For the **8,500+ children** who have been treated with SPINRAZA worldwide, victories are personal.*

*Based on commercial patients, early access patients, and clinical trial participants through May 2022.

INDICATION

SPINRAZA® (nusinersen) is a prescription medicine used to treat spinal muscular atrophy (SMA) in pediatric and adult patients.

SELECTED IMPORTANT SAFETY INFORMATION

Increased risk of bleeding complications has been observed after administration of similar medicines. Your healthcare provider should perform blood tests before you start treatment with SPINRAZA and before each dose to monitor for signs of these risks. Seek medical attention if unexpected bleeding occurs.

Please see additional Important Safety Information on page 23 and click for full Prescribing Information.

SPINRAZA® (nusinersen) injection 12 mg/5 mL

Spinal muscular atrophy starts in the central nervous system and can affect all the muscles in the body

Spinal muscular atrophy (SMA) is what's known as a neuromuscular disease because it affects the motor neurons that power the muscles in the body. SMA is degenerative, which means people who have it will lose muscle strength and function throughout their life.

SMA is a genetic disorder caused by a lack of survival motor neuron (SMN) protein, a protein that's key for muscle development and movement.

Muscles need signals from the CNS

// Motor neurons from the central nervous system (CNS) send signals to the body's muscles. These neurons need SMN protein in order to work. Without enough SMN protein, motor neurons die off. With no signals from the CNS, muscles get weaker and weaker.

SMN1 is mutated in SMA

// People with SMA can't generate enough SMN protein because the *survival motor neuron 1* (*SMN1*) gene is mutated or missing.

SMA=insufficient SMN protein

// People with SMA can't make enough SMN protein because they have a mutated or missing *survival motor neuron 1 (SMN1)* gene. The gene they do have, *SMN2*, does not produce enough SMN protein that is needed for motor neurons to survive.

Because muscle loss is permanent and can happen quickly in children, it's important to treat SMA as soon as possible

How quickly can muscle loss occur? It's hard to say. The rate of motor function loss varies from person to person, and there is no sure way to tell how quickly muscle function loss will happen or how severe it will be.

Genetic testing can confirm an SMA diagnosis.

Genetic testing is often required to start treatment. Ask your healthcare provider (HCP) for more information about genetic testing.

Please see additional Important Safety Information on page 23 and click for full Prescribing Information.

These are moments and stories. These are personal victories. This is SPINRAZA

13,000+

have been treated with SPINRAZA worldwide*

8,500+

children have been treated with SPINRAZA worldwide*

From 3 days to 80 years old,*†

there's someone from almost every age group who has taken SPINRAZA

*Based on commercial patients, early access patients, and clinical trial participants through May 2022.
†SPINRAZA pivotal studies included patients from 3 days to 16 years of age at first dose and did not include sufficient numbers of subjects aged 65 and older to determine whether they respond differently from younger patients.

SELECTED IMPORTANT SAFETY INFORMATION

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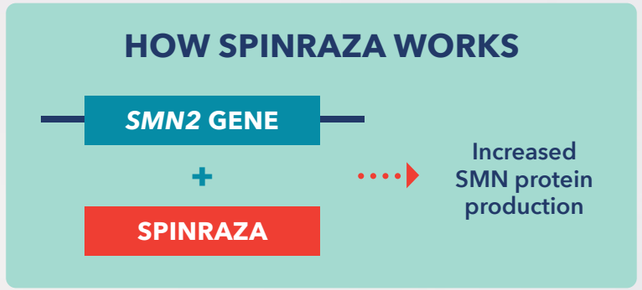
SMA is a disease of the CNS. SPINRAZA is delivered directly into the CNS

People with SMA can't generate enough SMN protein, the protein their motor neurons need to survive. That's where SPINRAZA can help.

// Gets to the source of motor neuron loss

// While you continue on treatment, SPINRAZA helps your body's SMN protein production

SPINRAZA specifically targets an underlying cause of muscle weakness



7-year old Emma explains how SPINRAZA works. Watch at SPINRAZA.com/HowSPINRAZAWorks

Please see additional Important Safety Information on page 23 and click for full Prescribing Information.

The effect of SPINRAZA has been studied for more than 8 years in the largest SMA clinical development program to date

ENDEAR pivotal study

Studied survival without permanent ventilation and motor milestone response in 121 children with early-onset SMA

CHERISH pivotal study

Studied changes in motor function in 126 nonambulatory individuals with later-onset SMA

NURTURE supportive study

Studied survival without respiratory intervention in 25 infants who have yet to show symptoms of SMA

CS2/CS12 supportive study

Studied overall safety and changes in motor function in 28 ambulatory and nonambulatory individuals with later-onset SMA

This list does not include all SPINRAZA clinical trials.

SELECTED IMPORTANT SAFETY INFORMATION

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Study information

SPINRAZA studies use scales to track improvements, but these scales can often be complex or unfamiliar. Definitions for all the scales in this brochure are listed for you below.

Motor function scales

// WHO motor milestones

The World Health Organization motor milestones are a set of 6 milestones—such as sitting without support, hands-and-knees crawling, and walking alone—that healthy children are expected to achieve by 2 years of age.

// HINE-2

Section 2 of the Hammersmith Infant Neurological Examination is used to assess improvements in motor function. The scale includes activities such as head control, independent sitting, and standing.

// HFMSE

The Hammersmith Functional Motor Scale—Expanded is an SMA-specific scale used to measure how well someone can do daily tasks like lifting their head, sitting, and stair-climbing. Each item is scored from 0 to 2, with a maximum score of 66.

// RULM

The Revised Upper Limb Module is a scale used to measure upper limb strength and function. It measures how well someone can do daily tasks like pushing buttons and opening containers. Each item is scored from 0 to 2, with a maximum score of 37.

// ULM

The Upper Limb Module is just a slightly older version of the RULM. See definition above. It is scored from 0 to 18 points, with higher scores indicating better function.

// 6MWT

The 6-Minute Walk Test is used to measure how far a person can walk in 6 minutes.

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SPINRAZA® (nusinersen) injection 12 mg/5 mL

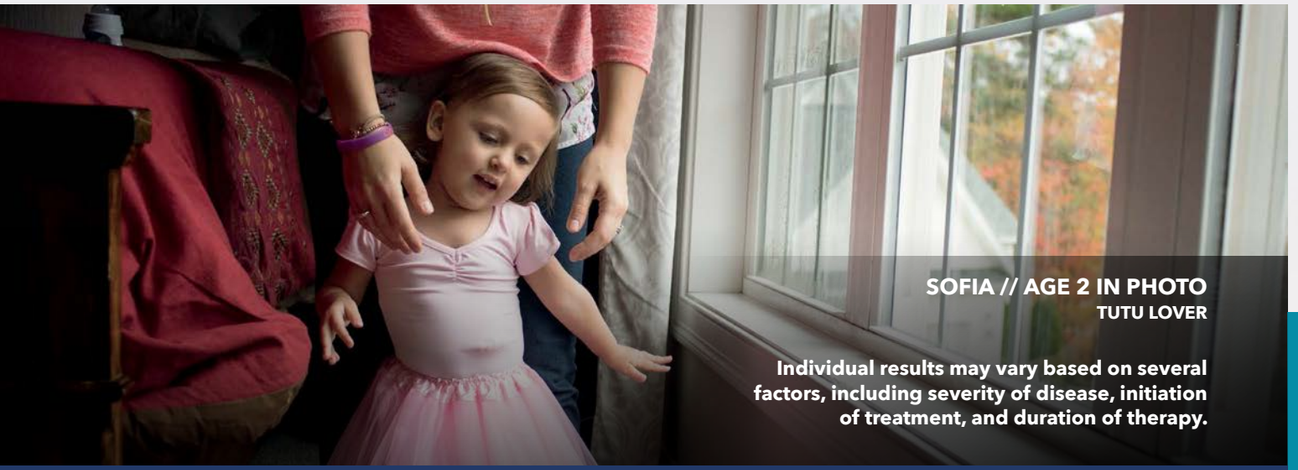
On average, children with SMA experienced improved survival and motor function

// **Who:** 121 children 7 months of age and younger

// **Study time:** 13 months

// **Safety:** The most common side effects were lower respiratory infection (55%) and constipation (35%). Serious adverse reactions of atelectasis (collapsed lung) were more frequent in the SPINRAZA-treated group (18%) than in the control group (10%)

// **Primary outcomes:**
- Time to death or use of permanent assisted ventilation
- The proportion of children who had an improvement in motor milestones, according to HINE-2



SOFIA // AGE 2 IN PHOTO
TUTU LOVER

Individual results may vary based on several factors, including severity of disease, initiation of treatment, and duration of therapy.

SELECTED IMPORTANT SAFETY INFORMATION

Increased risk of bleeding complications has been observed after administration of similar medicines. Your healthcare provider should perform blood tests before you start treatment with SPINRAZA and before each dose to monitor for signs of these risks. Seek medical attention if unexpected bleeding occurs.

On average, those with Type 1 SMA showed improvements in motor milestones that are rarely, if ever, achieved in untreated children

51% vs 0% untreated were motor milestone responders (children who improved in the categories listed below) according to HINE-2* at 13 months. Motor milestones included:

Head control

Rolling

Independent sitting

Standing

*A child who has had at least a 2-point increase in ability to kick, or at least a 1-point increase in categories like head control, rolling, sitting, crawling, standing, or walking.

47% reduced risk of mortality or permanent ventilation in the SPINRAZA group

Please see additional Important Safety Information on page 23 and click for full Prescribing Information.

SPINRAZA® (nusinersen) injection 12 mg/5 mL

Presymptomatic infants with SMA experienced significant improvements in survival and motor function

- **Who:** 25 infants 6 weeks of age and younger who had not yet shown symptoms of SMA
- **Study time:** This supportive study is ongoing
- **Primary outcome:** Time to death or respiratory intervention
- **Secondary outcome:** The effect SPINRAZA has on reaching WHO motor milestones
- **Limitations:** Small number of participants. The study is open-label, which means all infants received SPINRAZA
- **Safety:** Consistent with the SPINRAZA prescribing information

Individual results may vary based on several factors, including severity of disease, initiation of treatment, and duration of therapy. Some individuals featured may be involved in ongoing clinical trials.

SELECTED IMPORTANT SAFETY INFORMATION

Increased risk of kidney damage, including potentially fatal acute inflammation of the kidney, has been observed after administration of similar medicines. Your healthcare provider should perform urine testing before you start treatment with SPINRAZA and before each dose to monitor for signs of this risk.

After 14 months:

- An interim analysis performed after all infants had received SPINRAZA for at least 14 months (median, 25 months; range, 14 to 34 months), 100% (25/25) of infants were alive without the need for permanent respiratory intervention, 100% (25/25) were sitting without support, 88% (22/25) were walking with assistance, and 77% (17/22) of infants were walking independently.

After nearly 5 years of follow-up*:

- 100% (25/25) of presymptomatic infants were alive without permanent ventilation after a median follow-up of 4.9 years in the study. 84% (21/25) never required respiratory intervention.†

The majority of infants achieved the following WHO motor milestones at age-appropriate times:

100%

25 out of 25 were sitting without support

96%

24 out of 25 were walking with assistance

92%

23 out of 25 were walking independently

*Median, 4.9 years; range, 3.9-5.7 years.

†Respiratory intervention was defined as ventilation for ≥6 hours/day continuously for ≥7 days, or tracheostomy. Permanent intervention is defined as = or > 16 hours/day continuously for = or > 21 days in absence of an acute reversible event or tracheostomy.

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SPINRAZA® (nusinersen) injection 12 mg/5 mL

On average, individuals treated with SPINRAZA who have later-onset SMA experienced improvements in overall motor function

// **Who:** 126 children ages 2-9 years with later-onset SMA

// **Study time:** 15 months

// **Primary outcome:** Changes in motor function, measured with HFMSE

// **Secondary outcomes:** Changes in upper limb function, measured with RULM and percentage of individuals who had a clinically meaningful (3 or more points) improvement from baseline in HFMSE score

// **Limitation:** The dosing schedule was different from the approved SPINRAZA dosing schedule

// **Safety:** The most common side effects were fever (43%), headache (29%), vomiting (29%), and back pain (25%)

SELECTED IMPORTANT SAFETY INFORMATION

The most common side effects of SPINRAZA include lower respiratory infection, fever, constipation, headache, vomiting, back pain, and post-lumbar puncture syndrome.

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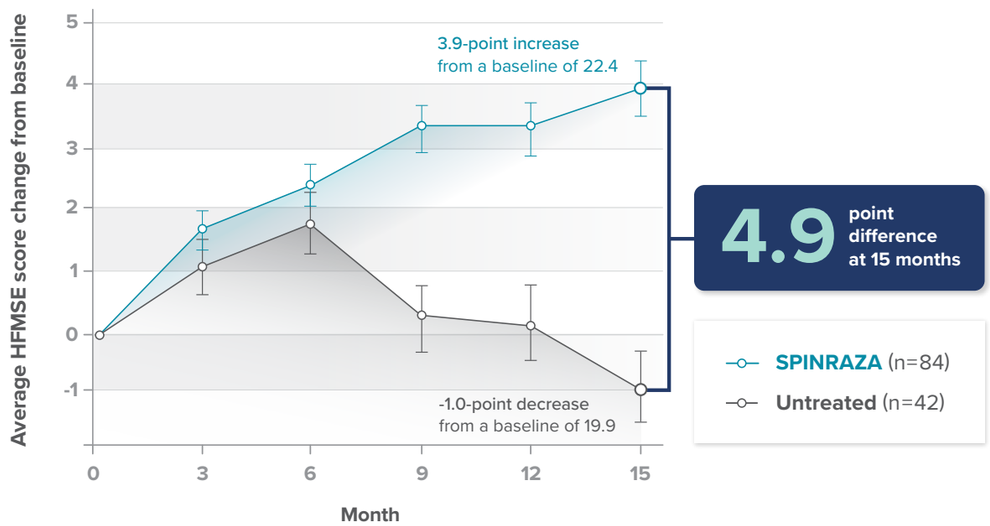
Primary outcome: Average change from baseline in HFMSE total score at 15 months versus untreated individuals



Those treated with SPINRAZA significantly improved their motor function

Motor function began to steadily improve in just 6 months compared to the untreated group

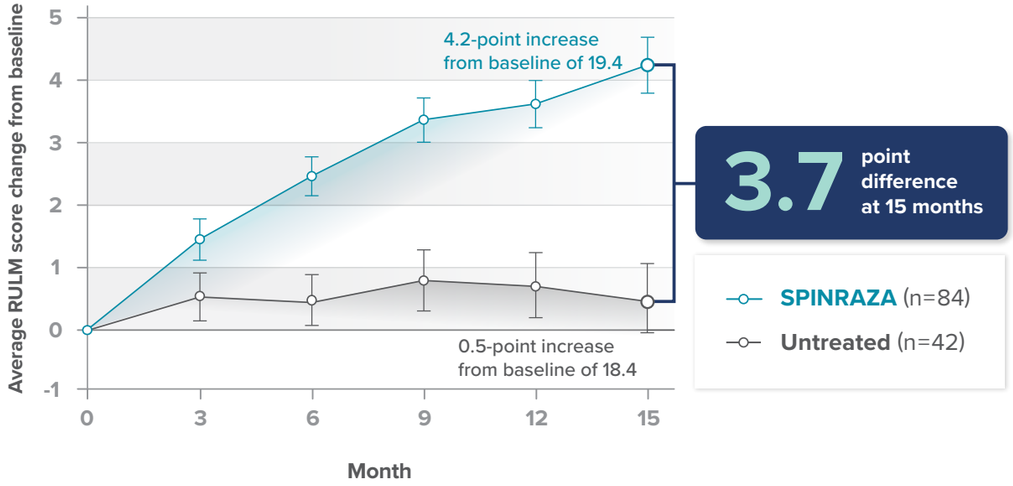
Please see additional Important Safety Information on page 23 and click for full Prescribing Information.

A 1- or 2-point improvement in HFMSE is considered a positive change, and 3 or more point improvement a clinically meaningful change

Secondary outcome: Percentage of individuals with a 3 or more point increase from baseline in HFMSE score

Treated with SPINRAZA	Untreated
56.8% (n=84)	**26.3%** (n=42)

Secondary outcome: Average change from baseline in upper limb function score at 15 months



Those treated with SPINRAZA on average increased their upper limb function

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SPINRAZA® (nusinersen) injection 12 mg/5 mL

Individuals within this study, on average, showed improvements in overall motor function and walking ability

// **Who:** 28 individuals ages 2 to 16 years old with later-onset SMA treated with SPINRAZA

// **Study time:** Approximately 3 years

// **Primary outcome:** Safety of SPINRAZA

// **Other outcomes:** The safety and longer-term effects of SPINRAZA on overall motor function, upper limb function, and walking ability were also studied

// **Limitations:** The dosing was different than the approved SPINRAZA schedule and these studies had no controls and small number of participants

// **Safety:** Side effects were similar with those reported in the pivotal trials

SELECTED IMPORTANT SAFETY INFORMATION

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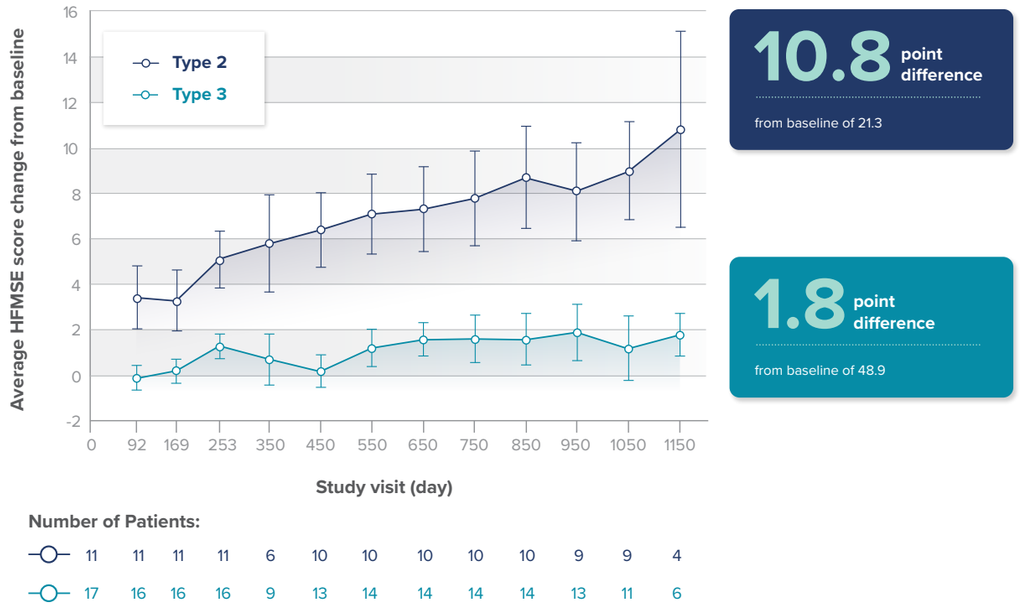
Individuals treated with SPINRAZA, on average, saw increases in motor function over 3 years



10.8 point difference

from baseline of 21.3

1.8 point difference

from baseline of 48.9

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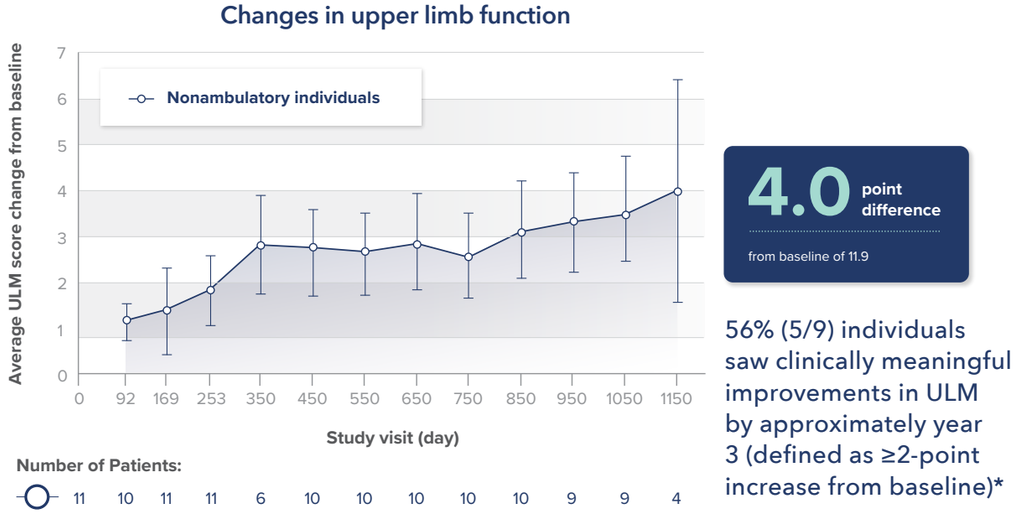
CS2/CS12 SUPPORTIVE STUDY

On average, nonambulatory individuals treated with SPINRAZA saw improvement from baseline in their upper limb function



4.0 point difference

from baseline of 11.9

56% (5/9) individuals saw clinically meaningful improvements in ULM by approximately year 3 (defined as ≥2-point increase from baseline)*

*Due to a gap between study visits, some data points do not contain results for all children.

SELECTED IMPORTANT SAFETY INFORMATION

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SPINRAZA® (nusinersen) injection 12 mg/5 mL

100% (8/8) of people who had the ability to walk achieved improvements in their walking distance by approximately year 3 (improvements defined as ≥30 meters from baseline)†

†Due to a gap between study visits, some data points do not contain results for all children.

AVERAGE WALKING DISTANCE INCREASED

301 feet (92 m)

1 of the 11 patients with Type 2 SMA gained the ability to walk.

2 of the 4 patients with Type 3 SMA regained the ability to walk.

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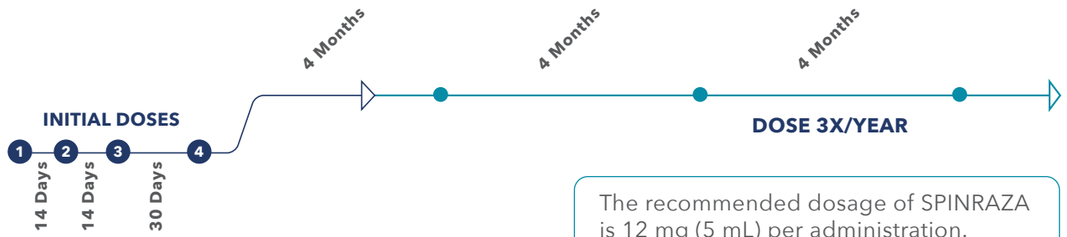
SPINRAZA® (nusinersen) injection 12 mg/5 mL

Dosing designed to get your body the medicine it needs, when it needs it



The recommended dosage of SPINRAZA is 12 mg (5 mL) per administration.

SPINRAZA is an intrathecal injection, or an injection into the fluid in the spine, given by a healthcare provider (HCP) experienced in performing lumbar punctures.

The dosing schedule begins with 4 initial loading doses; the first 3 occur in 14-day intervals and the fourth dose 30 days after the third dose. After these initial doses, SPINRAZA is administered in maintenance doses 3 times a year. Ask your HCP for additional information about the dosing schedule and treatment procedure.

Blood and urine testing

Because an increased risk of bleeding and kidney damage has been seen with similar medications, individuals taking SPINRAZA may be at similar risk. It is recommended your HCP perform blood and urine testing once before starting treatment and again before each dose to monitor for signs of these risks.

There are SPINRAZA treatment centers all across the US

Find one at SPINRAZA.com/locator

Please see additional Important Safety Information on page 23 and click for full Prescribing Information.

SMA360°
Your SPINRAZA circle of support

Biogen's SMA360° support program provides certain services that address nonmedical barriers to access.*

- Treatment coordination
- SPINRAZA education
- Insurance benefits investigation
- Financial assistance for eligible individuals

*SMA360° services from Biogen are available only to those who have been prescribed SPINRAZA. SMA360° is intended for US residents only.

See all of the SMA360° support services at SPINRAZA.com/support

SMA360™
Support services from Biogen

Join our community.

Speak with a Lead Case Manager
1-844-477-4672 Monday through Friday from 8:30 AM to 8:00 PM ET

With SMA 360°, you get a full SMA circle of support
Use your phone's camera to scan this code to learn more

"The Family Access Managers (FAMs) do a lot of coordinating with our care team, a lot of organization, all the logistics: we just show up, which has been really nice."

–Carlee's Mom

SPINRAZA® (nusinersen) injection 12 mg/5 mL

INDICATION

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IMPORTANT SAFETY INFORMATION

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Biogen