimilars and related indications and dosages

Addendum:

Itvisma was approved November 2025 and is indicated for the treatment of spinal muscular atrophy in adults and pediatric patients 2 years of age and older who have a confirmed mutation in survival motor neuron 1 (SMN1) gene. Itvisma is an adeno-associated virus (AAV) vector-based therapy indicated for single dose injection. It is not indicated for those patients who have previously been treated with Zolgensma.

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.

Criteria for initial approval must meet all of the following:

1. The patient is of the FDA-labeled or compendial approved age
2. The medication requested is prescribed in accordance with a 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
3. For Spinraza and Evrysdi documentation is provided of patient's baseline disease status, for example Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorder (CHOP-INTEND), Hammersmith Infant Neurological Examination (HINE) Section 2 motor milestone score, Revised Hammersmith Scale (RHS), or Upper Limb Module (ULM)
4. The patient does not have any contraindications to therapy
5. Diagnosis is confirmed by one of the following:
 - a. Molecular genetic testing showing homozygous deletions of exon 7 of the SMN1 gene
 - b. Compound heterozygous mutation of SMN1 gene
6. Prescribed by or in consultation with a pediatric/adult neurologist or a physician who is an expert in the treatment of SMA
7. For drugs with weight-based dosing, the patient's most recent weight is provided
8. The requested medication is not used concomitantly with another drug approved for SMA

Spinraza (must meet all of the following):

1. Documentation is provided at baseline and prescriber attests to performing the following laboratory tests prior to each Spinraza dose:
 - a. Platelet count
 - b. Prothrombin time; activated partial thromboplastin time
 - c. Quantitative spot urine protein concentration
2. Spinraza is administered by a healthcare professional experienced in performing lumbar punctures

Zolgensma (must meet all of the following):

1. The patient does not have advanced SMA (e.g., complete paralysis of limbs, permanent ventilator-dependence)
2. Patient will not receive concomitant surviving motor neuron (SMN) modifying therapy (e.g., Spinraza or Evrysdi)
3. Documentation is provided for the following prior to Zolgensma infusion:
 - a. The patient does not have any signs or symptoms of infection
 - b. Liver function (clinical exam, AST, ALT, total bilirubin, albumin, prothrombin time, partial thromboplastin (PTT), and INR)
 - c. Creatinine and complete blood count counts (platelet count)
 - d. Baseline testing for presence of anti-AAV9 antibodies
 - e. Vaccination status is up-to-date
4. Prescriber attests the patient will receive systemic corticosteroid therapy 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
5. Prescriber attests the patient has not received Zolgensma or Itvisma in their lifetime
6. Prescriber attests request for Zolgensma is for single-dose administration per patient's lifetime

Itvisma (must meet all of the following):

1. Documentation is provided for the following prior to Itvisma infusion:
 - a. The patient does not have any signs or symptoms of infection
 - b. Liver function (clinical exam, AST, ALT, total bilirubin, albumin, prothrombin time, partial thromboplastin (PTT), and INR)
 - c. Creatinine and complete blood count counts (hemoglobin and platelet count)
 - d. Baseline testing for presence of anti-AAV9 antibodies
 - e. Vaccination status is up-to-date
2. The patient does not have advanced SMA (e.g., complete paralysis of limbs, permanent ventilator-dependence)
3. Prescriber attests the patient will receive systemic corticosteroid therapy equivalent to oral prednisolone 1mg/kg/day at least 1 day prior to Itvisma infusion and will continue to receive corticosteroid therapy for at least a total of 30 days
4. Prescriber attests the patient has not received Itvisma or Zolgensma in their lifetime
5. Prescriber attests request for Itvisma is for single-dose administration per patient's lifetime
6. Itvisma is being administered by a healthcare professional experienced in performing lumbar punctures

Itvisma has a black box warning for serious liver injury. Zolgensma has a black box warning for serious liver injury and acute liver failure. See full prescribing information for complete boxed warning.

Continuation of therapy (For Evrysdi and Spinraza Requests):

1. Documentation is provided of clinical improvement and/or disease stabilization while on requested drug
2. The patient's most recent weight is provided
3. The requested medication is not used concomitantly with another drug approved for SMA
4. The medication requested is prescribed in accordance with a 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

5. For Spinraza requests:

- a. The medication is administered by a healthcare professional experienced in performing lumbar punctures
- b. Documentation is provided of the following laboratory tests:
 - i. Platelet count
 - ii. Prothrombin time; activated partial thromboplastin time
 - iii. Quantitative spot urine protein concentration

Approval:

- **Spinraza:** 12 months
- **Evrysdi:** 12 months
- **Zolgensma:** 4 weeks
- **Itvisma:** One time only

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
- **Itvisma:**
 - Children 2 years of age and older, including adults: 1.2×10^{14} vector genomes (vg) as a single intrathecal injection; safety and efficacy of IV formulation have not been established.
 - Children 1 year: 1.1×10^{14} vg/kg as a single IV dose; safety and efficacy of intrathecal formulation have not been established.
 - Infants: 1.1×10^{14} vector genomes (vg)/kg as a single IV dose; safety and efficacy of intrathecal formulation have not been established.
 - Term neonates: 1.1×10^{14} vector genomes (vg)/kg as a single IV dose; safety and efficacy of intrathecal formulation have not been established.
 - Premature neonates: Delay onasemnogene abeparvovec IV infusion until term gestational age is reached; safety and efficacy of intrathecal formulation have not been established.

References:

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2. Spinraza [package insert]. Biogen. Cambridge, MA. April 2024.
3. Zolgensma [package insert] Novartis Gene Therapies, Inc. Bannockburn, IL. February 2025.
4. Itvisma [package insert]. Novartis Gene Therapies, Inc. Bannockburn, IL. November 2025.
5. 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.
6. Clinical Pharmacology® Gold Standard Series [Internet database]. Tampa FL. Elsevier 2016. Updated periodically.
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9. D'Amico, A., Mercuri, E., Tiziano, F.D. et al. Spinal muscular atrophy. *Orphanet J Rare Dis* 6, 71 (2011).
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