CARECONTINUUM™

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Spinal Muscular Atrophy – Isembyld Utilization Management Medical Policy
- Isembyld™ (apitegromab-mstn intravenous infusion – Scholar Rock)

REVIEW DATE: 09/16/2026

OVERVIEW

Isembyld, a recombinant monoclonal antibody targeting proforms of myostatin, is indicated for the treatment of spinal muscular atrophy in adults and pediatric patients ≥ 2 years of age who are currently receiving a survival motor neuron 2 (SMN2) targeted treatment.[1]

Disease Overview

Spinal muscular atrophy is a genetic, autosomal recessive, progressive, neuromuscular disorder caused by biallelic deletions or pathogenic variants in the survival motor neuron 1 (*SMN1*) gene which can be identified by genetic testing.[2-5] The subsequent reduced levels of survival motor neuron (SMN) protein impact brainstem and spinal cord motor neurons. The estimated incidence in the US is one in 11,000 individuals.[3] The phenotypic expression of the disease is impacted by the *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 the 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/Motor Milestones*	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 or 2 for 80% of patients
Type 2 (30% of patients)	6 months to 18 months	Patients are able to sit. However, patients are unable to walk or stand without assistance.	Close to normal	2 or 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 (without use of FDA-approved therapies for spinal muscular atrophy); SMN2 – Survival motor neuron 2.

Clinical Efficacy

Isembyld was evaluated in one multinational, double-blind, placebo-controlled, 52-week, Phase III pivotal trial called SAPPHIRE (published) [n = 188] that evaluated the efficacy of Isembyld in nonambulatory patients 2 years to 21 years of age with Type 2 or Type 3 5q spinal muscular atrophy receiving Spinraza®

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(nusinersen intrathecal injection) or Evrysdi® (risdiplam tablets and oral solution).[1,6] Patients 2 years to 12 years of age (n = 156) were randomly assigned to receive Isembyld 10 mg/kg by intravenous (IV) infusion once every 4 weeks (n = 53), Isembyld 20 mg/kg IV once every 4 weeks (n = 53), or placebo (n = 50). Patients 13 years to 21 years of age (n = 32) were randomized (2:1) to receive Isembyld 20 mg/kg IV once every 4 weeks (n = 22) or placebo (n = 10).[1] Patients in all groups were on background therapy with either Spinraza or Evrysdi. The primary efficacy endpoint was the mean change from baseline at 1 year in the Hammersmith Functional Motor Scale Expanded (HFMSE) which evaluates motor function in patients with spinal muscular atrophy. The scale is comprised of 33 scored activities that provide objective information on motor ability and clinical progression (e.g., ability to site unassisted, stand, walk). The maximum score is 66 which reflects better motor function. In patients 2 years to 12 years of age, the mean HFMSE total score was 26 and approximately 21 for patients 13 years to 21 years of age. In children 2 years to 12 years of age, at the recommended dose of 10 mg/kg IV once every 4 weeks (n = 53), Isembyld (added to Evrysdi or Spinraza) led to a 1.0 point increase at 1 year on the HFMSE compared with a decrease of -1.2 points for placebo (n = 50) [P = 0.0121]. In this population, the proportion of patients with a change from baseline in the HFMSE total score ≥ 3 at 1 year was 34.2% in the Isembyld 10 mg/kg IV once every 4 weeks group (n = 53) compared with 13.5% in patients given placebo (n = 50) [odds ratio for overall response 3.8; P = 0.0125]. Efficacy evaluations in patients 13 years to 21 years of age receiving Isembyld 20 mg/kg IV once every 4 weeks (twice the recommended dose) [n = 22] showed a trend consistent with patients 2 years to 12 years of age who were given Isembyld 10 mg/kg IV once every 4 weeks.

Dosing

The recommended Isembyld dose is 10 mg/kg given once every 4 weeks as an IV infusion over approximately 60 minutes to 120 minutes.[1]

Guidelines

Isembyld is not addressed in guidelines. The Spinal Muscular Atrophy Newborn Screening Multidisciplinary Working Group is comprised of clinicians and geneticists with expertise in spinal muscular atrophy who 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 is more complicated.[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.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Isembyld. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Due to the specialized skills required for evaluation and diagnosis of patients treated with Isembyld as well as the monitoring required for adverse events and long-term efficacy, approval requires Isembyld to be prescribed by a physician who has consulted with or who specializes in the condition. If claims history is available, verification is required in certain criteria as noted by **[verification in claims history required]**. All reviews will be forwarded to the Medical Director for evaluation.

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Documentation: Documentation is required where 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 Isembyld is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Spinal Muscular Atrophy – Treatment.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 4 months if the patient meets ALL of the following (i, ii, iii, iv, v, vi and vii):
     - **i.** Patient is greater than or equal to 2 years of age; AND
     - **ii.** Baseline motor ability assessment that suggest spinal muscular atrophy (based on age, motor ability, and development) has been performed from ONE of the following exams (a, b, c, d, e, f, or g) **[documentation required]**:
       - **a)** Bayley Scales of Infant and Toddler Development; OR
       - **b)** Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND); OR
       - **c)** Hammersmith Functional Motor Scale Expanded (HFMSE); OR
       - **d)** Hammersmith Infant Neurological Exam Part 2 (HINE-2); OR
       - **e)** Motor Function Measure-32 Items (MFM-32); OR
       - **f)** Revised Upper Limb Module (RULM) test; OR
       - **g)** World Health Organization motor milestone scale; AND
     - **iii.** Patient has had a genetic test confirming the diagnosis of spinal muscular atrophy with bi-allelic 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.
     - **iv.** Patient meets ONE of the following (a or b):
       - **a)** Patient has two or three survival motor neuron 2 (*SMN2*) gene copies **[documentation required]**; OR
       - **b)** Patient meets BOTH of the following [(1) and (2)]:
         - **(1)** Patient has four survival motor neuron 2 (*SMN2*) gene copies **[documentation required]**; AND
         - **(2)** Patient has objective signs consistent with spinal muscular atrophy Types 1, 2, or 3 **[documentation required]**; AND
     - **v.** Patient has not received Zolgensma (onasemnogene abeparvovec-xioi intravenous infusion) or Itvisma (onasemnogene abeparvovec-brve intrathecal injection) in the past **[verification in claims history required]**; AND
       Note: If no claim for Zolgensma or Itvisma is present (or if claims history is not available), the prescribing physician confirms that the patient has not previously received Zolgensma or Itvisma.

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vi. Patient is using Isembyld in combination with one survival motor neuron 2 (SMN2)-targeted treatment; AND
Note: Examples of SMN2-targeted treatments include Spinraza (nusinersen intrathecal injection) and Evrysdi (risdiplam tablets and oral solution).

vii. 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; OR

B) Patient Currently Receiving Isembyld Therapy. Approve for 1 year if the patient meets ALL of the following (i, ii, iii, iv, v, and vi):

i. Patient is greater than or equal to 2 years of age; AND

ii. Patient has had a genetic test confirming the diagnosis of spinal muscular atrophy with bi-allelic pathogenic variants in the survival motor neuron 1 (*SMN1*) gene; AND
Note: Pathogenic variants may include homozygous deletion, compound heterozygous mutation, or a variety of other rare mutations.

iii. Patient meets ONE of the following (a or b):

a) Patient has two or three survival motor neuron 2 (*SMN2*) gene copies; OR

b) Patient meets BOTH of the following [(1) and (2)]:

(1) Patient has four survival motor neuron 2 (*SMN2*) gene copies; AND

(2) Patient has objective signs consistent with spinal muscular atrophy Types 1, 2, or 3; AND

iv. Patient is using Isembyld in combination with one survival motor neuron 2 (SMN2)-targeted treatment; AND
Note: Examples of SMN2-targeted treatments include Spinraza (nusinersen intrathecal injection) and Evrysdi (risdiplam tablets and oral solution).

v. 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

vi. Patient must meet ONE of the following (a or b):

a) Patient must have had a positive clinical response (for example, improvement or stabilization) from pretreatment baseline status with Isembyld from ONE of the following [(1), (2), (3), (4), (5), (6), or (7)] **[documentation required]**:

(1) Bayley Scales of Infant and Toddler Development; OR

(2) Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND); OR

(3) Hammersmith Functional Motor Scale Expanded (HFMSE); OR

(4) Hammersmith Infant Neurological Exam Part 2 (HINE-2); OR

(5) Motor Function Measure-32 Items (MFM-32); OR

(6) Revised Upper Limb Module (RULM) test; OR

(7) World Health Organization motor milestone scale; OR

b) According to the prescribing physician, the patient has responded to Isembyld and continues to benefit from ongoing Isembyld therapy by the most recent physician monitoring/assessment tools **[documentation required]**.
Note: Examples include pulmonary function tests showing improvement, bulbar function test results suggest benefits, reduced need for respiratory support, decrease in the frequency of respiratory infections or complications, and/or prevention of permanent assisted ventilation.

Dosing. Approve 10 mg/kg given by intravenous infusion not more frequently than once every 4 weeks.

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CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Isembyld is not recommended in the following situations:

1. **Patient has Complete Paralysis of All Limbs.** Data are needed to determine if this patient population with advanced spinal muscular atrophy would derive benefits from Isembyld.

2. **Patient has Permanent Ventilator Dependence.** Data are needed to determine if this patient population with advanced spinal muscular atrophy would derive benefits from Isembyld.

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

REFERENCES

1. Isembyld™ intravenous infusion [prescribing information]. Cambridge, MA: Scholar Rock; September 2026.
2. Schroth M, Deans J, Arya K, et al. Spinal muscular atrophy update in best practices. Recommendations for diagnosis considerations. *Neurology*. 2024;14:e200310.
3. Yeo CJJ, Tizzano EF, Darras BT. Challenges and opportunities in spinal muscular atrophy therapeutics. *Lancet Neurol*. 2024;23:205-218.
4. Ramdas S, Oskoui M, Servais L. Treatment options in spinal muscular atrophy: a pragmatic approach for clinicians. *Drugs*. 2024;84:747-762.
5. Prior TW, Leach ME, Finanger E. Spinal Muscular Atrophy. 2000 Feb 24 [Updated 2026 Feb 12]. In: Adam MP, Bick S, Mirzaa GM, et al, editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2026. Available at: https://www.ncbi.nlm.nih.gov/books/NBK1352/pdf/Bookshelf_NBK1352.pdf. Accessed on September 15, 2026.
6. Crawford TO, Servais L, Mercuri E, et al, for the SAPPHIRE study group. The safety and efficacy of apitegromab in nonambulatory type 2 or type 3 spinal muscular atrophy (SAPPHIRE): a phase 3, double-blind, randomized, placebo-controlled trial. *Lancet Neurol*. 2025;24:727-739.
7. Glascock J, Sampson J, Haidet-Phillips A, et al. Treatment algorithm for infants diagnosed with spinal muscular atrophy through newborn screening. *J Neuromuscul Dis*. 2018;5:145-158.
8. 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.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	09/16/2026

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