

## **Spinraza treatment for SMA at Stanford**

Spinraza, is the first FDA-approved drug that increases SMN protein content in motor nerve cells; deficiency of SMN in these cells is the underlying cause of SMA. Spinraza is now available commercially throughout the United States. The Stanford SMA program continues to investigate Spinraza in pediatric trials and is currently studying its effects in adults with SMA. Additionally, we are investigating other ways to increase SMN production in neurons, and we are working to determine the benefits of combining SMN increases with other therapies that can optimize strength and function.. To find out more about our research program, or to participate in studies, we encourage interested members of the SMA community to register in our research program at: <https://med.stanford.edu/day-lab/recruitment.html>.

Stanford has six years of experience using Spinraza and we are excited to offer it clinically to patients of all ages with SMA – pending insurance approval. Individuals who want Spinraza may receive it as part of their overall care at either the pediatric or adult Stanford Neuromuscular Clinics. Stanford has weekly multi-disciplinary clinics for infants, children and adults with SMA, and now incorporates Spinraza into the comprehensive care of these patients. Both the Pediatric Neuromuscular Clinic at Lucile Packard Children’s Hospital (LPCH) and the Adult Neuromuscular Clinic at the Stanford Neuroscience Health Center (SNHC) have accomplished teams of physicians, nurse practitioners, therapists, nurses, pharmacists and other providers who are experienced in the care and support of individuals affected by SMA.

### **The Stanford Neuromuscular Spinraza Treatment Program includes the following elements:**

- To receive Spinraza at Stanford, all individuals must be registered at, and receiving their care at, either the Stanford pediatric (LPCH) or adult (SNHC) Neuromuscular Clinic (see contact information below)
- The Stanford Neuromuscular team will work with each patient and family to obtain required prior authorization from the patient’s insurance.
- Spinraza injections follow a pre-specified schedule
  - Patients receive 4 injections in the first 2 months, and then injections every 4 months thereafter
- **Because Spinraza takes time to work, to maximize the possible benefits of Spinraza, all patients must receive clinical care that meets SMA care guidelines provided at Stanford or similar multi-disciplinary neuromuscular centers.**
- All Stanford patients who receive Spinraza, whether at Stanford or another facility, are scheduled to return to our comprehensive clinic every 4 months to monitor their response to the drug and adjust their management. During these clinic visits, patients will be evaluated using standard tests to measure the response to Spinraza. These assessments are required by insurance companies in all patients receiving Spinraza; lack of these assessments will result insurance companies cancelling authorization for continued access to Spinraza.

### **Contact Us (see also below)**

Stanford SMA Research Program – (650) 725-4341; email address [NeuromuscularResearch@stanford.edu](mailto:NeuromuscularResearch@stanford.edu)

LPCH Pediatric Neuromuscular and SMA Clinic – New patient scheduling: (650) 723-0993, select option 3 then option 2

LPCH Pediatric Neuromuscular and SMA Clinic – Established patient scheduling: (650) 723-0993 option 3 then option 1

SNHC Adult Neuromuscular and SMA Clinic – New patient scheduling: (650) 723-6469 option 2

SNHC Adult Neuromuscular and SMA Clinic – Established patient scheduling: (650) 723-6469 option 1

## **Pediatric Patients**

1. If your child has previously been seen at LPCH Neuromuscular Clinic but has not had a follow-up visit in the last 6 months, please schedule an appointment by calling (650) 723-0993, select option 3, then option 1.
2. If your child has not previously been seen at LPCH Neuromuscular Clinic, please call the new patient scheduler to make an appointment at (650) 723-0993, selecting option 3 and then option 2; have your doctor fax referrals to (650) 721-2884. To assure rapid procession, please tell the scheduler, and have your doctor indicate, that your child has SMA and you are interested in Spinraza.
3. During your appointment you can: ask about Spinraza treatment for your child or alternate research options; discuss assistance options from Biogen Support Services; complete the Spinraza Start Form from Biogen.
4. Patients already seen at the LPCH Neuromuscular Clinic in the last 6 months can fax in their Spinraza Start form (downloaded from the Biogen website) to (650) 721-6350 attention Jessica, or submit it through MyHealth, or bring it to the next appointment for finalization.
5. Tests needed to establish eligibility for Spinraza can be performed at your clinic appointment. These tests include: blood work, urine tests, cardiac tests, X-rays, review of genetic results, etc.

## **Adult Patients**

1. If you have previously been seen at the SNHC Neuromuscular Clinic but have not been seen in the last 6 months, please schedule an appointment by calling (650) 723-6469 and select option 1.
2. If you have not previously been seen at the SNHC Neuromuscular Clinic, please call the New Patient Coordinators at (650) 723-6469 and select option 2; have your doctor fax in referrals to (650) 723-6002. Please have your doctor indicate that you are interested in Spinraza for more accurate processing.
3. During your appointment you can: ask about Spinraza treatment; discuss assistance options from Biogen Support Services; and complete the Spinraza Start Form from Biogen.
4. Tests needed to establish eligibility for Spinraza can be performed at your clinic appointment. These tests include: blood work, urine tests, cardiac tests, X-rays, review of genetic results, etc.

## **General information about drug treatment**

### **About the drug:**

#### ***How often does the drug need to be injected?***

The drug is administered at Day 1, 15, 30, and 60. After these four loading doses, patients must come back every 4 months to receive a follow-up injection of the drug.

#### ***How much does the drug cost?***

The wholesale cost for the drug alone is \$125,000 per dose. This does not include the cost of neurology clinic visits, routine testing and procedures for injecting the drug. Furthermore, each institution negotiates its own contract with each insurance company to cover the costs of drugs, so that specific arrangements to cover the costs of the drug need to be worked out individually for each patient.

#### ***Does insurance cover it?***

We will obtain prior authorization from insurance before administering the drug. Some insurance companies have covered the test so far, but the individual insurance providers continue to change the policies regarding Spinraza. We work with the insurers, Biogen and Stanford hospitals to assure that each patient can obtain the treatment.

#### ***Does it work? What will it do?***

SMA results from the loss of a specific gene, SMN1 (survival motor neuron 1) in all patients with SMA. This gene produces the SMN protein, which allows nerves that control muscles to function properly. All patients with SMA also have at least one copy of a back-up gene, the SMN2 gene, which produces a smaller amount of SMN protein. SMN2 makes the exact SMN protein that is needed, but not make enough of it for the nerves to be healthy. Spinraza targets the SMN2 gene to help it make more SMN protein and improve the health of the nerves that control muscles. There is not as much published data on Spinraza's effects in adults as we have for children, but results in previous

studies suggest that it improves nerve function in patients with all types of SMA (SMA1, SMA2 and SMA3) who are aged 0-20 years of age. Because of the dramatic effects of Spinraza seen in tissue from patients, as well as its dramatic and consistent effects in patients with all types of SMA, the FDA approved the drug for all patients with SMA without any restrictions regarding the type of SMA, the age of the patient or the severity of the patient's disabilities. Our primary goal with the treatment of Spinraza is to stabilize a patient's course of disease and decrease or eliminate any additional loss of function, but in some instances there has actually been a varying degree of functional improvement.

***How is it administered?***

The drug is injected into the spinal fluid in the lower back in what is called an "intrathecal injection". This involves a lumbar puncture, or spinal tap, with injection of medication directly into the spinal fluid. The injection is very similar to the type of injection that many people get to relieve pain in the back (like "epidural" anesthesia for childbirth). The lumbar puncture and drug injection can take about 15-20 minutes, but the whole process of setting up the procedure, completing the procedure and lying still for a period of time after the injection may take about 2 hours from start to finish.

***Is anesthesia involved?***

Most adults tolerate the spinal injection easily with a local injection of lidocaine (Novocain), so that no other anesthesia or sedation is needed. Anesthesia may be used for some children receiving Spinraza depending on their age, physical strength, respiratory status, and other variables. For example, many children between the ages of 2-12 years are not able to lie still during the brief injection, so that anesthesia may be used to ensure that the drug all goes into the spinal fluid.

***Does the procedure hurt?***

There is an initial burning sensation during the lidocaine injection and a feeling of pressure during the procedure. There are many nerves in the lower back, so it is not uncommon to bump a nerve during the injection, which causes a brief pulse of pain that goes away quickly. Most patients do not feel this is a particularly painful procedure. Some patients (usually <10%) may develop a headache after the procedure. If a headache does occur, it usually goes away on its own but can be effectively treated if necessary.

***Can patients with spinal curvatures or rods receive the drug?***

Patients with spinal curvatures or rods are eligible for treatment. Each case will be reviewed individually to determine if a route can be identified in the lower back by which the injection can be given. We are still working with colleagues at Stanford and in SMA centers around the world to optimize treatment options for all patients.

***Can patients that are ventilator-dependent receive the drug?***

Yes, the medical team assesses each individual to determine if they can undergo the procedure safely and effectively. The medical team will identify the best way to safely undergo the treatment.

***Could the injection damage my spinal cord?***

The spinal cord terminates several inches higher in the back than the site of the injection, so cannot be directly injured by the needle or injection. The space within the spinal canal below the level of the spinal cord contains nerves that move away if bumped by the needle, and fluid that protects the nerves. A small amount of fluid is removed before the same volume of Spinraza is injected.

***Are there any side effects? Is it safe?***

Although no significant side effects have been seen with Spinraza, we are still working with Biogen and the FDA to monitor patients to identify potential side effects that not already listed. The potential side effects of Spinraza are listed on Biogen's website here: [https://www.spinraza.com/en\\_us/home/safety/profile.html](https://www.spinraza.com/en_us/home/safety/profile.html). Spinal injections of any material carries some risk of infection, so it is critically important that injections be performed at experienced sites.

***Why do I have to do physical therapy assessments? Can't I just get the injection?***

Physical therapy assessments are important to your health care, and also allow us to see how the medication is affecting you as an individual. Spinraza is not a "magic wand" and cannot simply eliminate the effects of SMA that have developed over months and years. However, the potential benefit of Spinraza in stabilizing each person's abilities depends on our

ability to detect changes that develop, and then optimizing positioning, support, functioning and on-going therapy so that the benefits are maximized. We recommend that all patients receiving Spinraza return every four months to a dedicated clinic of SMA experts (physicians, therapists, nurses and practitioners, such as at the Stanford Neuromuscular Clinics) to assure that the effects of this treatment are as beneficial as possible. Insurance companies require that evidence of benefit from the drug be submitted in order to receive authorization to continue Spinraza, which is an important reason why following-up in clinic for evaluation by the Neuromuscular Team is essential.

***Do I need to have had genetic testing done?***

Yes. Spinraza will only benefit patients who have an absence of the SMN1 gene, and have one or more copies of the SMN2 gene. If you have had testing done previously, please bring a copy of the original report to your visit if it is not already part of your Stanford medical record. This is important because sometimes there are other disorders that can mimic SMA, but are genetically different. If you have not had genetic testing done previously, because it was not covered by insurance, please let us know. Now that there is an approved treatment for SMA, we can appeal to your insurance company and expect that we will get approval for the testing very quickly. The Stanford Neuromuscular Genetic Counselor is available to help with this process. We expect to be able to get genetic results within a matter of days, or at most a week or two, so it shouldn't slow up the process and is essential for us to get Spinraza approved.

***Can people with all types of SMA receive the drug?***

Yes – as far as Biogen, the FDA and Stanford are concerned. Based on the data presented to the FDA, Spinraza has been approved for all patients with SMA irrespective of the type of SMA (SMA1, SMA2, SMA3 and SMA4 are all eligible for treatment), the age of the patient (infants, children and adults are all eligible), or the degree of disability (ambulatory and non-ambulatory individuals, those who require ventilatory support, and those who have had spinal surgery are all eligible). Each insurance company has the right to decide if the patients it covers will be treated or not, but there are no restrictions placed by the FDA, Biogen or Stanford.

**About treatment at Stanford:**

***What insurance is accepted at Stanford?***

Stanford accepts patients covered by most major insurance companies. If Stanford is “out of network” for your policy, there is also a possibility that your insurance would approve this specialized treatment at Stanford. The Stanford (LPCH and SNHC) clinic staff can help you determine whether your appointment at Stanford and any subsequent treatment would be covered by your insurance.

***Can we come from out-of-state for treatment?***

Yes, as long as your medical insurance is accepted at Stanford. Keep in mind that the first few months have more frequent injections (Day 1, 15, 30, and 60), and that we expect all patients treated at Stanford to continue their follow-up care at Stanford.

***Can we come from outside the USA for treatment?***

We are currently not set up to treat patients from outside the USA. We are open to developing this on a case-by-case basis, but in general patients wanting to receive on-going Spinraza treatment at Stanford will need to move to the U.S.A. and have U.S. medical insurance in place that will approve treatment.

***Are initial pre-treatment exams needed?***

Yes. Each patient will be seen for a pre-treatment clinic consultation by the Stanford Neuromuscular Team. This will include evaluations by the neuromuscular neurologist, nurse practitioner, physical therapist, occupational therapist, speech and language therapist, nutritionist, respiratory therapist and pulmonologist, as well as meeting with the genetic counselor, social worker and nurse coordinator. The appointment will include the exam, labs, and spine imaging required to establish eligibility for Spinraza treatment. Once the drug is authorized by the insurance company, patients will be contacted to set up a treatment schedule.

***Is this an in-patient or out-patient procedure?***

All Spinraza treatments are provided by an outpatient procedure. The entire visit should last no more than 2 hours, though might take slightly longer if general anesthesia (typically for children 2-12 years of age) or radiologic guidance of

the injection is required.

***What are the age ranges for Stanford's Pediatric (LPCH) and Adult (SNHC) Neuromuscular Clinics?***

We follow pediatric patients at LPCH until age 21 years so that we can optimize interaction with California Children's Services, which is provided to neuromuscular patients less than 21 years of age.

Most patients at the Stanford's SNHC Adult Neuromuscular Clinic are 18 years of age or older, though individuals 15 years or older can easily be seen at SNHC if desired.

For patients desiring Spinraza treatment at Stanford: 1) all patients under 16 years of age will be treated at LPCH; 2) all patient 21 years of age or older will be treated at SNHC; 3) patients aged 16-21 years can receive Spinraza at either LPCH or SNHC, whichever hospital is more appropriate based on the patient's needs.

***If I start drug treatment elsewhere, can I still get treated at Stanford?***

Yes. We encourage all our patients to continue receiving neuromuscular care at Stanford even if you receive Spinraza at a different institution. We recommend that we continue to monitor your condition in Stanford Neuromuscular Clinic at visits every 4 months while receiving Spinraza, at which we would undertake our standard neurological and therapy assessments to measure symptom progression or regression. Results of our evaluations every 4 months are needed to adjust the on-going management, treatment and therapy plans to optimize benefits of Spinraza and maximize functional capabilities. **We strongly emphasize, in order to optimize function and control the effects of SMA, that regular comprehensive care be maintained at an established multidisciplinary neuromuscular clinic, such as either the pediatric or adult Stanford Neuromuscular Clinic. Optimizing your health and neuromuscular function remains of great importance, whether or not you are on Spinraza.**

***Will Stanford continue to refine and improve their Spinraza Policy?***

Of course. We are eager to get feedback about what works and what could work better regarding all aspects of our SMA and Neuromuscular Program. This is a very active time for the neuromuscular field, and we remain committed to bring as many novel treatments for SMA as possible to the Northern California and greater SMA communities. Please feel free to contact us so that we can continue to improve our program and our interactions with the SMA patient and provider communities. We are committed to doing all that we can, as well as we can, as soon as we can to combat SMA and related disorders. Thanks for your help.

## **Contact Us**

If you are interested in participating in SMA research at Stanford, or want to be notified about on-going research possibilities, please register in the Stanford Neuromuscular Database by communicating with the Stanford Neuromuscular Program.

**Stanford SMA and Neuromuscular Research Program – (650) 725-4341; email [NeuromuscularResearch@stanford.edu](mailto:NeuromuscularResearch@stanford.edu)**

Patients with SMA who are between the ages of birth and 21 years old are welcome to receive comprehensive care in the Lucile Packard Children's Hospital (LPCH) Pediatric Neuromuscular Clinic. If you want to be seen at the LPCH Pediatric Neuromuscular Clinic please contact us at:

**LPCH (pediatric) New patient scheduling: (650) 723-0993 select option 3 then option 2**

**LPCH (pediatric) Established patients: (650) 723-0993 option 3 then option 1**

Patients with SMA who are 18 years of age or older are welcome to receive comprehensive care in the Stanford Adult Neuroscience Health Center (SNHC) Neuromuscular Clinic. If for particular reasons patients aged 16-21 years of age want

to receive Spinraza treatment at SHNC, even though they are receiving their on-going care at LPCH, they are welcome to schedule an appointment in the SNHC Neuromuscular Clinic or to talk with the LPCH Neuromuscular Team regarding their preferences. If you want to be seen at the SNHC Adult Neuromuscular Clinic please contact us at the numbers listed below.

**SNHC (adult) Established patients: (650) 723-6469 option 1** and ask to speak with the Neuromuscular Patient Care Coordinator to schedule your Spinraza evaluation appointment. As our call volume is high, you may be asked to leave a message and your call will be returned within 24 hours.

**SNHC (adult) New patients: (650) 723-6469 option 2** and ask to speak with our New Patient Coordinators. You will be asked to have your current physician submit a referral and any relevant medical records such as genetic testing results. To aid in processing, your physician should state that you are interested in Spinraza treatment. **Referrals should be faxed to (650) 723-6002.** Once processed, our New Patient Coordinator will contact you to schedule an appointment.