SPINRAZA® (nusinersen) injection 12 mg/5 mL

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

4,600+ adults have been treated with SPINRAZA worldwide*

See how SPINRAZA may help.

*Pivotal trials did not include adult patients with spinal muscular atrophy (SMA). 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.

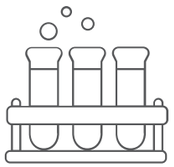
Please see additional Important Safety Information on page 27 and full Prescribing Information.

People living with SMA will experience motor function loss throughout their lives

SMA is a genetic disorder caused by insufficient levels of survival motor neuron (SMN) protein, a protein that is needed for motor neurons to survive. Motor neurons send signals to muscles from the central nervous system (CNS). Without sufficient SMN protein, motor neurons die off. With no signals from the CNS, muscles get weaker and weaker.

Natural history shows that all people living with SMA will experience motor function loss throughout their lives. For people living with later-onset SMA, these losses may become more noticeable with age.

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.

It is difficult to know when you will experience motor function loss

The rate of motor function loss varies from person to person, and it is difficult to predict when someone living with SMA will experience motor function loss. Although some people may experience periods where motor function appears stable, people living with later-onset SMA will experience motor function loss over time. Below are some key facts about SMA disease progression.

Motor function loss can become more obvious over time.

It can be hard to notice motor function loss with annual checkups because it may be happening slowly. But that doesn't mean it isn't happening. Such loss becomes more obvious as it continues over time.

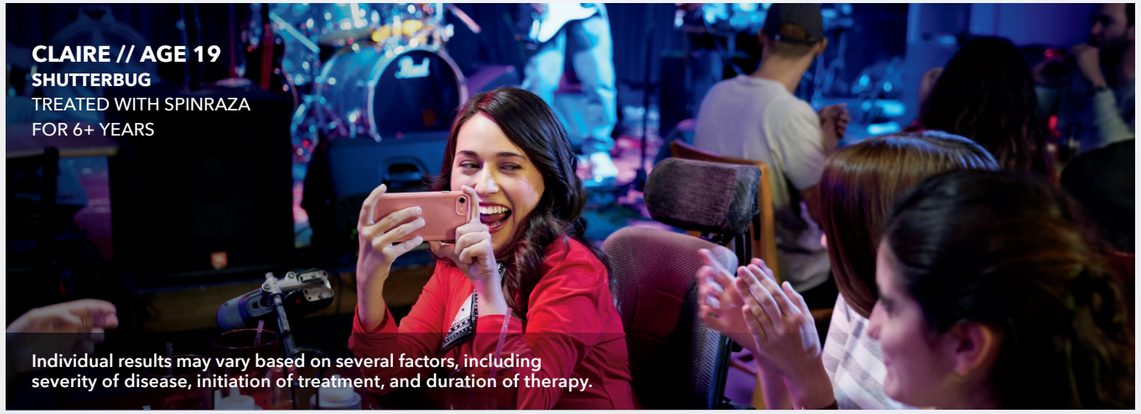
Type and age aren't true predictors of motor function loss.

Because everyone experiences SMA differently, it is difficult to predict when motor function loss will happen or even who will experience it.

Talk to your doctor about changes in your motor function.

SPINRAZA® (nusinersen) injection 12 mg/5 mL

SPINRAZA has extensive real-world experience across a broad range of ages



13,000+

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

4,600+ adults

have been treated with SPINRAZA worldwide*

*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

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.

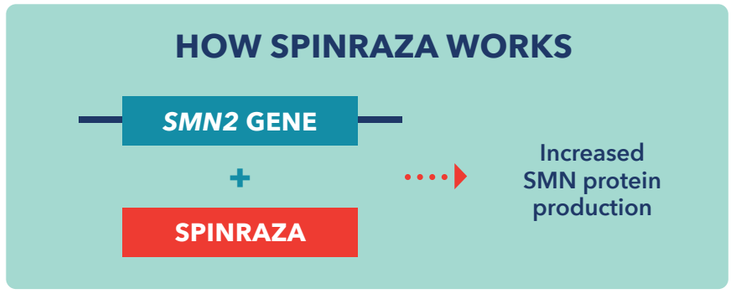
SMA is a disease of the CNS. SPINRAZA is delivered directly into the CNS

People with SMA can't generate enough SMN protein, the protein their motor neurons need to function. 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.

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 of the SMN protein that is needed for motor neurons to survive.



Watch a video about how SPINRAZA works at SPINRAZA.com/HowSPINRAZAWorks

Please see additional Important Safety Information on page 27 and full Prescribing Information.

SPINRAZA® (nusinersen) injection 12 mg/5 mL

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

Understanding Clinical Development Programs

Pivotal study: A study used to get FDA approval for a drug. The study is conducted by the company seeking approval for the drug. It is designed so that we are sure that the efficacy and safety we see in the study are because of the drug. This is the strongest type of study.

Supportive study: A study that is not needed to gain FDA approval, but it provides additional information on a drug's safety and efficacy.

Independent study: A study that is not conducted or controlled by a drug company.

Observational study: A study that can be observed as a part of routine medical care used to gain more knowledge about a drug after FDA approval. This type of study is valuable, but not as strong as a pivotal study.

Controls: People who don't get the study drug. Controls can be compared with people who did get the study drug.

Retrospective design: A retrospective study uses the medical records to look over past experience.

Outcomes

Primary: Studies are often designed to answer 1 main question, or outcome. This is known as the primary outcome. This question will determine how many patients are enrolled. It will also affect how the findings are analyzed. Results for this type of outcome are more conclusive than those for secondary outcomes.

Secondary: Aside from the main outcome, studies also ask other questions. These are called secondary outcomes. This is done to gather more information on how the drug works. The study is not built around these secondary questions, so the results can be less conclusive or inconclusive.

This list does not include all SPINRAZA clinical trials.

Please see additional Important Safety Information on page 27 and full Prescribing Information.

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

// **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.

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.

These are not all of the possible side effects of SPINRAZA. Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

Before taking SPINRAZA, tell your healthcare provider if you are pregnant or plan to become pregnant.

This information is not intended to replace discussions with your healthcare provider.

SPINRAZA® (nusinersen) injection 12 mg/5 mL

Individuals with later-onset SMA experienced improvements in overall motor function

// **Who:** 126 individuals with later-onset SMA, aged 2 to 9 years

// **Study time:** 15 months

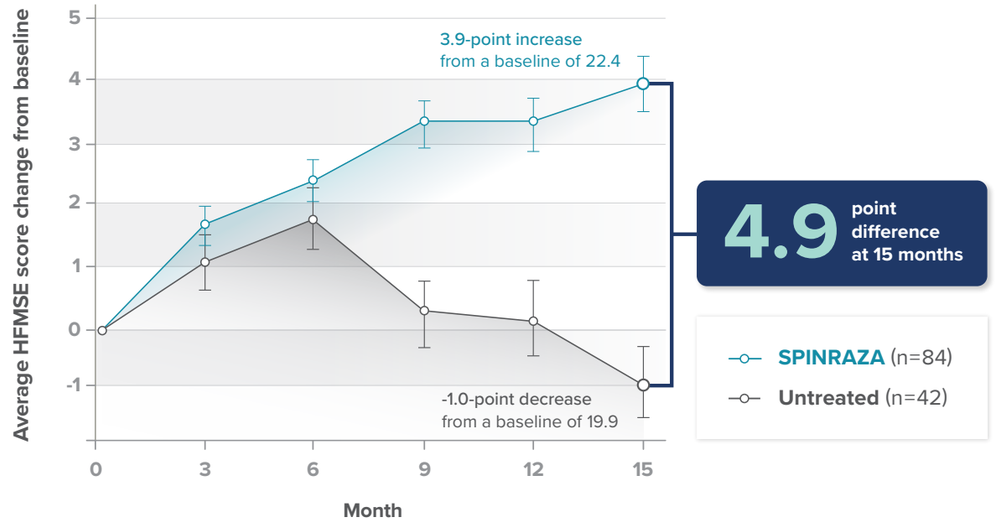
// **Primary outcome:** Changes in motor function measured on the HFMSE

// **Secondary outcomes:** Changes in upper limb function measured on the RULM and percentage of individuals who had a clinically meaningful (≥3-point) improvement from baseline in HFMSE score

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

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

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 with the untreated group

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.

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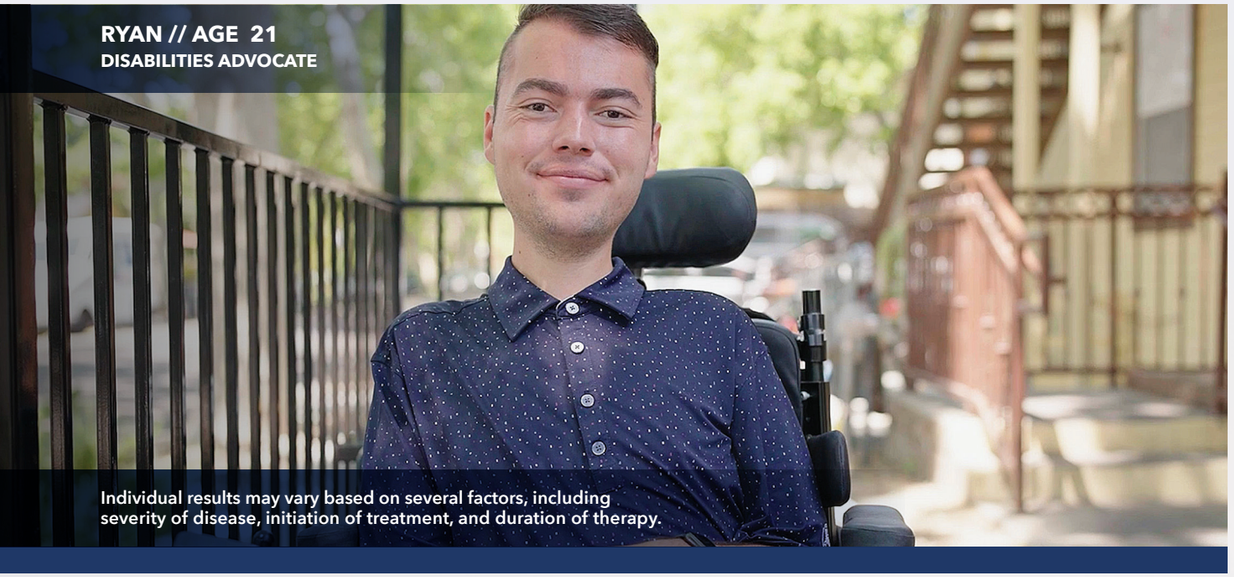
SPINRAZA® (nusinersen) injection 12 mg/5 mL

HFMSE scores showed a clinically meaningful change

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

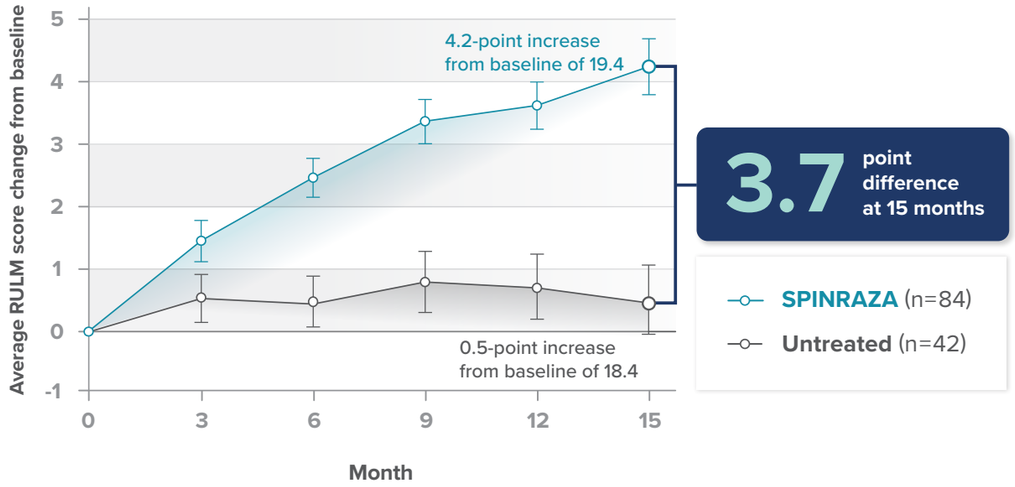
56.8% of the 84 adults treated with SPINRAZA **vs** **23.3%** of the 42 adults in the untreated control group saw a clinically meaningful change in HFMSE scores



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

Please see additional Important Safety Information on page 27 and full Prescribing Information.

Average revised upper limb function scores improved at 15 months



Revised upper limb module (RULM) scores range from 0 to 37, with higher scores indicating better function

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.

SPINRAZA® (nusinersen) injection 12 mg/5 mL

On average, individuals with later-onset SMA showed greater improvements in walking and overall motor function

// **Who:** 28 individuals aged 2 to 15 years old with later-onset SMA treated with SPINRAZA

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

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

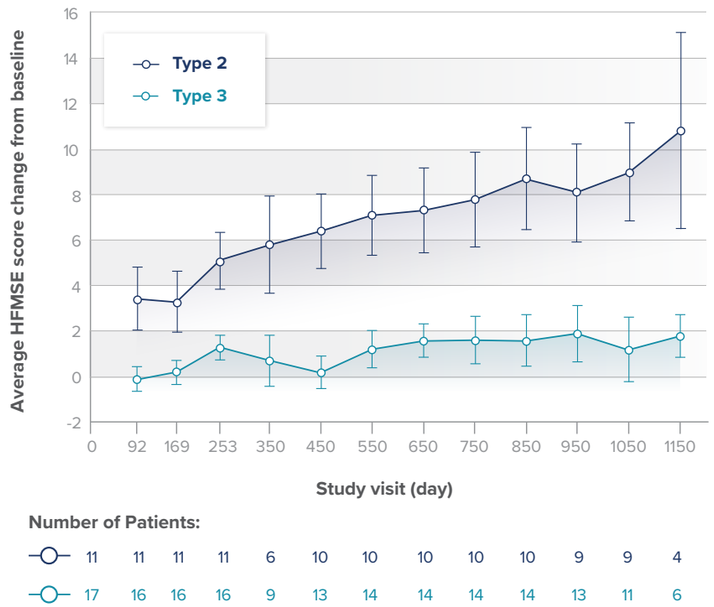
// **Other outcomes:** The safety and longer-term effects of SPINRAZA on overall motor function, upper limb function, and walking ability were also studied

// **Limitations:** The dosing was different than the approved SPINRAZA schedule. Additionally, these studies had a small number of participants and did not have untreated control groups

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

On average, individuals treated with SPINRAZA saw greater increases in motor function over 3 years

Average changes in motor function*



10.8 point difference

from baseline of 21.3

1.8 point difference

from baseline of 48.9

*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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These are not all of the possible side effects of SPINRAZA. Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

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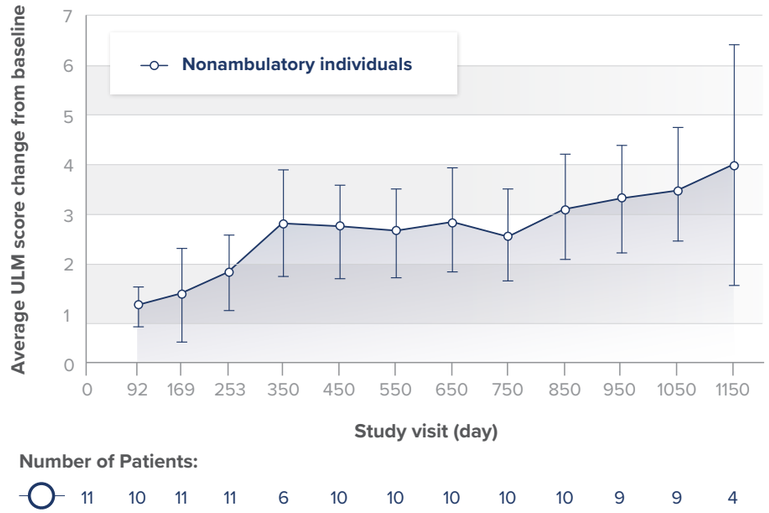
Please see additional Important Safety Information on page 27 and full Prescribing Information.

CS2/CS12 SUPPORTIVE STUDY

Nonambulatory individuals treated with SPINRAZA saw improvement from baseline in their upper limb function

Changes in upper limb function*



4.0 point difference

from baseline of 11.9

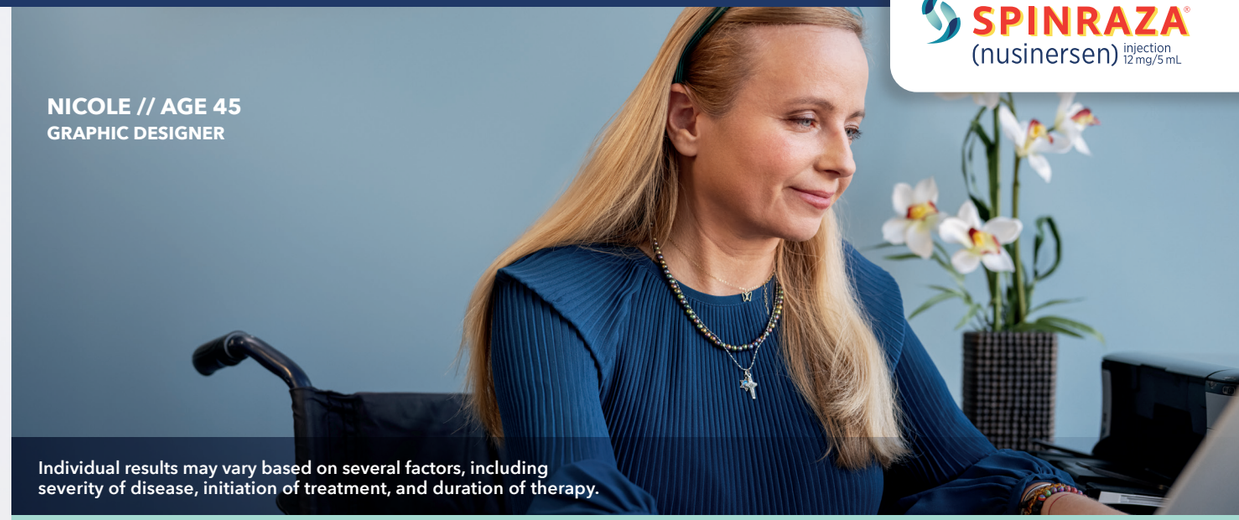
56% (5/9) of individuals saw clinically meaningful improvements in ULM by approximately year 3 (defined as ≥2-point increase from baseline)

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

SELECTED IMPORTANT SAFETY INFORMATION

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.

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.

Please see additional Important Safety Information on page 27 and full Prescribing Information.

SPINRAZA® (nusinersen) injection 12 mg/5 mL

An independent, observational study in adults ages 16-65 years with later-onset SMA

// **Who:** 139 adults ages 16-65 years with later-onset SMA, 2 with Type 1, 47 with Type 2, 89 with Type 3, and 1 with Type 4

// **Study time:** 14 months

// **Primary outcome:** Changes in motor function at 6, 10, and 14 months, measured on HFMSE

// **Secondary outcomes:**

- Changes in upper limb function at 6, 10, and 14 months, measured on RULM
- Changes in walking ability measured on 6MWT

// **Limitations:**

- **No controls:** Controls are people who don't get the study drug. Controls can be compared with people who do get the study drug. This study did not have an untreated control group
- **No blinding:** Blinding is when the doctors and nurses caring for those in the trial don't know who is getting the study drug. This study was not blinded
- **Measured for primary outcome only:** Remember, primary outcomes answer the main question, or outcome, of a study. Secondary outcomes provide answers to other questions in a study

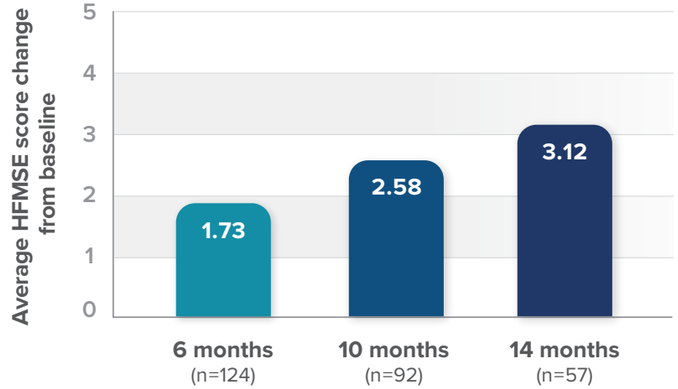
Safety:
Most of the side effects were consistent with those in the SPINRAZA pivotal trials.
The most common side effects in the trial were headache, back pain, and nausea.
Others reported were:

- Bladder disorder not otherwise specified
- Diffuse pain
- Infection
- Constipation
- Meningitis, aseptic
- Vertigo
- Ear infection

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.

Primary outcome: Average change in HFMSE scores from baseline



Patients who achieved a clinically meaningful ≥3-point increase in HFMSE score*

28% (35/124) at 6 months

35% (33/92) at 10 months

40% (23/57) at 14 months

The number of individuals at each assessment varied. This is because 4 individuals withdrew from the study, and some had either missed assessments or had not received treatment long enough to be included.

*Exploratory endpoint.

Most adults stabilized or significantly improved their motor function. Some adults did not improve or maintain motor function

- Those with less severe symptoms at the start of the trial had greater improvements in motor function
- **11%** (14/124) showed worsening motor function while on treatment

Please see additional Important Safety Information on page 27 and full Prescribing Information.

SPINRAZA® (nusinersen) injection 12 mg/5 mL

Secondary outcome: Average change from baseline in RULM

On average, adults stabilized or improved their upper limb function
After 6 months of treatment:

23% (28/120)
meaningfully improved their current level of strength and of these, **75% (21/28)** remained stable after 14 months of treatment

61% (74/120)
stabilized their current level of strength

15% (18/120)
showed a decline of 1 point or more, and 8% (10/120) showed a decline of 2 points or more

Please see additional Important Safety Information on page 27 and full Prescribing Information.

Secondary outcome: Average change from baseline in 6MWT scores of ambulatory adults with Type 3 SMA

73 ft
(22.1 m)

AT 6 MONTHS
(n=47)

102 ft
(31.1 m)

AT 10 MONTHS
(n=37)

151 ft
(46.0 m)

AT 14 MONTHS
(n=25)

SELECTED IMPORTANT SAFETY INFORMATION

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These are not all of the possible side effects of SPINRAZA. Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

SPINRAZA® (nusinersen) injection 12 mg/5 mL

A retrospective, observational study in adults ages 18-72 with later-onset SMA

// **Who:** 116 adults ages 18-72 years with later-onset SMA: 13 with Type 2 and 103 with Type 3

// **Study time:** 14 months. Assessments were made at 6, 10, and 14 months

// **Primary outcomes:** Changes in overall motor function measured by HFMSE, changes in upper limb function measured by RULM, and changes in walking ability measured by 6MWT

// **Limitations:**

- **No controls:** Controls are people who don't get the study drug. Controls can be compared with people who do get the study drug. This study did not have an untreated control group
- **Retrospective design:** A retrospective study uses the medical records and information of those who previously took the drug
- **Missing data for some outcomes:** Missing data may impact a study's conclusion
- **Small number of patients with SMA Type 2:** Of the 116 adults who participated in the study, 13 had SMA Type 2
- These limitations may have affected the outcomes

Safety: No new side effects were identified in this study; those that were reported were consistent with the safety profile of SPINRAZA. **The most common side effects were headache and back pain.** Additionally:

- **41.4% of patients** reported a side effect
- **Most headaches were generally mild to moderate** and went away spontaneously in a few days
- **5 patients were hospitalized for headache**
- 2 patients stopped therapy at 6 months. The reasons were that they felt no improvement and that they were unable to take the therapy

Please see additional Important Safety Information on page 27 and full Prescribing Information.

Primary outcome 1: Median change from baseline in HFMSE scores of adults with later-onset (Type 3) SMA

AT 6 MONTHS | +1 point improvement in half of the 103 adults

AT 10 MONTHS | +2 point improvement in half of the 75 adults

AT 14 MONTHS | +3 point improvement in half of the 46 adults

Adults with SMA Type 3 saw significant improvement in motor function as early as 6 months

Median is the middle value of a range of numbers.

SELECTED IMPORTANT SAFETY INFORMATION

Before taking SPINRAZA, tell your healthcare provider if you are pregnant or plan to become pregnant.

This information is not intended to replace discussions with your healthcare provider.

SPINRAZA® (nusinersen) injection 12 mg/5 mL

Primary outcome 2: Median change from baseline in RULM score in nonambulatory adults with Type 3 SMA

AT 6 MONTHS | function was maintained in at least half of the 51 adults

AT 10 MONTHS | +1 point improvement in half of the 33 adults

AT 14 MONTHS | +2 point improvement in half of the 19 adults

Nonambulatory adults with Type 3 SMA saw significant improvements in upper limb strength and motor function.

When adults with Type 3 SMA were analyzed, those who could walk (ambulatory) did not have an improvement at any time point (0 at all time points).

Primary outcome 3: Median change from baseline in 6MWT scores of ambulatory adults with Type 3 SMA

36 ft
(11 m)

AT 6 MONTHS
(n=48)

82 ft
(25 m)

AT 10 MONTHS
(n=35)

66 ft
(20 m)

AT 14 MONTHS
(n=24)

The majority of adults saw clinically meaningful changes in at least 1 of 3 types of motor function at month 14

Meaningful change can be described as the following:

- **+3 points on HFMSE,** which occurred in 49% of adults by month 14
- **+2 points on RULM,** which occurred in 35% of adults by month 14
- **+98 ft (30 m) on 6MWT,** which occurred in 42% of ambulatory adults by month 14

Median is the middle value of a range of numbers.

SELECTED IMPORTANT SAFETY INFORMATION

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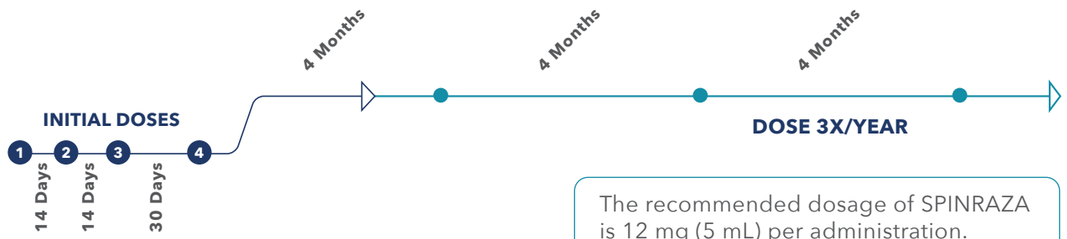
Please see additional Important Safety Information on page 27 and full Prescribing Information.

SPINRAZA® (nusinersen) injection 12 mg/5 mL

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

Staying on time with your treatment can help you get the most out of SPINRAZA

Here are a few things to consider:

- ☑ Understand your health plan's coverage and approval criteria (genetic testing, motor function testing, labs, clinical notes)
- ☑ Communicate with your care team and FAM to ensure timely submission of authorizations
- ☑ Prioritize and track clinic, physical therapy, and dosing appointments

There are SPINRAZA treatment centers all across the US

FIND ONE AT
SPINRAZA.com/locator

Please see additional Important Safety Information on page 27 and 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
- Insurance benefits investigation
- SPINRAZA education
- 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
1-844-4SPINRAZA
1-844-477-4672
Monday through Friday
from 8:30 AM to 8:00 PM ET

With SMA360°, you get a full circle of support

SPINRAZA® (nusinersen) injection 12 mg/5 mL

INDICATION

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

IMPORTANT SAFETY INFORMATION

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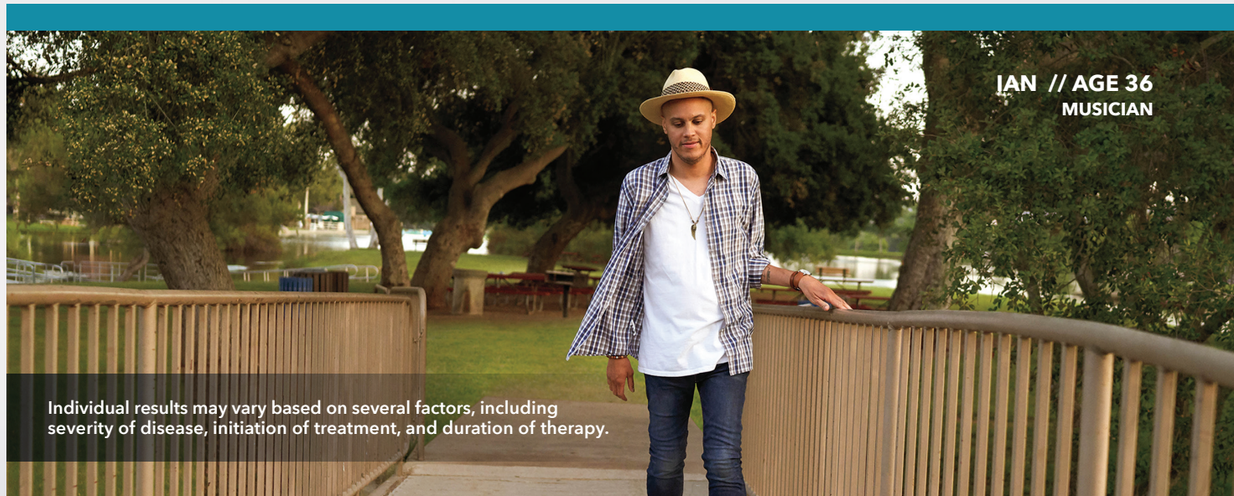
Please see full Prescribing Information.

This information is not intended to replace discussions with your healthcare provider.



SELECTED IMPORTANT SAFETY INFORMATION

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Please see additional Important Safety Information on page 27 and full Prescribing Information.

225 Binney Street, Cambridge, MA 02142

SPINRAZA® (nusinersen) injection 12 mg/5 mL

Biogen