zolgensma®
(onasemnogene abeparvovec-xioi)
suspension for intravenous infusion

Pathways to Approval for Insurance Coverage

Please see Indication and Important Safety Information on page 3 and the accompanying Full Prescribing Information, including Boxed Warning for Serious Liver Injury and Acute Liver Failure.

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Indication and Important Safety Information

zolgensma® (onasemnogene abeparvovec-xioi) suspension for intravenous infusion

Indication

ZOLGENSMA is an adeno-associated virus (AAV) vector-based gene therapy indicated for the treatment of pediatric patients less than 2 years of age with spinal muscular atrophy (SMA) with bi-allelic mutations in the *survival motor neuron 1* (*SMN1*) gene.

Limitations of Use

The safety and effectiveness of repeat administration or the use in patients with advanced SMA (e.g., complete paralysis of limbs, permanent ventilator dependence) has not been evaluated with ZOLGENSMA.

Important Safety Information

BOXED WARNING: Serious Liver Injury and Acute Liver Failure

Cases of acute liver failure with fatal outcomes have been reported. Acute serious liver injury, acute liver failure, and elevated aminotransferases can also occur with ZOLGENSMA. Patients with preexisting liver impairment may be at higher risk. Prior to infusion, assess liver function of all patients by clinical examination and laboratory testing. Administer systemic corticosteroid to all patients before and after ZOLGENSMA infusion. Continue to monitor liver function for at least 3 months after infusion, and at other times as clinically indicated. If acute serious liver injury or acute liver failure is suspected, promptly consult a pediatric gastroenterologist or hepatologist.

WARNINGS AND PRECAUTIONS

Systemic Immune Response

Patients with underlying active infection, either acute or chronic uncontrolled, could be at an increased risk of serious systemic immune response. Administer ZOLGENSMA to patients who are clinically stable in their overall health status (e.g., hydration and nutritional status, absence of infection). Postpone ZOLGENSMA in patients with infections until the infection has resolved and the patient is clinically stable.

Thrombocytopenia

Transient decreases in platelet counts, some of which met the criteria for thrombocytopenia, were typically observed within the first two weeks after ZOLGENSMA infusion. Monitor platelet counts before ZOLGENSMA infusion and on a regular basis for at least 3 months afterwards.

Thrombotic Microangiopathy

Cases of thrombotic microangiopathy (TMA) were reported to occur generally within the first two weeks after ZOLGENSMA infusion. TMA can result in life-threatening or fatal outcomes. Obtain baseline creatinine and complete blood count before ZOLGENSMA infusion. Following infusion, monitor platelet counts closely as well as other signs and symptoms of TMA. Consult a pediatric hematologist and/or pediatric nephrologist immediately to manage as clinically indicated.

Elevated Troponin-I

Increases in cardiac troponin-I levels were observed following ZOLGENSMA infusion. Monitor troponin-I before ZOLGENSMA infusion and on a regular basis for at least 3 months afterwards. Consider consultation with a cardiologist if troponin elevations are accompanied by clinical signs or symptoms.

AAV Vector Integration and Risk of Tumorigenicity

There is a theoretical risk of tumorigenicity due to integration of AAV vector DNA into the genome. Cases of tumor have been reported in patients who received ZOLGENSMA post-approval; information on the cases is limited and causal relationship cannot be established. Report cases of tumor development in patients who received ZOLGENSMA to Novartis Gene Therapies, Inc. at 1-833-828-3947.

ADVERSE REACTIONS

The most commonly observed adverse reactions (incidence ≥5%) in clinical studies were elevated aminotransferases and vomiting.

Please see accompanying Full Prescribing Information.

Interactive Guide Overview

This interactive guide outlines best practices for the key steps in the approval process to help your patients get started on ZOLGENSMA® (onasemnogene abeparvovec-xioi) as soon as possible.

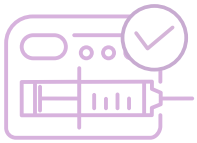
Approximately 98% of patients <2 years of age with SMA received insurance approval.[1,*] This guide details the process for various appeals along the pathway to approval. Coverage requirements may vary from patient to patient based on their individual health plan and circumstances, such as *survival motor neuron 2* (*SMN2*) gene copy number. Interactive checklists throughout the guide can help you prepare your submissions and track your progress.

Key Steps in the ZOLGENSMA Approval Process

01 Testing and Diagnosis

02 Submission to Health Plan

03 Approval and Treatment



If you have questions about the steps in the ZOLGENSMA access process, contact your Regional Account Associate Director (RAAD) or the OneGene Program at **855-441-GENE (4363), Monday-Friday (8 AM to 8 PM ET)**

*Data derived (May 2019-September 2021) from the OneGene Program, a patient support service offered by Novartis Gene Therapies. Data include all patients <2 years of age for whom payer decision was known and information was available to the OneGene Program.

Who is responsible for this step at your office/institution?

Name:

Step 1: Testing and Diagnosis of Spinal Muscular Atrophy

With the widespread adoption of newborn screening (NBS) for spinal muscular atrophy (SMA) in the United States, many patients with SMA will be identified by NBS, providing an opportunity for early treatment. As demonstrated on the **Cure SMA NBS map**, screening has been enacted in 48 states, covering 99% of newborn babies in the United States.[2]

Upon diagnosis, run the necessary lab tests required by the health plan for insurance approval to treat with ZOLGENSMA® (onasemnogene abeparvovec-xioi)

- ☐ Confirmation of SMA diagnosis
- ☐ Determination of *SMN2* copy number and SMA type
  - Reminder: the number of copies of the *SMN2* gene is not always indicative of SMA type or the severity of the disease[3]
- ☐ Adeno-associated virus 9 (AAV9) antibody test
  - Patients must have anti-AAV9 antibody titers of ≤1:50. If the patients have higher anti-AAV9 antibody titers (>1:50), you can retest to determine if the levels have decreased

Novartis Gene Therapies Laboratory Testing Program

Novartis partners with Athena Diagnostics and Cellular Technology Limited (CTL) to sponsor the Novartis Gene Therapies Laboratory Testing Program to provide test kits and cover the cost of diagnostic tests for SMA genetic testing and anti-AAV9 antibody tests.

Athena Diagnostics offers tests to confirm *SMN1* deletion and *SMN2* copy numbers and anti-AAV9 antibody tests. CTL offers anti-AAV9 antibody tests.

Prior to shipping specimens for this program, please call Athena at **800-394-4493, option 2, Monday-Friday (8:30 AM to 9:00 PM ET)**, which may help expedite processing time.

For technical questions regarding the ELISA: AAV9 Antibody Test, please contact CTL at **216-791-5084 ext 134** or email **CAT@immunospot.com**.

If you have any questions regarding the Novartis Gene Therapies Laboratory Testing Program or need to order additional specimen collection kits, please contact the OneGene Program at **855-441-GENE (4363), Monday-Friday (8 AM to 8 PM ET)**

Who is responsible for this step at your office/institution?

Name:

Testing and Diagnosis: Lab Tests

Prior to the initial prior authorization (PA) submission, additional lab tests for *SMN2* copy number or anti-AAV9 antibodies may be needed.

SMN2

Health plans may deny access to ZOLGENSMA® (onasemnogene abeparvovec-xioi) for your patient if the results do not provide a specific *SMN2* copy number.

Prior to submitting the PA, obtain a clarifying lab test to identify the specific *SMN2* copy number.

- To order additional specimen collection kits, please contact the OneGene Program at **855-441-GENE (4363), Monday-Friday (8 AM to 8 PM ET)**. Please allow 2 to 3 business days for your kits to arrive after they are shipped
- *SMN2* copy number test results are typically available within 4 days, but may take up to [21] days if the results do not identify the specific *SMN2* copy number (eg, a result indicating 4+ copies)

AAV9

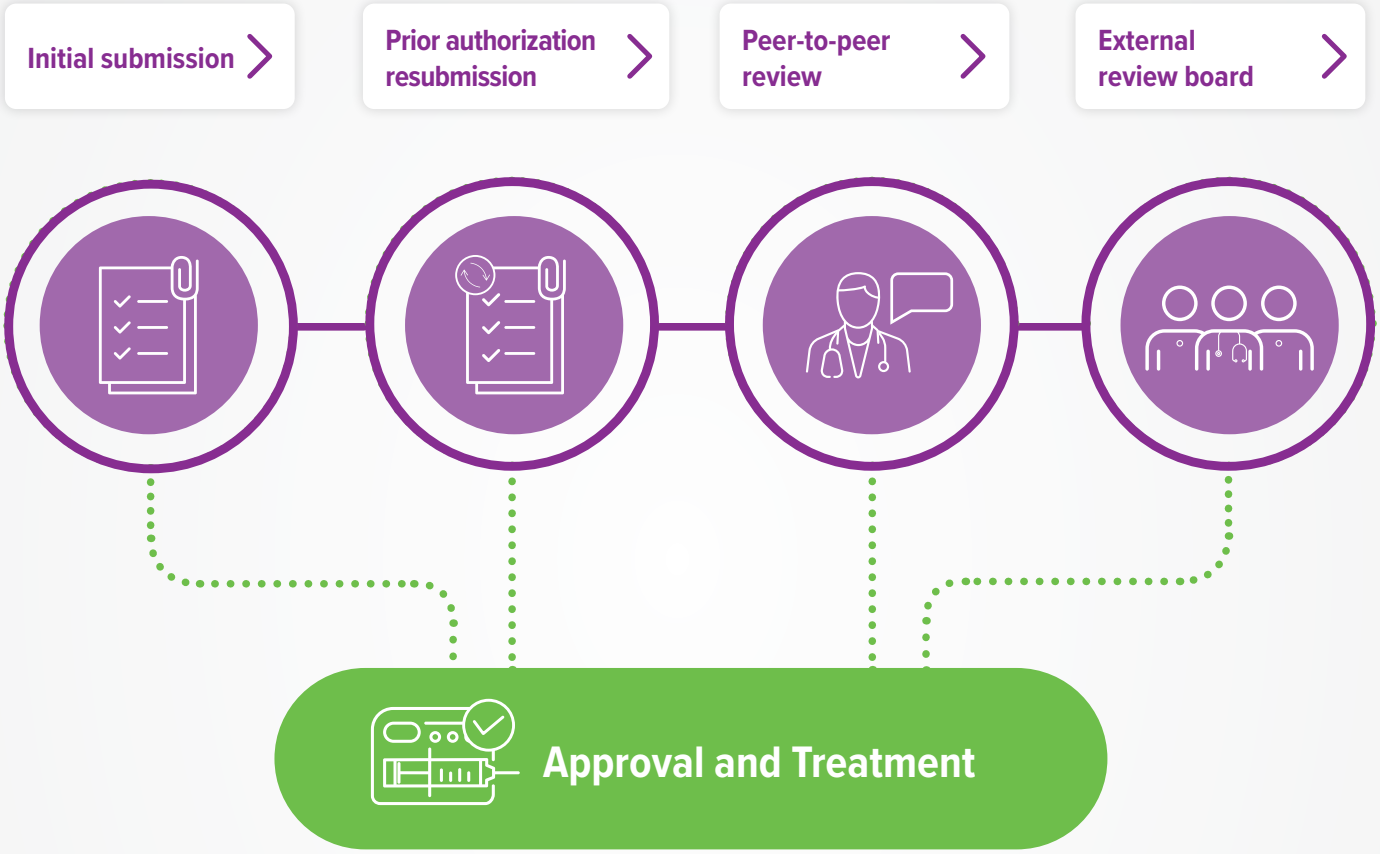
Patients must have anti-AAV9 antibody titers of ≤1:50. If the initial test results indicate titers of >1:50, test for anti-AAV9 antibodies again and do not submit the PA until test results indicate anti-AAV9 antibody titers of ≤1:50.

- To order additional specimen collection kits, fill out the Reorder Form—Novartis Gene Therapies/Athena Diagnostics/CTL Anti-AAV9 Antibody Collection Kit and email the completed form to [**Workorders@labconnect.com**] or fax the form to **423-722-3166**. Please allow 1 to 2 business days for the new kits to arrive
- Anti-AAV9 antibody results are typically available in 4 days

Perform all lab tests as soon as the diagnosis is made and confirm results align with PA requirements prior to submission

Step 2: Submissions to Health Plans

Although some patients receive approval after the initial submission for ZOLGENSMA® (onasemnogene abeparvovec-xioi), some may require escalation to additional types of reviews. This section provides best practices for submissions for each type of review.



Who is responsible for this step at your office/institution?

Name:

Preparing the Initial Submission to the Patient's Health Plan

Prepare a thorough submission to the health plan to help eliminate potential reasons for a denial.

Include all relevant information and required test results in your submission

- ☐ Dates of newborn screening and diagnostic confirmation
- ☐ Documentation of onset of clinical signs and symptoms of SMA
- ☐ Test confirming *survival motor neuron 1* (*SMN1*) gene deletion and number of *SMN2* copies
- ☐ Anti-AAV9 antibody test
- ☐ Motor function testing results (eg, the Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders [CHOP INTEND])
- ☐ Swallowing evaluation
- ☐ Patient weight
- ☐ Documentation that the prescriber is a specialist (ie, pediatric neurologist, neuromuscular specialist, or neurologist)
- ☐ Letter of medical necessity detailing the rationale for treating the patient with ZOLGENSMA® (onasemnogene abeparvovec-xioi)
- ☐ ZOLGENSMA product information
- ☐ Relevant supporting publications
- ☐ Mark that the PA is an urgent request to receive a response within 72 hours

Please see the **resources tab** or visit **zolgensmareimbursement.com** for additional information and support on prior authorization criteria, letters of medical necessity, appeals, and supporting literature for payer approval of ZOLGENSMA.

Assemble all the paperwork prior to submission to minimize possible reasons for denial

If you have questions about the steps in the ZOLGENSMA access process, contact your RAAD or the OneGene Program at **855-441-GENE (4363), Monday-Friday (8 AM to 8 PM ET)**

Who is responsible for this step at your office/institution?

Name:

Prior Authorization Resubmission Following a Denial

If the initial request is denied, you will need to submit an appeal to the health plan. Review the patient-specific denial and gather the necessary information to address the reason for the denial in your appeal.

In your appeal, make sure to

- ☐ Highlight the reason for denial and address it with specific rationale, being as detailed as possible
- ☐ Reiterate the request for treatment
- ☐ Request a peer-to-peer review with a specialist, such as a neuromuscular specialist or pediatric neurologist familiar with SMA, for further discussion and clarification
- ☐ Request a response be made within [72 hours] due to clinical urgency
- ☐ Include pertinent documentation from the initial submission

Please see the the **resources tab** or visit **zolgensmareimbursement.com** for additional information and support, including links to our letter of appeals guide and clinical reprint list with supporting literature for ZOLGENSMA.

If you have questions about the steps in the ZOLGENSMA access process, contact your RAAD or the OneGene Program at **855-441-GENE (4363), Monday-Friday (8 AM to 8 PM ET)**

Who is responsible for this step at your office/institution?

Name:

Submitting for a Prescriber Peer-to-peer Discussion

If your appeal is denied, you may request a peer-to-peer review. When meeting for a peer-to-peer discussion with a specialist such as a neuromuscular specialist or pediatric neurologist familiar with SMA, the reviewing peer may not have all the necessary documentation.

To prepare for your meeting, collect and review documentation submitted to the payer, such as

- [ ] Patient history and clinical documentation
- [ ] Claim form
- [ ] Prior authorization request
- [ ] Letter of medical necessity
- [ ] Denial letters
- [ ] Letter of appeal
- [ ] Drug information
- [ ] Relevant clinical guidelines
- [ ] Supporting publications

During your meeting, be sure to take thorough notes. Identify the outcome and ensure that the health plan has all the necessary documentation required for resubmission. Be on the lookout for next steps and timing for approval.

Who is responsible for this step at your office/institution?

Name:

Escalating to External Review Board or Oversight Committee

Federal consumer protection standards require insurance companies to offer an external review process through a state or federal board.[4]

Information on the organization that handles the external review for your patient is included on the denial of the health plan's internal review or the patient's Explanation of Benefits[4]

A written request for external review must be submitted within 4 months of receiving notice that the claim has been denied[4]

When submitting the written request, include additional supporting documentation related to the request

- [ ] Written request for external review
- [ ] Patient history and clinical documentation
- [ ] Drug information
- [ ] Letters sent to and received from the insurer regarding the claim
- [ ] Supporting publications

Who is responsible for this step at your office/institution?

Name:

Step 3: Receiving Approval and Preparing for Treatment with ZOLGENSMA® (onasemnogene abeparvovec-xioi)

You and your staff have secured access to ZOLGENSMA for your patient with SMA. Now it is time to schedule the infusion and prepare for treatment.

ZOLGENSMA is a one-time-only infusion provided as a kit customized for the patient's weight-based dosing requirements.

To prepare for infusion

- [ ] Ensure patients have baseline tests for anti-AAV9 antibodies, liver function, creatinine level, complete blood count (including hemoglobin and platelet count), and troponin-I
  - Continue monitoring liver function, platelet count, and troponin-I after infusion as described in the Prescribing Information

- [ ] Confirm patient weight
  - ZOLGENSMA dosing is weight-based. If there is a delay between ordering ZOLGENSMA and infusion, the patient may need to be re-weighed to ensure accuracy of ZOLGENSMA dose
  - Reconfirm the patient's weight on the day of the infusion

- [ ] Pre-infusion medication
  - Patients need to be treated with systemic corticosteroids 1 day prior to ZOLGENSMA infusion. Continued corticosteroid treatment is required following infusion

- [ ] Administer ZOLGENSMA to patients who are clinically stable in their overall baseline health status (eg, hydration and nutritional status, absence of infection)
  - Patients with underlying active infection, either acute or chronic uncontrolled, could be at an increased risk of serious systemic immune response
  - Postpone ZOLGENSMA in patients with infections until the infection has resolved and the patient is clinically stable

Ensure that you provide the OneGene Program or your RAAD the most current patient weight 7 days prior to the infusion date

The OneGene Program Provides Support and Ongoing Follow-up for Patients

The OneGene Program, offered by Novartis Gene Therapies, is a comprehensive, individualized patient support program for families and their health care providers throughout the ZOLGENSMA® (onasemnogene abeparvovec-xioi) treatment pathway.

The OneGene Program support includes

- **ANSWERS TO QUESTIONS** about ZOLGENSMA and SMA
- A dedicated **PERSONALIZED SUPPORT TEAM** focused on the needs of each family
- **LOGISTICAL AND COMMUNICATION SUPPORT** to ensure the appropriate delivery of ZOLGENSMA to the treatment center
- **VERIFICATION** of insurance benefits
- Support on **FINANCIAL ASSISTANCE** programs for eligible patients

OneGene program®

The ZOLGENSMA Prescription Form and a signed Patient Consent Form are required in order to receive support through the OneGene Program. The Patient Consent Form can be submitted with the ZOLGENSMA Prescription Form by the Prescriber's office, or separately by the patient's parent/legal guardian.

For questions about the OneGene Program, call **855-441-GENE (4363), Monday-Friday (8 AM to 8 PM ET)**

Additional Resources are Available to Help Navigate the Pathway to Approval

Click on the resources below to access them on zolgensmareimbursement.com

Prior Authorization Criteria Guide

Letter of Medical Necessity Guide

Sample Letter of Medical Necessity

Letter of Appeals Guide

Clinical Reprint List

ZOLGENSMA Prescription Form

Visit zolgensmareimbursement.com for more information and resources

Notes

References: 1. Data on file. Novartis Gene Therapies, Inc. 2021. **2.** Cure SMA. States screening & not screening for SMA. https://www.curesma.org/wp-content/uploads/2023/02/NBS_Maps_Screening_States_CKD_v1-26-2023.pdf. Accessed October 31, 2023. **3.** Calucho M, Bernal S, Alias L, et al. Correlation between SMA type and *SMN2* copy number revisited: an analysis of 625 unrelated Spanish patients and a compilation of 2834 reported cases. *Neuromuscul Disord*. 2018;28(3):208-215. **4.** Department of Health and Human Services. Appealing a health plan decision. https://www.healthcare.gov/appeal-insurance-company-decision/external-review/. Accessed October 31, 2023.

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