Clinical Policy Title:	onasemnogene abeparvovec-xioi
Policy Number:	RxA.577
Drug(s) Applied:	Zolgensma®
Original Policy Date:	03/06/2020
Last Review Date:	10/19/2023
Line of Business Policy Applies to:	All lines of business (except Medicare)

Criteria

I. Initial Approval Criteria

A. Spinal Muscular Atrophy (must meet all):

1. Diagnosis of SMA Type I with onset of symptoms prior to 6 months of age;
2. Genetic testing confirming 1, 2, or 3 copies of SMN2 gene;
3. Genetic testing confirms the presence of one of the following (a, b, or c):
   a. Homozygous deletions of SMN1 gene (e.g., absence of the SMN1 gene);
   b. Homozygous mutation in the SMN1 gene (e.g., biallelic mutations of exon 7);
   c. Compound heterozygous mutation in the SMN1 gene (e.g., deletion of SMN1 exon 7 (allele 1) and mutation of SMN1 (allele 2));
4. Prescribed by or in consultation with a neurologist;
5. Age < 2 years;
6. Documentation of one of the following baseline scores(a or b):
   a. Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorder (CHOP-INTEND) score;
   b. Hammersmith Infant Neurological Examination (HINE) Section 2 motor milestone score;
7. Documentation of both of the following (a and b):
   a. Baseline laboratory tests demonstrating Anti-AAV9 antibody titers ≤ 1:50 as determined by ELISA binding immunoassay;
   b. Baseline liver function test, platelet counts, and troponin-I;
8. Member has not been previously treated with Zolgensma®;
9. Zolgensma® is not prescribed concurrently with Spinraza® or Evrysdi®;
10. If the member is currently on Spinraza®, must meet the following (a and b):
    a. Provider must submit evidence of clinical deterioration (e.g., sustained decrease in CHOP-INTEND score over a period of 3 to 6 months);
    b. Documentation of provider attestation of clinical deterioration and that Spinraza® will be discontinued upon the initiation of Zolgensma®;
11. If the member is currently on Evrysdi®, must meet the following (a and b):
    a. Provider must submit evidence of clinical deterioration (e.g., sustained decrease in CHOP-INTEND score over a period of 3 to 6 months);
    b. Documentation of provider attestation of clinical deterioration and Evrysdi® discontinuation;
12. Member does not have an active viral infection;
13. Total dose does not exceed 1.1 x 10^{14} vector genomes (vg) per kilogram (kg).

Approval Duration

Commercial: 28 days (one time infusion per lifetime)

Medicaid: 28 days (one time infusion per lifetime)

II. Continued Therapy Approval

A. Spinal Muscular Atrophy

1. Re-authorization is not permitted.

Approval Duration

Commercial: Not applicable

Medicaid: Not applicable

References

1. Mendell JR, Al-zaidy S, Shell R, et al. Single-Dose Gene-Replacement Therapy for Spinal Muscular Atrophy. N Engl J Med. 2017;377(18):1713-1722. Available at: https://pubmed.ncbi.nlm.nih.gov/29091557/. Accessed July 28, 2022.
2. ClinicalTrials.gov [Internet]. Identifier: NCT03421977, Long-Term Follow-up Study for Patients From AVXS-101-CL-101 (START). https://clinicaltrials.gov/ct2/show/NCT03421977. Accessed July 28, 2022.
3. ClinicalTrials.gov [Internet]. Identifier: NCT00381729, Study of Intrathecal Administration of AVXS-101 for Spinal Muscular Atrophy (STRONG). https://clinicaltrials.gov/ct2/show/NCT03381729. Accessed July 28, 2022.
4. ClinicalTrials.gov [Internet]. Identifier: NCT03505099, Pre-Symptomatic Study of Intravenous AVXS-101 in Spinal Muscular Atrophy (SMA) for Patients With Multiple Copies of SMN2 (SPR1NT). https://clinicaltrials.gov/ct2/show/NCT03505099. Accessed July 28, 2022.
5. ClinicalTrials.gov [Internet]. Identifier: NCT03306277, Single-Dose Gene Replacement Therapy Clinical Trial for Patients With Spinal Muscular Atrophy Type 1 (STR1VE). https://clinicaltrials.gov/ct2/show/NCT03306277. Accessed July 28, 2022.
6. ClinicalTrials.gov [Internet]. Identifier: NCT03461289, Single-Dose Gene Replacement Therapy Clinical Trial for Patients With Spinal Muscular Atrophy Type 1 (STRIVE-EU). https://clinicaltrials.gov/ct2/show/NCT03461289. Accessed July 28, 2022.
7. Institute for Clinical and Economic Review (ICER): Final Evidence Report –Zolgensma® and Spinraza®. https://icer.org/news-insights/press-releases/icer-issues-final-report-on-sma/. Accessed July 28, 2022.
8. 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. Available at: https://pubmed.ncbi.nlm.nih.gov/29290580/. Accessed July 28, 2022.
9. Finkel RS, Mercuri E, Meyer OH, et al. Diagnosis and management of spinal muscular atrophy: Part 2: Pulmonary and acute care; medications, supplements and immunizations; other organ systems; and ethics. Neuromuscul Disord. 2018;28(3):197-207. Available at: https://pubmed.ncbi.nlm.nih.gov/29305137/. Accessed July 28, 2022.
10. Cobben JM, de Visser M, Scheffer H, et al. Confirmation of clinical diagnosis in requests for prenatal prediction of SMA type I. J Neurol Neurosurg Psychiatry 1993; 56: 319-21. Available at: https://pubmed.ncbi.nlm.nih.gov/8459253/. Accessed July 28, 2022.
11. Maitre NL, Chorna O, Romeo DM, and Guzzetta A. Implementation of the Hammersmith Infant Neurological Examination in a High-Risk Infant Follow-Up Program. Pediatric Neurology 2016; 65:31-38. Available at: https://pubmed.ncbi.nlm.nih.gov/27765470/. Accessed July 28, 2022.
12. Finkel RS, McDermott MP, Kaufmann P, et al. Observational study of spinal muscular atrophy type I and implications for clinical trials. Neurology 2014; 83: 810-7. Available at: https://pubmed.ncbi.nlm.nih.gov/25080519/. Accessed July 28, 2022.
13. De Sanctis R, Coratti G, Pasternak A, et al. Developmental milestones in type I spinal muscular atrophy. Neuromuscul Disord 2016; 26: 754-9. Available at: https://pubmed.ncbi.nlm.nih.gov/27769560/. Accessed July 28, 2022.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	03/06/2020

Policy was reviewed: 1. Clinical Policy title updated 2. Line of policy business applies to was updated to All lines of business 3. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 4. References were reviewed and updated. 5. Clarified I.A.10.b.	12/03/2020	12/07/2020
Policy was reviewed: 1. Generic name for the drug was updated from “onasemnogene abeparvovec” to “onasemnogene abeparvovec-xioi”. 2. References were reviewed and updated.	10/9/2021	12/7/2021
Policy was reviewed: 1. Initial Approval Criteria, I.A.7.c: Updated to remove prior documentation criteria "Member does not have advanced SMA (e.g., complete paralysis of limbs, permanent ventilator dependence, tracheostomy, non-invasive ventilation beyond the use for sleep)." 2. Initial Approval Criteria, I.A.9: Updated combination therapy criteria to include new drug Evrysdi®. 3. Initial Approval Criteria, I.A.11: Updated to include new documentation criteria If the member is currently on Evrysdi®, must meet the following (a and b): a. Provider must submit evidence of clinical deterioration (e.g., sustained decrease in CHOP-INTEND score over a period of 3 to 6 months); b. Documentation of provider attestation of clinical deterioration and Evrysdi® discontinuation. 4. References were reviewed and updated.	7/28/2022	10/19/2022
Policy was reviewed.	10/19/2023	10/19/2023