



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



**A CAREGIVER'S
GUIDE TO
ZOLGENSMA**

**A one-time-only dose
for the treatment of SMA
in children under the age
of 2 years old.**

Ryker, treated with ZOLGENSMA at 5 months old and pictured at 2 years old with his father, Glen, was diagnosed with SMA Type 1. Before receiving treatment with ZOLGENSMA, Ryker received another SMA treatment.

Indication

ZOLGENSMA[®] (onasemnogene abeparvovec-xioi) is a prescription gene therapy used to treat children less than 2 years old with spinal muscular atrophy (SMA). ZOLGENSMA is given as a one-time infusion into a vein. ZOLGENSMA was not evaluated in patients with advanced SMA.

Important Safety Information

ZOLGENSMA can increase liver enzyme levels and cause acute serious liver injury or acute liver failure. Patients will receive an oral corticosteroid before and after infusion with ZOLGENSMA and will undergo regular blood tests to monitor liver function. Contact the patient's doctor immediately if the patient's skin and/or whites of the eyes appear yellowish, if the patient misses a dose of corticosteroid or vomits it up, or if the patient experiences a decrease in alertness.

Please see additional Important Safety Information on [page 27](#) and the accompanying [Full Prescribing Information](#).

Table of contents

Click the page number for detailed information on these topics about ZOLGENSMA® (onasemnogene abeparvovec-xioi) and more.

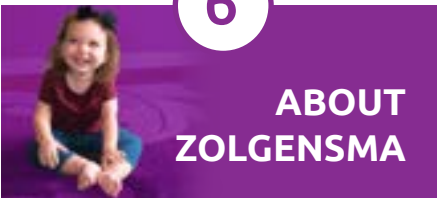


3

FACTS ABOUT SMA

Understand the genetic cause of SMA and how it impacts the body.

[Go to page 3](#) ➤




6

ABOUT ZOLGENSMA

Learn about the one-time-only dose and how it works.

[Go to page 6](#) ➤




9

TREATMENT WITH ZOLGENSMA

Learn the steps to starting ZOLGENSMA and what you can expect before, during, and after treatment.

[Go to page 9](#) ➤




18

CLINICAL STUDIES RESULTS

Discover the efficacy and safety results from the clinical studies.

[Go to page 18](#) ➤




25

SAFETY PROFILE OF ZOLGENSMA

Read about the safety data and side effects.

[Go to page 25](#) ➤



28

EVERY DAY WITH SMA

Find valuable resources that provide guidance and inspiration for life with SMA before and after treatment.

[Go to page 28](#) ➤

Important Safety Information

Decreased platelet counts could occur following infusion with ZOLGENSMA. Seek immediate medical attention if the patient experiences unexpected bleeding or bruising.

Please see the Indication and Important Safety Information on page 27 and the accompanying Full Prescribing Information.

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

FACTS ABOUT SMA

“

Treatment day gave us hope for Brady's future. We celebrate that day because we feel like that's the day Brady got the chance to be a kid again.”

Nicole, mother of Brady

Brady, treated with ZOLGENSMA at 14 months old and pictured at 2 years old, was diagnosed with SMA Type 2.

Important Safety Information

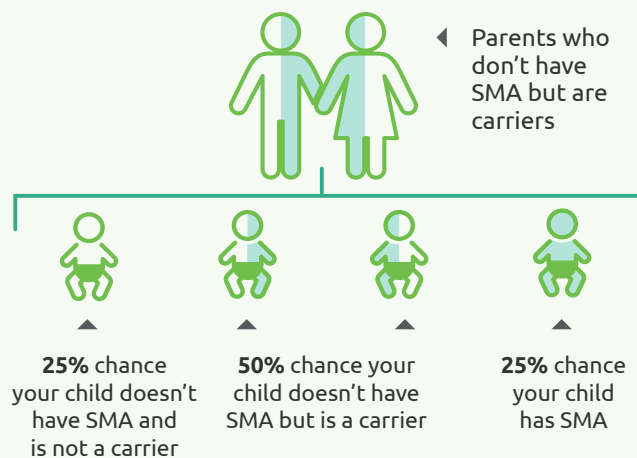
Infections before or after ZOLGENSMA[®] (onasemnogene abeparvovec-xioi) infusion can lead to more serious complications. Contact the patient's doctor immediately if you see any signs of a possible infection such as coughing, wheezing, sneezing, runny nose, sore throat, or fever.

Please see the Indication and Important Safety Information on [page 27](#) and the accompanying [Full Prescribing Information](#).

SMA is a rare genetic disease and, if diagnosed early, can be treated quickly to stop the progression of the disease

How SMA is inherited

Spinal muscular atrophy (SMA) is an autosomal recessive disorder. This means that in order to have SMA, a person must have 2 copies of a nonworking *survival motor neuron 1 (SMN1)* gene or be missing both copies of the *SMN1* gene.



About 1 in 50

people in the United States (or 6.6 million* Americans) is a genetic carrier of SMA, and most don't know it.

*Calculations are based on an estimated US population of 330 million.



/ 11K

SMA affects about 1 in every 11,000 babies born in the US.

As more children are diagnosed early through newborn screening, treatment can be started immediately to stop the progression of SMA and improve outcomes.

Important Safety Information

Decreased platelet counts could occur following infusion with ZOLGENSMA. Seek immediate medical attention if the patient experiences unexpected bleeding or bruising.

Please see the Indication and Important Safety Information on page 27 and the accompanying Full Prescribing Information.


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

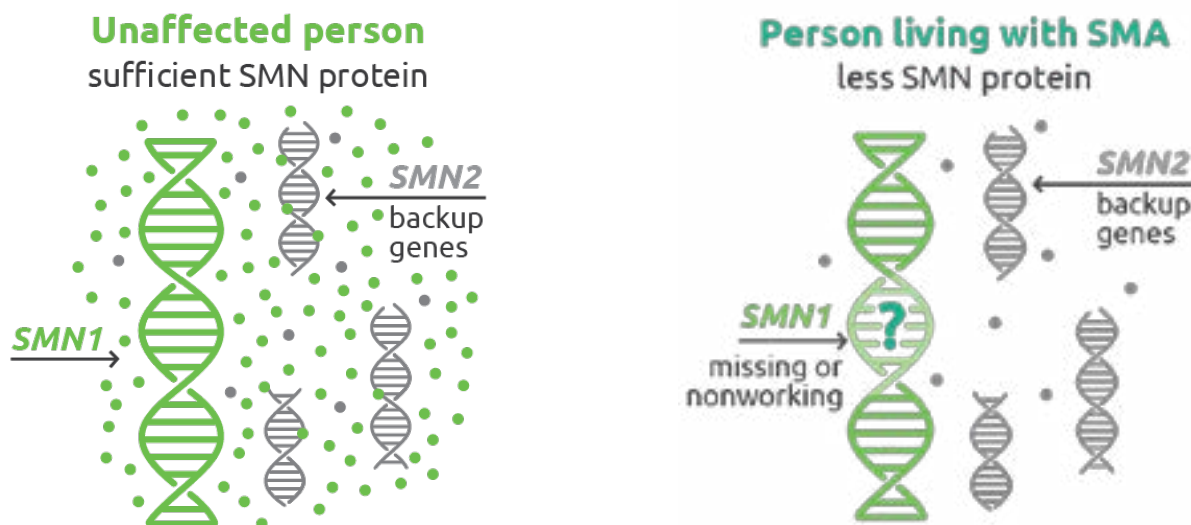
What causes SMA?

The genetic root cause of SMA is the *SMN1* gene that is missing or not working properly. When this main gene is missing or not working properly, the body cannot make enough survival motor neuron (SMN) protein, which is needed for motor neuron cell survival. Everyone is born with a certain amount of motor neuron cells, which are responsible for communicating with the arms, legs, throat, and many other areas in the body to tell them to work properly. Without enough SMN protein, select motor neuron cells throughout the body may lose function and die. As a result, patients with SMA experience muscle weakness and may develop difficulty in breathing, swallowing, or speaking.

The role of a backup gene

There is a backup gene for the *SMN1* gene called the *SMN2* gene. People can have 1 or more copies of this backup gene. This gene, like the *SMN1* gene, tells the body to make SMN protein. For people with SMA, the *SMN2* gene is the only source of SMN protein; however, it is unable to produce as much working protein as the *SMN1* gene. **In fact, the *SMN2* gene makes only about 10% of working protein compared to the protein produced by the *SMN1* gene. That is why it is essential to address the genetic root cause of SMA by replacing the function of the missing or nonworking *SMN1* gene.** Even people with several copies of the *SMN2* gene may not produce as much SMN protein as those with the working *SMN1* gene, and their motor neuron cells may not work as they should. Usually, the more copies of the *SMN2* gene a person has, the less severe his or her SMA is.

The *SMN1* and *SMN2* genes



Important Safety Information

Thrombotic microangiopathy (TMA) has been reported to occur approximately one week after ZOLGENSMA infusion. Caregivers should seek immediate medical attention if the patient experiences any signs or symptoms of TMA, such as unexpected bruising or bleeding, seizures, or decreased urine output.

Please see the Indication and Important Safety Information on page 27 and the accompanying Full Prescribing Information.


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

ABOUT ZOLGENSMA

“

She received treatment and that gives me hope for the future. She's only a toddler now, but I want her to feel like she can do anything she wants.”

Aaron, father of Natalie

Natalie, treated with ZOLGENSMA at ~14 months old and pictured at 1½ years old, was diagnosed with SMA Type 2.

Watch family videos and hear caregivers share their experiences.



Important Safety Information

Talk with the patient's doctor to decide if adjustments to the vaccination schedule are needed to accommodate treatment with a corticosteroid. Protection against respiratory syncytial virus (RSV) is recommended.

Please see the Indication and Important Safety Information on [page 27](#) and the accompanying [Full Prescribing Information](#).



The one-time-only dose for the treatment of SMA

With one dose, ZOLGENSMA® (onasemnogene abeparvovec-xioi) can stop the progression of SMA. It is a gene therapy that is designed to replace the function of the missing or nonworking *SMN1* gene that causes SMA. ZOLGENSMA is not a cure and cannot reverse damage already caused by SMA before treatment.

ZOLGENSMA targets the genetic root cause of SMA

1

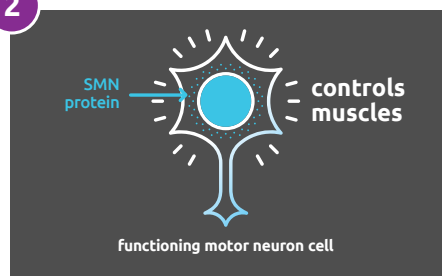


SMN1 gene missing or nonworking

A targeted approach

ZOLGENSMA targets the genetic root cause of SMA by replacing the function of a missing or nonworking gene called the *SMN1* gene. This gene is critical for making SMN protein.

2



SMN protein

controls muscles

functioning motor neuron cell

The importance of SMN protein

SMN protein is essential to motor neuron cell survival. These cells control muscle function. Without SMN protein, motor neuron cells die, causing muscles to become so weak that breathing, eating, and moving become difficult, and the condition can become life threatening in its most severe forms.

Important Safety Information

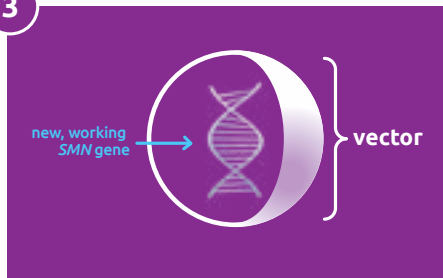
Temporarily, small amounts of ZOLGENSMA may be found in the patient's stool. Use good hand hygiene when coming into direct contact with bodily waste for 1 month after infusion with ZOLGENSMA. Disposable diapers should be sealed in disposable trash bags and thrown out with regular trash.

Please see the Indication and Important Safety Information on page 27 and the accompanying Full Prescribing Information.

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

ZOLGENSMA targets the genetic root cause of SMA (continued)

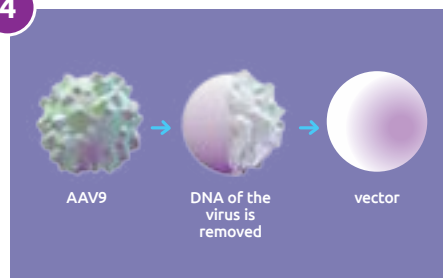
3



The role of the vector

ZOLGENSMA® (onasemnogene abeparvovec-xioi) is made up of a new, working copy of a human *SMN* gene that is placed inside a vector. A vector's job is to take the new, working *SMN* gene to the motor neuron cells in the body.

4



Delivery of the *SMN* gene

The vector that delivers the *SMN* gene is made from a virus called adeno-associated virus 9, or AAV9. This type of virus is not known to make people sick. To make the vector, the DNA of the virus is removed so that the new *SMN* gene can be put inside. Vectors are used because they can travel throughout the body and deliver the new, working gene to the cells where it is needed.

5



Production of *SMN* protein

When the new gene reaches its destination, it tells the motor neuron cells to start making *SMN* protein. This happens throughout the body, delivering a new, working copy of the *SMN* gene to motor neuron cells. The new gene does not become part of the child's DNA.

6



Motor neuron cells maintained

With the motor neuron cells now able to make sufficient *SMN* protein, motor neuron cells that have not died may survive, function, and be maintained.

Watch an animated video
of how ZOLGENSMA works.



Important Safety Information

The most common side effects that occurred in patients treated with ZOLGENSMA were elevated liver enzymes and vomiting.

Please see the Indication and Important Safety Information on page 27 and the accompanying Full Prescribing Information.


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

TREATMENT WITH ZOLGENSMA

“

It means a lot to us to have a one-time-only treatment. It gives us more time to be a family at home.”

Tina, mother of Malachi

Malachi, treated with ZOLGENSMA at ~4 months old and pictured at 4 years old, was diagnosed with SMA Type 1.

Watch family videos and hear caregivers share their experiences.



Important Safety Information

ZOLGENSMA[®] (onasemnogene abeparvovec-xioi) can increase liver enzyme levels and cause acute serious liver injury or acute liver failure. Patients will receive an oral corticosteroid before and after infusion with ZOLGENSMA and will undergo regular blood tests to monitor liver function. Contact the patient's doctor immediately if the patient's skin and/or whites of the eyes appear yellowish, if the patient misses a dose of corticosteroid or vomits it up, or if the patient experiences a decrease in alertness.

Please see the Indication and Important Safety Information on [page 27](#) and the accompanying [Full Prescribing Information](#).

STEP
1

Pretreatment testing to determine if your child qualifies for ZOLGENSMA

ZOLGENSMA[®] (onasemnogene abeparvovec-xioi) is a prescription gene therapy used to treat children less than 2 years old with SMA. It is given as a one-time infusion into a vein. If you and your child's doctor have chosen ZOLGENSMA, there are a few steps that need to be taken to determine if your child qualifies for ZOLGENSMA.

● Complete necessary lab tests

● Confirm a diagnosis

Before ZOLGENSMA can be given to your child, a diagnosis of SMA has to be confirmed through a genetic test.

● Perform an AAV9 antibody test

An adeno-associated virus 9 (AAV9) antibody test measures the amount of anti-AAV9 antibodies in your child's blood. If your child's immune system has built up a certain level of anti-AAV9 antibodies, he or she may not qualify for ZOLGENSMA right away. If your child's anti-AAV9 antibodies are too high, your doctor has the option to retest. Speak with your doctor about the AAV9 antibody test that is offered through the Novartis Gene Therapies complimentary lab program.

● Perform blood tests

Your doctor should perform blood tests to check your child's liver function and obtain creatinine, complete blood count (including hemoglobin and platelet count), and troponin-I. These measurements before dosing will help your doctor and care team monitor your child's levels after dosing. These tests may happen while waiting for approval or as you get closer to treatment.

Watch a video to learn more about the steps to starting treatment.



Important Safety Information

Infections before or after ZOLGENSMA infusion can lead to more serious complications. Contact the patient's doctor immediately if you see any signs of a possible infection such as coughing, wheezing, sneezing, runny nose, sore throat, or fever.

Please see the Indication and Important Safety Information on page 27 and the accompanying Full Prescribing Information.

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



Shane, pictured and treated with ZOLGENSMA at ~17 months old, was diagnosed with SMA Type 2. Before receiving treatment with ZOLGENSMA, Shane received another SMA treatment.

- **Have your doctor submit a ZOLGENSMA Prescription Form and a Patient Consent Form**

While waiting for test results, your doctor may submit a ZOLGENSMA® (onasemnogene abeparvovec-xioi) Prescription Form and/or a Patient Consent Form to the OneGene Program®. This starts the process to assess insurance coverage and authorization requirements and helps you learn about the patient support the **OneGene Program** offers. You will need to sign the Patient Consent Form to access all of the support provided by the OneGene Program.

Once the Prescription Form and/or Patient Consent Form is completed, a representative from the OneGene Program will call you to discuss the patient support available to you.

Important Safety Information

Decreased platelet counts could occur following infusion with ZOLGENSMA. Seek immediate medical attention if the patient experiences unexpected bleeding or bruising.

Please see the Indication and Important Safety Information on page 27 and the accompanying Full Prescribing Information.

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

1

2

3

4

5

STEP
2

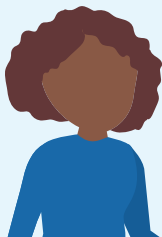
Connect with the OneGene Program[®]

The **OneGene Program**, a team of highly trained and dedicated people, is a resource brought to you by Novartis Gene Therapies. It is designed to support and guide you and your family at every step during treatment.



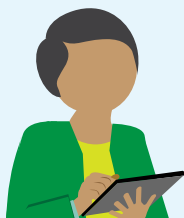
Contact at 855-441-GENE (4363),
Monday-Friday (8 AM-8 PM ET), to learn more.

Novartis Gene Therapies is there for your family, providing additional assistance throughout the treatment journey.



Patient Resource Manager

A Patient Resource Manager is your main point of contact on behalf of Novartis Gene Therapies, providing expert guidance and answering questions about ZOLGENSMA[®] (onasemnogene abeparvovec-xioi) as your child goes through the treatment journey.



Case Coordinator

A Case Coordinator acts as a go-between to connect you to resources you may need and assists doctors with insurance processes. Other support includes verification of insurance benefits and coordination of financial assistance programs for eligible patients.

Important Safety Information

Thrombotic microangiopathy (TMA) has been reported to occur approximately one week after ZOLGENSMA infusion. Caregivers should seek immediate medical attention if the patient experiences any signs or symptoms of TMA, such as unexpected bruising or bleeding, seizures, or decreased urine output.

Please see the Indication and Important Safety Information on page 27 and the accompanying Full Prescribing Information.



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

1

2

3

4

5

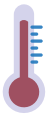
STEP
3

Prepare for treatment day

If your child is approved for treatment with ZOLGENSMA® (onasemnogene abeparvovec-xioi), your child's doctor and care team will help ensure you know exactly what to expect on the day of treatment and how to prepare. Additionally, your Patient Resource Manager will work with you to understand how he or she can best support your family on treatment day.



If not completed already, your doctor should perform blood tests to check your child's liver function and to establish baseline levels for creatinine, complete blood count (including hemoglobin and platelet count), and troponin-I. These tests will help your doctor and care team monitor your child after dosing.



Infections before or after ZOLGENSMA infusion can lead to more serious complications. If symptoms of infection appear before infusion, you may be asked to postpone treatment until the infection has resolved. Contact your doctor immediately if you see any signs of a possible infection such as coughing, wheezing, sneezing, runny nose, sore throat, or fever.



A course of an oral corticosteroid* should be started the day before infusion with ZOLGENSMA. This helps manage elevated liver enzyme reactions to ZOLGENSMA by the body's immune system.



Confirm your child's infusion date, time, and location with your doctor. Determine your family's transportation plan and get directions to the treatment center, including the address and available parking areas if you're driving. Ask the treatment center how many family members can be with you and your child on the day of infusion.

*The specific treatment course for each patient will be determined by the treating doctor. The treatment course is based on several clinical factors and the judgment of the doctor. Caregivers should discuss specific treatment recommendations with their treating doctor.

Important Safety Information

Talk with the patient's doctor to decide if adjustments to the vaccination schedule are needed to accommodate treatment with a corticosteroid. Protection against respiratory syncytial virus (RSV) is recommended.

Please see the Indication and Important Safety Information on page 27 and the accompanying Full Prescribing Information.


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

STEP
4

Treatment day

On the day of treatment, your child will be infused with ZOLGENSMA

You should give your child the second dose of the oral corticosteroid on the day of infusion as prescribed by your doctor to help manage reactions to ZOLGENSMA[®] (onasemnogene abeparvovec-xioi) by the body's immune system. The actual infusion will take 60 minutes. However, ask your child's doctor or care team for additional details on the schedule for the day.

Remember to talk to your doctor and care team about any family members you would like to have with you on treatment day. If possible, you may have the option of having your Patient Resource Manager present on the day of treatment to support your family.

You will be given a Post-Treatment Kit on treatment day that details additional medical monitoring and types of specialists that may be part of your child's healthcare team. Ensure you receive the kit from your doctor or ask your Patient Resource Manager for one.



Sienna, pictured and treated with ZOLGENSMA at 17 months old, was diagnosed with SMA Type 1. Before receiving treatment with ZOLGENSMA, Sienna received another SMA treatment.

Important Safety Information

Temporarily, small amounts of ZOLGENSMA may be found in the patient's stool. Use good hand hygiene when coming into direct contact with bodily waste for 1 month after infusion with ZOLGENSMA. Disposable diapers should be sealed in disposable trash bags and thrown out with regular trash.

Please see the Indication and Important Safety Information on [page 27](#) and the accompanying [Full Prescribing Information](#).

1

2

3

4

5

What to do and know before you leave the hospital

Talk with your doctor about post-treatment follow-up and additional monitoring. You will continue to give your child the corticosteroid as prescribed by your doctor. Contact your doctor immediately if you see any signs of a possible infection such as coughing, wheezing, sneezing, runny nose, sore throat, or fever.

Your doctor will monitor your child's liver function for at least 3 months after infusion through weekly clinical exams and blood tests for the first month and every other week for the second and third months. Your doctor will determine when to gradually reduce the dose of the corticosteroid and when to stop it.

- You should contact your doctor immediately if a dose of the corticosteroid is missed or vomited up. Keep track of dosing time so you can share details with your doctor of when the last dose was given or vomited up
- Talk to your doctor about potential side effects that may occur after treatment, especially what to do if vomiting or fever occur. Ask your doctor about potential side effects of ZOLGENSMA® (onasemnogene abeparvovec-xioi)

In addition to liver function, your doctor will perform blood tests to measure platelet counts and troponin-I levels. See below for a sample post-treatment monitoring schedule.

BASELINE ASSESSMENTS PRIOR TO INFUSION												
At baseline, assess liver function, creatinine, complete blood count (including hemoglobin and platelet count), and troponin-I												
MONITORING AFTER INFUSION												
TEST	MONTH 1				MONTH 2				MONTH 3			
	WEEK 1	WEEK 2	WEEK 3	WEEK 4	WEEK 5	WEEK 6	WEEK 7	WEEK 8	WEEK 9	WEEK 10	WEEK 11	WEEK 12
Liver function	✓	✓	✓	✓		✓		✓		✓		✓
Platelet count	✓	✓	✓	✓		✓		✓		✓		✓
Troponin-I	✓	✓	✓	✓				✓				✓

✓ = monitoring performed.

Important Safety Information

The most common side effects that occurred in patients treated with ZOLGENSMA were elevated liver enzymes and vomiting.

Please see the Indication and Important Safety Information on [page 27](#) and the accompanying [Full Prescribing Information](#).


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

STEP
5

After treatment with ZOLGENSMA

Once your child has been treated with ZOLGENSMA® (onasemnogene abeparvovec-xioi), it is important to learn how to continue managing your child's SMA. This includes speaking with a neuromuscular specialist and creating an extended healthcare team.

Continuing your child's SMA care

While ZOLGENSMA replaces the function of your child's missing or nonworking *SMN1* gene, your child still has SMA. That's why it is important to speak with your neuromuscular specialist and healthcare team to review supportive care (like physical and occupational therapy, working with a nutritionist, and meeting with a pulmonologist) to determine what kind of care may be best for your child following treatment. Additional therapies, accommodations, and support may be needed to guide your child's ongoing development. Work with your healthcare team to evaluate your child's progress after treatment.

ZOLGENSMA is not a cure. Your child may continue to show signs of SMA. These may include difficulty swallowing or breathing or muscle weakness. Discuss any signs or symptoms with your child's doctor and healthcare team.

The SMA community is here for you



To connect with other caregivers and discover valuable resources, check out [CureSMA.org](https://www.curesma.org).

Important Safety Information

ZOLGENSMA can increase liver enzyme levels and cause acute serious liver injury or acute liver failure. Patients will receive an oral corticosteroid before and after infusion with ZOLGENSMA and will undergo regular blood tests to monitor liver function. Contact the patient's doctor immediately if the patient's skin and/or whites of the eyes appear yellowish, if the patient misses a dose of corticosteroid or vomits it up, or if the patient experiences a decrease in alertness.

Please see the Indication and Important Safety Information on [page 27](#) and the accompanying [Full Prescribing Information](#).



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



Pictured left to right: Matthew, Ellie, Montgomery, and Emily. Ellie, treated with ZOLGENSMA at 15 days old and pictured at 9 months old, was diagnosed with SMA *in utero*.

Connect with families to discover more

See what children treated with ZOLGENSMA[®] (onasemnogene abeparvovec-xioi) are up to, hear from SMA caregivers, and learn more about treatment.



Important Safety Information

Infections before or after ZOLGENSMA infusion can lead to more serious complications. Contact the patient's doctor immediately if you see any signs of a possible infection such as coughing, wheezing, sneezing, runny nose, sore throat, or fever.

Please see the Indication and Important Safety Information on page 27 and the accompanying Full Prescribing Information.


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

CLINICAL STUDIES RESULTS



“

Tenley has gained strength after treatment. She is able to maneuver a wheelchair by herself and get around and feel more like a kid. So that’s really important for us.”

Lacretia, mother of Tenley

Tenley, treated with ZOLGENSMA at ~5½ months old and pictured at 4½ years old, was diagnosed with SMA Type 1.

Important Safety Information

Decreased platelet counts could occur following infusion with ZOLGENSMA[®] (onasemnogene abeparvovec-xioi). Seek immediate medical attention if the patient experiences unexpected bleeding or bruising.

Please see the Indication and Important Safety Information on [page 27](#) and the accompanying [Full Prescribing Information](#).

ZOLGENSMA increased achievements for symptomatic patients across all measures studied

The purpose of the STR1VE study was to review the efficacy and safety of ZOLGENSMA[®] (onasemnogene abeparvovec-xioi). The STR1VE study enrolled 22 symptomatic patients,* which means they displayed symptoms of SMA before receiving treatment. All patients were diagnosed with SMA Type 1, had 2 copies of the *SMN2* backup gene, and were 6 months of age or younger at the time of IV infusion.

- The average age at dosing was 3.7 months (range 0.5-5.9 months)
- All patients received the therapeutic dose of ZOLGENSMA (dose approved by the FDA)
- Patients were followed through their 18 months of age study visit

*One patient was initially classified as presymptomatic but was later confirmed to be symptomatic and was included in the final clinical study findings.

The STR1VE study looked at 5 key measurements



See full results from the STR1VE clinical study.

Important Safety Information

Thrombotic microangiopathy (TMA) has been reported to occur approximately one week after ZOLGENSMA infusion. Caregivers should seek immediate medical attention if the patient experiences any signs or symptoms of TMA, such as unexpected bruising or bleeding, seizures, or decreased urine output.

Please see the Indication and Important Safety Information on page 27 and the accompanying Full Prescribing Information.

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

Patients survived without breathing support

At the 14 months of age study visit,



(20/22)* of patients were alive and did not need permanent breathing support

In the natural history of SMA Type 1 (children who haven't received treatment), about 25% of children were alive without permanent breathing support at 14 months of age.

- 1 patient passed away at 7.8 months of age from causes unrelated to treatment
- 1 patient withdrew from the study at 11.9 months of age and required permanent ventilation at 11 months of age prior to leaving the study

*One patient was initially not part of the data set but is included in the final data analysis.

What is an event?

Event is defined as death, the need for permanent ventilatory support (such as tracheostomy), or the need for respiratory assistance (not due to illness or surgery) for 16 hours or more a day for at least 14 days.

Patients could sit without help



(13/22) of patients could sit without support for at least 30 seconds at the 18 months of age study visit

In the natural history of SMA Type 1, patients are not able to sit independently.

Important Safety Information

Talk with the patient's doctor to decide if adjustments to the vaccination schedule are needed to accommodate treatment with a corticosteroid. Protection against respiratory syncytial virus (RSV) is recommended.

Please see the Indication and Important Safety Information on page 27 and the accompanying Full Prescribing Information.



Patients maintained milestones for over 5 years after treatment with ZOLGENSMA

The START clinical study was the first study of ZOLGENSMA[®] (onasemnogene abeparvovec-xioi) and is completed. This study enrolled 15 symptomatic patients diagnosed with SMA Type 1 who were 8 months of age or younger at the time of infusion. Patients were split into 2 groups. Three patients in group 1 received a low dose and 12 patients in group 2 received a high dose (~therapeutic dose).

The primary purpose of the study was to evaluate the safety of ZOLGENSMA. Other endpoints measured were event-free survival (event was defined as death, the need for permanent ventilatory support, such as tracheostomy, or the need for respiratory assistance*) and the change from baseline in CHOP INTEND (or the Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders). CHOP INTEND measures the motor development of children with SMA Type 1. At the end of the START clinical study, all 12 patients in the high-dose group were alive and free of permanent breathing support 24 months after treatment.

92% (11/12) of patients could sit without support for at least 5 seconds

75% (9/12) of patients could sit without support for at least 30 seconds

92% (11/12) of patients achieved or maintained CHOP INTEND scores higher than 40 points

The START long-term follow-up (LTFU) study is designed to monitor the safety of ZOLGENSMA over 15 years. Ongoing study results show the safety and efficacy of ZOLGENSMA up to 5 years after treatment and 5 years of age or older. The study enrolled 13 patients from the START study—3 patients from group 1 (low dose) and 10 patients from group 2 (high dose).

Study results for START LTFU group 2



(10/10) of patients were alive and did not need permanent breathing support (as of June 2020)

(10/10) have maintained motor milestones achieved at the end of the START study (as of December 2019)

*≥16 hours of respiratory assistance each day continuously for ≥14 days.

Important Safety Information

Temporarily, small amounts of ZOLGENSMA may be found in the patient's stool. Use good hand hygiene when coming into direct contact with bodily waste for 1 month after infusion with ZOLGENSMA. Disposable diapers should be sealed in disposable trash bags and thrown out with regular trash.

Please see the Indication and Important Safety Information on page 27 and the accompanying Full Prescribing Information.

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



“

When I grow up, I want to be a cowgirl. I want to wear my boots and my hat and own a ranch.”

Evelyn

Evelyn, treated with ZOLGENSMA at ~2 months old and pictured at 4½ years old, was diagnosed with SMA Type 1 and participates in the START LTFU study.

Learn more about milestones achieved in the START clinical study.

Important Safety Information

Decreased platelet counts could occur following infusion with ZOLGENSMA® (onasemnogene abeparvovec-xioi). Seek immediate medical attention if the patient experiences unexpected bleeding or bruising.

Please see the Indication and Important Safety Information on [page 27](#) and the accompanying [Full Prescribing Information](#).

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

ZOLGENSMA helped presymptomatic patients reach age-appropriate milestones and survive without permanent breathing support

The purpose of the SPR1NT study was to evaluate the efficacy and safety of ZOLGENSMA[®] (onasemnogene abeparvovec-xioi) in patients younger than 6 weeks of age and showing no symptoms (presymptomatic) of SMA. The study enrolled 29 presymptomatic patients diagnosed with SMA who had 2 or 3 copies of the *SMN2* backup gene.*

The average age at treatment:

- 2 copies of *SMN2* (14 patients): 20.6 days
- 3 copies of *SMN2* (15 patients): 28.7 days
- Patients received the therapeutic dose of ZOLGENSMA (dose approved by the FDA)

*The following SPR1NT study results are as of June 2020 (this study is ongoing).

Alive and free of permanent ventilation (as of June 2020)



(29/29) of patients were alive and free of permanent breathing support

See full results from the SPR1NT clinical study.

Important Safety Information

The most common side effects that occurred in patients treated with ZOLGENSMA were elevated liver enzymes and vomiting.

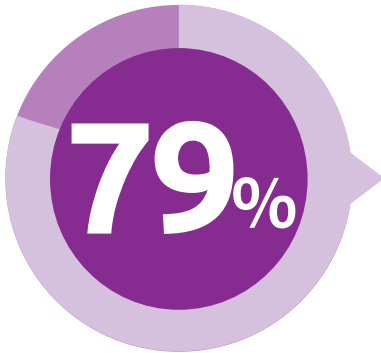
Please see the Indication and Important Safety Information on page 27 and the accompanying Full Prescribing Information.

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

Patients could sit without help

Patients reached age-appropriate milestones

In the SPR1NT study, the Bayley-III was used to determine children's motor skills compared to what is expected for unaffected developing children. The WHO-MGRS (World Health Organization Multicentre Growth Reference Study) was used to provide a timeline for motor milestone development in unaffected children.



(11/14) of **patients with 2 copies of *SMN2* backup gene could sit without assistance** (30 seconds or more) as measured by Bayley-III at any visit up to 18 months of age

In the natural history of SMA Type 1, patients are never able to sit, stand, or walk independently.

The 3 remaining patients were older than the age-appropriate window but are still younger than 18 months of age.

Patients could stand by themselves



(8/15) of **patients with 3 copies of *SMN2* backup gene could stand without assistance** (3 seconds or more) as measured by Bayley-III at any visit up to 24 months of age
8/8 patients achieved this milestone within an age-appropriate time

The 7 remaining patients have not passed the age-appropriate window to achieve this milestone.

Important Safety Information

Infections before or after ZOLGENSMA infusion can lead to more serious complications. Contact the patient's doctor immediately if you see any signs of a possible infection such as coughing, wheezing, sneezing, runny nose, sore throat, or fever.

Please see the Indication and Important Safety Information on [page 27](#) and the accompanying [Full Prescribing Information](#).

SAFETY PROFILE OF ZOLGENSMA

“

I expected ZOLGENSMA to stop the progression of the disease. Just halt it. And now she's hitting milestones that were once a dream. I think my little girl's going to do things that I never even pictured.”

Ciji, mother of Maisie

Maisie, treated with ZOLGENSMA at ~20 months old and pictured at 2 years old, was diagnosed with SMA Type 1. Before receiving treatment with ZOLGENSMA, Maisie received another SMA treatment.

Watch family videos and hear caregivers share their experiences.



Important Safety Information

ZOLGENSMA[®] (onasemnogene abeparvovec-xioi) can increase liver enzyme levels and cause acute serious liver injury or acute liver failure. Patients will receive an oral corticosteroid before and after infusion with ZOLGENSMA and will undergo regular blood tests to monitor liver function. Contact the patient's doctor immediately if the patient's skin and/or whites of the eyes appear yellowish, if the patient misses a dose of corticosteroid or vomits it up, or if the patient experiences a decrease in alertness.

Please see the Indication and Important Safety Information on [page 27](#) and the accompanying [Full Prescribing Information](#).

Safety profile

ZOLGENSMA[®] (onasemnogene abeparvovec-xioi) has an established safety profile demonstrated in 3 clinical studies and 1 observational long-term follow-up study.

- **44 patients were treated with ZOLGENSMA and ranged in age from 0.3 to 7.9 months at the time of infusion**
- **The most common side effects (5% or more) that occurred in patients treated with ZOLGENSMA were elevated liver enzymes and vomiting**
- **Reports of pyrexia (or fever), thrombotic microangiopathy (TMA), thrombocytopenia, acute liver failure, acute liver injury, and increased troponin were identified during postmarketing experience**

Safety data update

As of June 2020, 102 patients have been treated with ZOLGENSMA intravenously (IV) in clinical studies.*

- The most common side effects (5% or more) that occurred in patients treated with ZOLGENSMA were elevated liver enzymes and vomiting
- Safety data continue to be collected

*Patients from 5 open-label studies, including 2 completed and 3 ongoing clinical studies: START (completed, N = 15), STR1VE (completed, N = 22), STR1VE-EU (ongoing, N = 33), STR1VE-AP (ongoing, N = 2), SPR1NT (ongoing, N = 30). Three patients in the START study received a lower dose.

Important Safety Information

Infections before or after ZOLGENSMA infusion can lead to more serious complications. Contact the patient's doctor immediately if you see any signs of a possible infection such as coughing, wheezing, sneezing, runny nose, sore throat, or fever.

Please see the Indication and Important Safety Information on page 27 and the accompanying Full Prescribing Information.

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

Indication and Important Safety Information

What is ZOLGENSMA?

ZOLGENSMA® (onasemnogene abeparvovec-xioi) is a prescription gene therapy used to treat children less than 2 years old with spinal muscular atrophy (SMA). ZOLGENSMA is given as a one-time infusion into a vein. ZOLGENSMA was not evaluated in patients with advanced SMA.

What is the most important information I should know about ZOLGENSMA?

- ZOLGENSMA can increase liver enzyme levels and cause acute serious liver injury or acute liver failure.
- Patients will receive an oral corticosteroid before and after infusion with ZOLGENSMA and will undergo regular blood tests to monitor liver function.
- Contact the patient's doctor immediately if the patient's skin and/or whites of the eyes appear yellowish, if the patient misses a dose of corticosteroid or vomits it up, or if the patient experiences a decrease in alertness.

What should I watch for before and after infusion with ZOLGENSMA?

- Infections before or after ZOLGENSMA infusion can lead to more serious complications. Contact the patient's doctor immediately if you see any signs of a possible infection such as coughing, wheezing, sneezing, runny nose, sore throat, or fever.
- Decreased platelet counts could occur following infusion with ZOLGENSMA. Seek immediate medical attention if the patient experiences unexpected bleeding or bruising.
- Thrombotic microangiopathy (TMA) has been reported to occur approximately one week after ZOLGENSMA infusion. Caregivers should seek immediate medical attention if the patient experiences any signs or symptoms of TMA, such as unexpected bruising or bleeding, seizures, or decreased urine output.

What do I need to know about vaccinations and ZOLGENSMA?

- Talk with the patient's doctor to decide if adjustments to the vaccination schedule are needed to accommodate treatment with a corticosteroid.
- Protection against respiratory syncytial virus (RSV) is recommended.

Do I need to take precautions with the patient's bodily waste?

Temporarily, small amounts of ZOLGENSMA may be found in the patient's stool. Use good hand hygiene when coming into direct contact with bodily waste for 1 month after infusion with ZOLGENSMA. Disposable diapers should be sealed in disposable trash bags and thrown out with regular trash.

What are the possible or likely side effects of ZOLGENSMA?

The most common side effects that occurred in patients treated with ZOLGENSMA were elevated liver enzymes and vomiting.

The safety information provided here is not comprehensive.

Talk to the patient's doctor about any side effects that bother the patient or that don't go away.

You are encouraged to report suspected side effects by contacting the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch, or Novartis Gene Therapies, Inc. at 833-828-3947.

Please see the [Full Prescribing Information](#).

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

EVERY DAY WITH SMA

“

It's taken some time to get to the point where we're really accustomed to our routine, but we've figured out what works for us. It's not at all what we planned, but we are rolling with the punches every day.”

Daryn, father of Slade

Slade, treated with ZOLGENSMA at ~7 months old and pictured at 1 year old, was diagnosed with SMA Type 1. Before receiving treatment with ZOLGENSMA, Slade received another SMA treatment and continues on that treatment today.

Important Safety Information

Decreased platelet counts could occur following infusion with ZOLGENSMA[®] (onasemnogene abeparvovec-xioi). Seek immediate medical attention if the patient experiences unexpected bleeding or bruising.

Please see the Indication and Important Safety Information on [page 27](#) and the accompanying [Full Prescribing Information](#).

Every Day With SMA is here to help you navigate life with SMA

Even after treatment with ZOLGENSMA® (onasemnogene abeparvovec-xioi), it's important to remember that your child still has SMA, and it will need to be managed. **Every Day With SMA** is a valuable resource designed to help you navigate the next chapter of your SMA journey.

Every Day With SMA provides information, guidance, and inspiration from experienced caregivers about life with SMA. You can get tips for daily living, watch videos of children to see how they are doing after treatment, and learn what families with children who have been treated are doing to change SMA in the future.



Eli, treated with ZOLGENSMA at ~4 months old and pictured at 5 years old with his mom, Natalie, was diagnosed with SMA Type 1.

Evelyn, treated with ZOLGENSMA at ~2 months old and pictured at 4½ years old with her parents, Elena and Milan, was diagnosed with SMA Type 1.

Discover more resources and community support.

Important Safety Information

Thrombotic microangiopathy (TMA) has been reported to occur approximately one week after ZOLGENSMA infusion. Caregivers should seek immediate medical attention if the patient experiences any signs or symptoms of TMA, such as unexpected bruising or bleeding, seizures, or decreased urine output.

Please see the Indication and Important Safety Information on [page 27](#) and the accompanying [Full Prescribing Information](#).


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

“

Our Patient Resource Manager was really vital in helping us address questions we had before, during, and after treatment. It was comforting to be able to speak to someone throughout the process.”

Annie, mother of Quinn

Quinn, treated with ZOLGENSMA at ~15 months old and pictured at 2½ years old, was diagnosed with SMA Type 2.

