SPINRAZA® (nusinersen) FREQUENTLY ASKED QUESTIONS

Please remember your healthcare provider (HCP) is your primary resource for information about spinal muscular atrophy (SMA) and SPINRAZA

LAUREN // AGE 20
LATER-ONSET SMA
TREATED WITH SPINRAZA

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.

INDICATION
SPINRAZA 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 14 and click for full Prescribing Information.

WHAT YOU'LL FIND INSIDE

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 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.

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STEPHEN // AGE 38
LATER-ONSET SMA
TREATED WITH SPINRAZA

POTENTIAL BENEFITS AND RISKS

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01 What are the potential benefits of treatment?

SPINRAZA is the only FDA-approved therapy for all patients with SMA regardless of age. The effect of SPINRAZA on survival, overall motor function, and walking ability had been studied in the longest clinical trial program in SMA to date.

The pivotal trial, ENDEAR, studied 121 infants 7 months of age and younger with Type 1 (early-onset) SMA. The pivotal trial, CHERISH, evaluated 126 individuals aged 2 to 9 years with later-onset SMA. The supportive trial, NURTURE, studied 25 infants 6 weeks of age and younger who had not yet shown symptoms of SMA.

SPINRAZA has also been studied in real-world, independent, observational studies in adults up to age 72.

SPINRAZA pivotal studies included patients from 3 days to 16 years of age at first dose but did not include sufficient numbers of subjects aged 65 and older to determine whether they respond differently from younger patients.

02 What are the risks and common side effects of SPINRAZA?

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

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. Speak with your HCP for medical advice about side effects.

03 How many people with SMA have been treated with SPINRAZA?

More than 11,000 people have been treated with SPINRAZA worldwide, including 3700 adults.

*Based on commercial patients, early access patients, and clinical trial participants as of July 2021.

SELECTED IMPORTANT SAFETY INFORMATION

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04 What improvements were observed in infants treated with SPINRAZA?

The pivotal trial, ENDEAR, studied 121 infants 7 months of age and younger with Type 1 (early-onset) SMA over 13 months. The primary outcomes were time to death or use of permanent assisted ventilation and the proportion of responders (or number of children) who showed an improvement in motor milestones according to Section 2 of the Hammersmith Infant Neurological Examination (HINE).

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

Children with Type 1 SMA showed improvements in motor milestones that are rarely, if ever, achieved in untreated children. 51% of children treated with SPINRAZA vs 0% untreated were motor milestone responders* according to HINE 2 at 13 months. Motor milestones included head control, rolling, independent sitting, and standing. There was a 47% reduced risk of mortality or permanent ventilation in the SPINRAZA group versus the untreated group. Also, there was a 63% reduced risk of mortality in the SPINRAZA group.

*A child who 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

Visit SPINRAZA.com/earlyonset to see more results of the ENDEAR clinical study.

05 What achievements were observed in presymptomatic infants treated with SPINRAZA?

The ongoing, supportive trial, NURTURE, studied 25 infants 6 weeks of age and younger who had not yet shown symptoms of SMA. The primary outcome was time to death or respiratory intervention and the secondary outcome was the effect SPINRAZA has on reaching World Health Organization (WHO) motor milestones. The limitations of the study are the small number of participants and the study is open-label, which means all infants received SPINRAZA. Safety is consistent with the SPINRAZA prescribing information.

Visit SPINRAZA.com/presymptomatic to see the results of the NURTURE clinical study.

SELECTED IMPORTANT SAFETY INFORMATION
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06 Were motor function improvements also found in individuals with later-onset (Types 2 and 3) SMA?

The pivotal trial, CHERISH, evaluated 126 individuals aged 2 to 9 years with later-onset SMA over 15 months. The primary outcome was change in motor function, measured with Hammersmith Functional Motor Scale–Expanded (HFMSE). The secondary outcomes were changes in upper limb function, measured with Revised Upper Limb Module (RULM) and percentage of individuals who had a clinically meaningful (3 or more points) improvement from baseline in HFMSE score. The limitation of the study was that the dosing schedule was different from the approved SPINRAZA dosing schedule. The most common side effects were fever (43%), headache (29%), vomiting (29%), and back pain (25%).

People treated with SPINRAZA had a 3.9-point increase from a baseline of 22.4 in HFMSE total score while untreated people saw a mean 1.0-point decrease from a baseline of 19.9. This means that those treated with SPINRAZA significantly improved their motor function.

The supportive trial, CS2/CS12, studied 28 individuals ages 2 to 16 years old with later-onset SMA over 3 years. The primary outcome was the safety of SPINRAZA. Other outcomes included the safety and longer-term effects of SPINRAZA on overall motor function, upper limb function, and walking ability. The limitations of the study were that the dosing was different than the approved SPINRAZA schedule and these studies had no controls. Side effects were similar to those reported in the pivotal trials.

Visit SPINRAZA.com/lateronset to see more results of the CHERISH and CS2/CS12 clinical studies.

07 I/my child take(s) a variety of medications each day. Is it still OK to take SPINRAZA?

There are no known drug-drug interactions and no contraindications in the SPINRAZA prescribing information. Your HCP can help answer questions regarding your/your child's specific medications and SPINRAZA.

08 How will I know if I am/my child is responding to treatment?

Your HCP can evaluate changes in motor function to determine how you are/your child is responding to treatment. We recommend working with your HCP to set expectations and establish treatment goals.

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PHYSICAL ASSESSMENTS

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01 What is the Hammersmith Infant Neurological Exam (HINE) Section 2?

Section 2 of the HINE is an assessment tool that uses a point system to measure progress in various categories of motor milestone development for infants between 2 and 24 months of age. The motor milestone categories include voluntary grasp, ability to kick, head control, rolling, sitting, crawling, standing, and walking. The score ranges from 0 to 26.

02 What is the Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND)?

The CHOP INTEND is a clinical scale that measures incremental motor function changes, such as increased movement, flexibility, or strength. In a clinical study, it is primarily used in infants with SMA who are 1 to 38 months of age or weak individuals with SMA Type 1 who have only achieved an infant's level of motor function. There are 16 motor function activities and each is scored on a scale from 0 to 4 with a total score range from 0 to 64.

03 What is the Hammersmith Functional Motor Scale–Expanded (HFMSE)?

The HFMSE is an assessment tool that uses a point system for measuring motor functions, such as standing, walking, stepping, and other movements. The HFMSE can be used to assess the motor function of individuals with later-onset (Types 2 and 3) SMA. It measures 33 items and the score ranges from 0 to 66, with a low score indicating poor motor function and a high score indicating higher motor function.

04 What is the 6-Minute Walk Test (6MWT)?

The 6MWT is a clinical test that measures ambulatory capacity and is a more dynamic assessment than most other motor function tests. Participants are instructed to walk as far as possible along a 25-meter course and return in the opposite direction for 6 minutes. The time it takes to complete each 25-meter segment and the total distance is recorded.

PHYSICAL ASSESSMENTS

05 What is the Revised Upper Limb Module (RULM)?

The RULM is an assessment tool that uses a point system to measure upper limb functions. It covers a wide spectrum of individuals with SMA, from weak and strong to ambulatory and nonambulatory. The RULM includes 20 tasks, such as raising arms above the head and lifting weighted objects. Scores can range from 0 (if all activities are failed) to 37 (if all activities are completed).

06 What is the difference between the RULM and the Upper Limb Module (ULM)?

The ULM is an assessment tool for weaker, nonambulatory individuals with SMA, while the RULM is a revised version of the ULM that covers stronger, ambulatory individuals as well.

07 Which physical assessments can measure my/my child's progress?

A trained HCP may perform different motor function assessments depending on your age and the severity of your SMA. For individuals who've only achieved an infant's level of motor skills, HCPs may use physical assessments like the HINE Section 2 and CHOP INTEND. In a clinical study, the HFMSE was used to evaluate general motor function and RULM evaluated upper limb function in both ambulatory and nonambulatory individuals. For individuals who can walk, a trained HCP may use the 6MWT to assess walking ability and endurance.

08 Can I perform any of these physical assessments at home?

The physical assessments mentioned above should be performed by trained clinical specialists (eg, physical therapists).

CLAIRE // AGE 19
LATER-ONSET SMA
TREATED WITH SPINRAZA

HOW SPINRAZA WORKS

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01 Does every person with SMA have a *survival motor neuron 2* (*SMN2*) gene?

All individuals with SMA have at least one copy of the *SMN2* gene, a closely related gene that is not believed to be affected by SMA. But *SMN2* does not produce enough survival motor neuron (SMN) protein to compensate for the missing or mutated *survival motor neuron 1* (*SMN1*) gene in individuals with SMA.

02 How does SPINRAZA work?

SMA is a disease of the central nervous system (CNS), caused by an insufficient amount of SMN protein in motor neurons. SPINRAZA is delivered directly to the CNS, where it increases SMN protein production, targeting an underlying cause of SMA.

Visit SPINRAZA.com/howitworks for more information about how SPINRAZA works, including a short video from an individual receiving treatment.

03 How long will I/my child receive SPINRAZA?

In the first 2 months, you/your child will receive 4 loading doses of SPINRAZA followed by maintenance doses administered once every 4 months. Your physician is the best person to answer this question, but remember that SMA is a chronic genetic disease.

SELECTED IMPORTANT SAFETY INFORMATION

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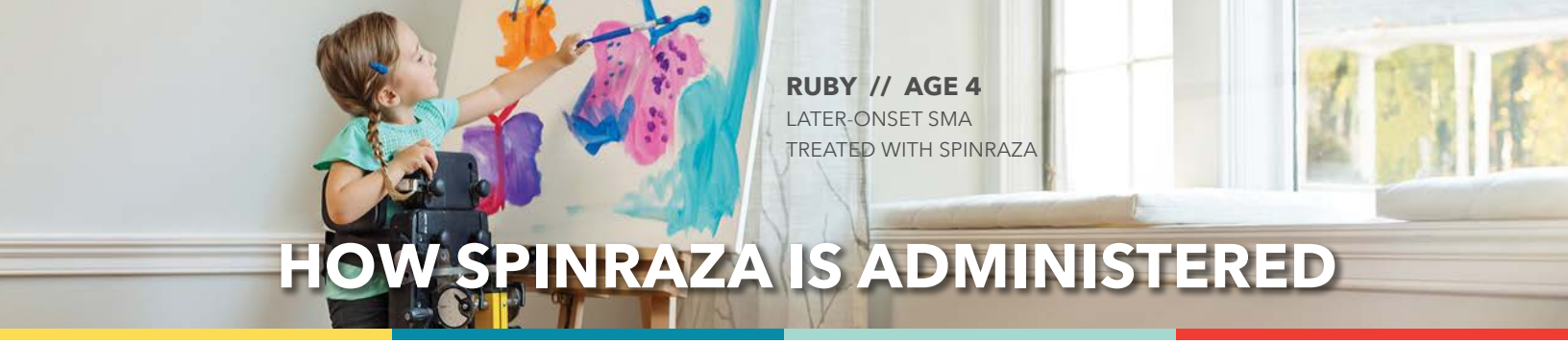

RUBY // AGE 4
LATER-ONSET SMA
TREATED WITH SPINRAZA

HOW SPINRAZA IS ADMINISTERED

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01 How is SPINRAZA administered?

SPINRAZA is given as an injection into cerebrospinal fluid (the fluid in the spine) via a medical procedure called an intrathecal injection, an established route of medication delivery used to target the central nervous system (CNS). Intrathecal injection is used across a broad range of diagnostic tests and therapies.

02 Why does SPINRAZA have to be injected into the back?

The lower back is the region used for intrathecal injection. This type of injection is performed to deliver medication directly into the CNS. SMA affects motor neurons in the CNS, which includes the brain and spinal cord. Medication delivered into the bloodstream often cannot reach motor neurons because the body keeps foreign substances out of the CNS via the blood-brain barrier.

Intrathecal injection of SPINRAZA into the cerebrospinal fluid (CSF) allows the medication to be distributed from the CSF to the target CNS tissues in order to circulate around the spine and brain.

03 Can you help me understand the treatment schedule for SPINRAZA?

The dosing schedule of SPINRAZA includes loading doses and maintenance doses that are administered at specific time intervals. The first 3 loading doses of SPINRAZA are administered every 14 days. The fourth and final loading dose is administered 30 days later. Maintenance doses are then administered every 4 months thereafter.

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WHAT YOU MAY EXPECT

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01 Who will perform the treatment procedure?

The treatment procedure is performed by, or under the direction of, HCPs experienced in performing lumbar punctures.

02 Is it possible that the individual receiving the injection will feel pain during and after the treatment procedure?

It's possible that the individual receiving the injection will feel pain during and after the injection. Local anesthetics and sedation may be used, depending on the individual's clinical condition. Discuss this with your/your child's HCP to determine the best plan.

03 Will I/my child require sedation as part of the treatment procedure?

Your HCP will determine if sedation will be necessary during the procedure. He or she is your primary resource when it comes to understanding the treatment procedure.

04 What lab tests are required?

It is recommended that your HCP perform blood and urine testing once before starting treatment with SPINRAZA and again before each dose. This is to monitor for potential risks of bleeding complications or kidney damage.

05 Will the treatment procedure require an overnight stay at the treatment center?

Your HCP will determine if an overnight stay is required.

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.

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WHAT YOU MAY EXPECT

06 Who will monitor me/my child during the procedure?

Your healthcare team will monitor you/your child during the procedure at the treatment center.

07 If there are any existing medical issues related to SMA, how might these factors affect receiving treatment with SPINRAZA?

Your HCP can best determine how any existing medical issues might affect the treatment change with SPINRAZA.

08 What typically happens during SPINRAZA intrathecal injection?

SPINRAZA is administered as an intrathecal injection over 1 to 3 minutes using a spinal needle. Ultrasound or other imaging techniques may be used to guide placement of the needle, particularly in younger patients. Your HCP is best equipped to address any questions or concerns about the procedure.

09 What happens if a scheduled treatment appointment is missed?

It's important to speak with your/your child's HCP in the event of a missed treatment appointment. He or she can determine the next course of action per the SPINRAZA Prescribing Information.

10 Why am I often being referred to my HCP for more information?

The information we provide is intended to help you understand SPINRAZA as it was evaluated in various clinical studies of individuals with SMA. SMA is a highly variable disease and experiences can differ. Your HCP is familiar with your medical history and is best equipped to address any specific questions or concerns.

SELECTED IMPORTANT SAFETY INFORMATION

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RESOURCES AND SUPPORT SERVICES

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01 How can I find an available treatment center near me?

The SPINRAZA Treatment Locator is a user-friendly search engine on SPINRAZA.com that can help you find the HCPs and treatment facilities closest to you that may be able to administer SPINRAZA. The search results show an interactive map with information about HCPs and facilities that have chosen to be listed.

Biogen is committed to making sure that individuals treated with SPINRAZA and their families are able to access treatment.

Before choosing a treatment center, be sure to speak with your primary HCP. To get started, visit SPINRAZA.com/locator.

02 Where can I learn more about SPINRAZA?

Biogen offers free educational events as part of the Support and Treatment Education Program (STEP) series. Learn more about SPINRAZA and connect with other caregivers and individuals with SMA. Get knowledge and support to help inform your treatment experience. Topics may include:

- Independent, Observational Adult Data
- Navigating Insurance Coverage
- Assessing Motor Function in SMA
- Understanding Intrathecal Injection
- Multidisciplinary Care Team in SMA
- Advocating for Optimal SMA Care
- What to Expect When Transitioning SMA Care

Call 1-866-955-9999 or visit SPINRAZA.com/event to find a webinar or live event near you.

Talk to your HCP to learn more about SPINRAZA and if it might be right for you. Your HCP is best equipped to address any specific questions or concerns.

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

SELECTED IMPORTANT SAFETY INFORMATION

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03 What resources or services are available to help me with things such as insurance issues and/or financial concerns?

Once you/your child is prescribed SPINRAZA, you can learn about and access SMA360° support services from Biogen. Biogen's SMA360° support program provides certain services that address nonmedical barriers to access.* The SMA360° team is made up of some important people: the **Family Access Manager (FAM)** and the **Lead Case Manager (LCM)**.

Your FAM can:

- **Coordinate** the logistics of getting started with treatment
- **Prepare** you for the treatment journey by educating you on what to expect
- **Connect** with you at the treatment center, if you choose, to help with logistics as necessary

Your LCM can:

- **Investigate** your insurance benefits to help you understand your current coverage
- **Facilitate** the prior authorization process for treatment
- **Provide** information in the event of denied insurance claims
- **Educate** you on the eligibility details of the **Biogen Copay Program**, which may lower the out-of-pocket costs for commercially insured patients to as low as $0
- **Supply** background and resources to refer you to third-party charity organizations
- **Counsel** you and your family on the possibility of adding or changing insurance coverage

Please remember that your doctor should be your primary resource for any questions related to SMA and SPINRAZA.

You can contact an LCM at **1-844-4SPINRAZA** (1-844-477-4672), Monday through Friday, from 8:30 AM–8:00 PM ET, to get more information about these services.

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

04 How will I know if my health insurance will cover the SPINRAZA prescription?

An LCM can help you understand your current insurance benefits or counsel you and your family on the possibility of adding or changing insurance coverage as needed.

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EMMA // AGE 7
LATER-ONSET SMA
TREATED WITH SPINRAZA

IMPORTANT SAFETY INFORMATION

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INDICATION

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IMPORTANT SAFETY INFORMATION

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