UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Spinal Muscular Atrophy – Gene Therapy – Itvisma Utilization Management Medical Policy

- Itvisma® (onasemnogene abeparvovec-brve intrathecal injection – Novartis)

REVIEW DATE: 07/22/2026

OVERVIEW

Itvisma, an adeno-associated virus vector-based gene therapy, is indicated for the treatment of **spinal muscular atrophy** with confirmed mutation in the survival motor neuron 1 (SMN1) gene in adult and pediatric patients ≥ 2 years of age.[1]

Disease Overview

Spinal muscular atrophy is a genetic, autosomal recessive, progressive, neuromuscular disorder caused by biallelic deletions or pathogenic variants in the SMN1 gene which can be identified by genetic testing.[2-5] The subsequent reduced levels of survival motor neuron (SMN) protein impacts brainstem and spinal cord motor neurons. The estimated incidence in the US is one in 11,000 patients.[3] The phenotypic expression of the disease is generally impacted by the survival motor neuron 2 (SMN2) gene copy number.[3-5] Patients with a higher number of SMN2 gene copies often have less severe disease with milder progression. Table 1 describes disease types. Of note, various motor ability assessments and different functional motor scales are used in clinical practice to characterize impairment in patients with spinal muscular atrophy. When motor neuron function is lost, it cannot be regained, which greatly impacts patients who have experienced progression (e.g., patients with complete paralysis of limbs or permanent ventilator dependence). A different manner of patient categorization classifies the three most common types as "non-sitters", "sitters", and "walkers".

Table 1. Types of Spinal Muscular Atrophy.[4,5]

	Age at Onset	Features/Clinical Presentation*	Lifespan*	SMN2 Gene Copy Number
Type 0 (< 1% of patients)	Birth	Severe hypotonia and weakness with respiratory failure at birth. There is no achievement of motor milestones.	A few weeks to days (< 6 months)	1
Type 1 (50% of patients)	< 6 months	Poor muscle tone and lack of movement. Respiratory assistance may be needed. Patients are never able to sit without support.	< 2 years	1 to 2 for 80% of patients
Type 2 (30% of patients)	6 to 18 months	Patients are able to sit. However, patients are unable to walk or stand without assistance.	Close to normal	2 to 3 for over 90% of patients
Type 3 (10% to 20% of patients)	≥ 18 months	Walks independently but may lose this ability as the disease progresses. There is loss of motor skills.	Normal	3 to 5 for most patients
Type 4 (< 1% of patients)	> 18 years	Independent walking. Fatigue and proximal muscle weakness.	Normal	4 for 75% of patients; 5 or 6 for 25% of patients

* With supportive care only; SMN2 – Survival motor neuron 2.

Clinical Efficacy

The STEER trial was a double-blind, sham-controlled, Phase III study that evaluated the efficacy of Itvisma in 126 treatment-naïve patients ≥ 2 to < 18 years of age with spinal muscular atrophy.[1,6] Patients involved in the trial were able to sit, but never able to walk independently.[1] Randomization was in a 3:2 ratio in which patients received Itvisma by single lumbar intrathecal injection or sham procedure. The mean patient age was 6 years (range 2 years to 17 years). Main races were Asian (59%), White (11%) and Black or

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African American (7%). Most patients (97%) had confirmed bi-allelic deletion (0 copies) of the SMN1 gene. The highest motor function ever achieved were as follows: 52% of patients sitting without support; 26% standing with assistance; 19% walking with assistance; and 2% standing independently.[1] Most patients had three survival motor neuron 2 (SMN2) gene copies (94.4%); 4.0% of patients had two SMN2 gene copies and 1.6% of patients had ≥ 4 SMN2 gene copies.[6] The presence of an elevated baseline serum anti-adeno-associated virus serotype 9 antibody titer (i.e., > 1:50) at screening prevented participation, as well as a platelet count at less than the lower limit of normal. Patients with an infectious process or febrile illness within 30 days prior to the treatment day were excluded. Those positive for human immunodeficiency virus, hepatitis B, or hepatitis C could not participate.[6] At baseline, the mean Hammersmith Functional Motor Scale Expanded (HFMSE) total score, which evaluates motor function in patients with spinal muscular atrophy who are ambulatory, was around 18 (range 1 to 42.5).[1] Of note, the maximum HFMSE score is 66 with higher scores indicative of better function. The primary endpoint was the change from baseline in the HFMSE total score at the end of follow-up, defined as the average of the Week 48 and Week 52 assessment for Itvisma compared with sham. The mean change from baseline in the HFMSE total score at the end of follow-up was 2.39 for Itvisma (n = 75) and 0.51 for sham (n = 51) [treatment difference 1.88].

Guidelines

The Spinal Muscular Atrophy Newborn Screening Multidisciplinary Working Group developed a treatment algorithm in 2018 for infants who have positive results from a newborn screening test for spinal muscular atrophy.[7] Spinal muscular atrophy Types 1 and 2 comprise a large majority of cases and account for many patients who screen positively for spinal muscular atrophy with three or fewer SMN2 gene copies. Immediate treatment is recommended in patients with two or three SMN2 gene copies. Treatment recommendations for patients who screen positive for spinal muscular atrophy and have only one SMN2 gene copy are more complicated. It is likely that patients with only one SMN2 gene copy will likely be symptomatic at birth and the physician should determine if treatment is warranted.[7] In 2020, the Working Group updated recommendations that infants diagnosed with spinal muscular atrophy via newborn screening with four SMN2 gene copies should receive immediate treatment.[8] Also, patients with five (or more) SMN2 gene copies should be observed and screened for symptoms.

Dosing

The recommended dose of Itvisma is 1.2×10^{14} vector genomes by intrathecal bolus injection over approximately 1 to 2 minutes.[1] Itvisma is for single-dose injection; do not re-administer Itvisma.

Safety

Itvisma has a Boxed Warning regarding acute serious liver injury.[1] Acute serious liver injury and elevated aminotransferases can occur with Itvisma. Patients with preexisting liver impairment may be at higher risk. Prior to intrathecal injection, evaluate liver function in all patients by clinical examination and laboratory testing (e.g., aspartate aminotransferase, alanine aminotransferase, prothrombin time, total bilirubin). Before administration of Itvisma, it is recommended to examine a creatinine level, as well as obtain a complete blood count (including hemoglobin and platelet count).

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Itvisma. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Because of the specialized skills required for evaluation and diagnosis of patients treated with Itvisma as well as the specialized training required for administration of Itvisma, approval requires Itvisma to be prescribed by a physician who has consulted with or who specializes in the condition. All approvals are provided for one-time (per lifetime) as a single dose. The approval duration is 90 days to allow for an adequate timeframe to prepare and

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administer one dose of therapy. If claims history is available, verification is required for certain criteria as noted by **[verification in claims history required]**. All reviews (approvals and denials) will be forwarded to the Medical Director for evaluation.

Documentation: Documentation is required for the use of Itvisma as noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to chart notes, laboratory results, medical test results, claims records, prescription receipts, and/or other information. All documentation must include patient-specific identifying information.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Itvisma is recommended in those who meet the following criteria:

FDA-Approved Indication

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1. **Spinal Muscular Atrophy – Treatment.** Approve for a one-time (per lifetime) single dose if the patient meets ALL of the following (A, B, C, D, E, G, H, I, J, K, L, M, N, and O):
   - **A)** Patient is ≥ 2 years to < 18 years of age; AND
   - **B)** Patient has not received Itvisma or Zolgensma (onasemnogene abeparvovec-xioi intravenous infusion) in the past **[verification in claims history required]**; AND
     Note: If no claim for Itvisma or Zolgensma is present (or if claims history is not available), the prescribing physician confirms that the patient has not previously received Itvisma or Zolgensma.
   - **C)** Patient has had a genetic test confirming the diagnosis of spinal muscular atrophy with pathogenic variants in the survival motor neuron 1 (SMN1) gene **[documentation required]**; AND
     Note: Pathogenic variants may include homozygous deletion, compound heterozygous mutation, or a variety of other rare mutations.
   - **D)** Patient meets ONE of the following (i or ii):
     - **i.** Patient has two or three survival motor neuron 2 (SMN2) gene copies **[documentation required]**; OR
     - **ii.** Patient meets BOTH of the following (a and b):
       - **a)** Patient has four SMN2 gene copies **[documentation required]**; AND
       - **b)** The number of SMN2 gene copies has been determined by a quantitative assay capable of distinguishing between four SMN2 gene copies and five or greater SMN2 gene copies; AND
   - **E)** Baseline anti-adeno-associated virus serotype 9 (AAV9) antibody titers are ≤ 1:50 **[documentation required]**; AND
   - **F)** Patient has undergone liver function testing within the past 30 days AND meets ALL of the following (i, ii, iii, and iv):
     - **i.** Alanine aminotransferase levels are ≤ 2 times the upper limit of normal **[documentation required]**; AND
     - **ii.** Aspartate aminotransferase levels are ≤ 2 times the upper limit of normal **[documentation required]**; AND
     - **iii.** Total bilirubin levels are ≤ 2 times the upper limit of normal **[documentation required]**; AND
     - **iv.** Prothrombin time results are ≤ 2 times the upper limit of normal **[documentation required]**; AND
   - **G)** Patient has undergone a renal function assessment within the past 30 days AND has a creatinine level < 1.0 mg/dL **[documentation required]**; AND

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H) A complete blood count has been obtained within the past 30 days AND the patient meets BOTH of the following (i and ii):
  i. White blood cell count is ≤ 20,000 cells per mm^3 **[documentation required]**; AND
  ii. Hemoglobin level is within the normal reference range **[documentation required]**; AND
  Note: Reference ranges for hemoglobin levels vary among laboratories and are dependent upon age and gender.

I) Patient does not have hepatitis B; AND

J) Patient does not have hepatitis C; AND

K) Patient is not human immunodeficiency virus positive; AND

L) For a patient currently receiving or who has received prior treatment with Spinraza (nusinersen intrathecal injection), the prescribing physician confirms that further therapy with Spinraza will be discontinued; AND

M) For a patient currently receiving or who has received prior treatment with Evrysdi (risdiplam oral solution and tablets), the prescribing physician confirms that further therapy with Evrysdi will be discontinued; AND

N) The medication is prescribed by a physician who has consulted with or who specializes in the management of patients with spinal muscular atrophy and/or neuromuscular disorders; AND

O) If criteria A through N are met, approve one dose of Itvisma to provide for a one-time (per lifetime) single dose of 1.2 x 10^{14} vector genomes by intrathecal injection.

Dosing. The recommended dose of Itvisma is one-time (per lifetime) as a single-dose intrathecal injection of 1.2 x 10^{14} vector genomes.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Itvisma is not recommended in the following situations:

1. **Patient has Complete Paralysis of All Limbs.** Data are needed to determine if this patient population would derive benefits from Itvisma.

2. **Patient has Permanent Ventilator Dependence.** Data are needed to determine if this patient population would derive benefits from Itvisma.

3. **Prior Receipt of Gene Therapy.** Itvisma has not been studied in patients who previously received gene therapy.

4. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	01/14/2026
Selected Revision	**Spinal Muscular Atrophy – Treatment:** The requirement that the patient has hemoglobin levels between 8 g/dL and 18 g/dL was changed to the hemoglobin level is within the normal reference range. A Note was added that reference ranges for hemoglobin levels vary among laboratories and are dependent upon age and gender.	01/28/2026
Selected Revision	**Spinal Muscular Atrophy – Treatment:** The approval duration was changed from 30 days to 90 days. Verification required was removed from the requirement to approve one dose of Itvisma to provide for a one-time (per lifetime) single dose of 1.2×10^{14} vector genomes by intrathecal injection.	02/04/2026
Early Annual Revision	No criteria changes.	07/22/2026

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