

## Spinraza treatment for SMA at Stanford

Spinraza, the first FDA-approved drug that corrects the underlying cause of SMA, is now available commercially in the United States. The Stanford SMA program has helped investigate Spinraza's effects, and is also helping to develop additional treatments. To find out more about our research program, or participate in studies, we encourage interested members of the SMA community to register in our research program using the contact information below.

Stanford has four years of experience using Spinraza and we are excited to now offer it clinically to patients of all ages with SMA – pending insurance approval. Individuals who want Spinraza can 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 Lucile Packard Children's Hospital (LPCH) Pediatric Neuromuscular Clinic and the Stanford Neuroscience Health Center (SNHC) Adult Neuromuscular Clinic have accomplished teams of physicians, nurse practitioners, therapists, nurses 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)
- We assign each patient desiring Spinraza to one of 4 groups based on their exam. These are non-overlapping groups at each hospital (pediatric and adult), with each group having its own schedule for Spinraza injections:
  - Grp 1. Newly diagnosed infants (at LPCH only)
    - We expect this to be the smallest group awaiting Spinraza, and anticipate being able to schedule their treatments in an ad hoc fashion that doesn't interfere with the other groups
  - Grp 2. Patients with SMA of any type in whom injections can be performed without X-ray guidance
  - Grp 3. Patients with SMA of any type in whom injections require X-ray guidance
  - Grp 4. Patients with SMA of any type in whom initial injections will require surgical intervention
- We expect to provide Spinraza as part of an ongoing comprehensive treatment program in a total of 60-100 pediatric patients at LPCH, and 60-100 adult patients at SNHC
- We expect to be able to initiate Spinraza for 8-12 new patients every 6-8 weeks at each hospital
- We believe Spinraza will benefit all SMA patients, but cannot predict which patients might benefit most. Since we can maximally treat 12 new patients every 6 weeks (at each hospital), if more than 12 patients are awaiting treatment in any of the groups (defined above) we will randomly select next patients to start Spinraza
- The Stanford Neuromuscular team will work with each patient and family to obtain prior authorization from the patient's insurance, which is required before Spinraza can be administered
- Spinraza injections follow a specific 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 its benefits patients must also receive clinical support meeting SMA care guidelines, as is 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
  - Stanford patients who start Spinraza at another institution can switch to Stanford for ongoing Spinraza injections after the patients who can only receive care at Stanford have their treatment initiated.

## 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. 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 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 Lisa, 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, 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, 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. Afterwards 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 we do not yet have a list of known approvers, and anticipate that this will take several months to become clear. We also expect that some insurance companies that have announced limits to their approval of the drug will modify their decisions.

#### ***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 can produce a small amount of SMN protein. SMN2 does not perform very well so does not make enough of the SMN protein 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.

We do not have as much data on Spinraza's effects in adults as we do in children, but we do have results that show 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 in using Spinraza is always to assure that the patient's course will stabilize, and that no additional function will be lost, but in some instances there is also some 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 can 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 about 2 years old and 12 years old are not able to lie still during the brief injection, so that anesthesia may be used to assure 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 twinge of pain that goes away quickly. Most patients do not feel this is a particularly painful procedure. Some patients (usually <10%) can 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, as long as the medical team believes it will still be safe to undergo the treatment.

***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 so that we can definitively identify any potential side effects. The potential side effects of Spinraza are listed on Biogen's website here: <https://www.spinraza-hcp.com/?cid=ppc-ggl-spinrazahcpnowapproved-lm-644-spinrazahcpnowapproved&gclid=CLf9oIv4ztECFU9efgodT5QOaA>

***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 being able to identify any 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 the Stanford Neuromuscular Clinic) to assure that the effects of this treatment are as beneficial as possible. Insurance companies may require that evidence of benefit from the drug be submitted in order to receive authorization to continue Spinraza after the first year, which is another reason for the follow-up in clinic for evaluation by the Neuromuscular Team.

**About patient prioritization:**

***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 few weeks, so it shouldn't slow up the process much and is essential for us to get Spinraza approved.

***What are the criteria for prioritization?***

There are no criteria established by Biogen, the FDA or Stanford for receiving Spinraza other than having a genetic diagnosis of SMA. Patients will be grouped dependent on the level of care their drug administration will require (see above). This will primarily depend on whether there is significant scoliosis or a spinal fusion that would make it impossible to give the drug without X-Ray guidance, or without surgical intervention. If there are more patients in each group than can be treated in the next 1-2 months, patients to be treated will be chosen randomly from the overall group.

***Are younger patients given a higher priority?***

Newly diagnosed infants with SMA1 have shown the most dramatic benefits of the drug, so they will be treated as soon as possible. We do not expect a large number of these patients, and expect to simply work them into our existing treatment schedule, so do not expect that they will impact the order and schedule of treatment for other (older) patients with SMA. Other than infants, we expect Spinraza to benefit all patients, making it impossible to determine who will benefit more. Consequently, all patients other than infants will be grouped into the described groups (2 - those not needing X-ray guidance for the injection; 3 - those needing X-ray guidance for the injection; 4 - those needing surgical intervention for the injection), and patients from each group will be treated as soon as possible, selecting next patients with the random process described above if the number of patients waiting for Spinraza exceeds our expected bandwidth of 12 patients every 6 weeks.

***How long will it take to get in for treatment?***

Stanford did the first Spinraza treatment of an infant almost 4 years ago, has done 3 of the first 6 commercial treatments of children in the USA since FDA approval, and will soon begin treatment of adults. The drug injection programs in the Stanford pediatric and adult clinics run in parallel, so both proceed at their maximal pace. Furthermore, we're establishing means by which each of the treatment groups defined above (based on the ease of spinal injection for each patient) can proceed with treatment at its own pace and schedule. We have currently been enrolling 2-4 new patients every 4-8 weeks in the pediatric hospital, but anticipate that in the very near future we will be able to enroll 8-12 patients in each hospital every 6 weeks. We are currently unable to predict exactly how long it will take for patients to receive treatment but are dedicated to providing information to the community in an ongoing way so that you can see our progress. Our target is to have all SMA patients who desire Spinraza started on treatment within 6-9 months, but this in part depends on whether insurance covers treatment of all patients, and will also be delayed for patients in whom injection of the drug requires a surgical intervention.

***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.

***How do I get on the waiting list?***

To receive Spinraza at Stanford individuals will need to be clinic patients at either the pediatric (LPCH) or adult (SNHC) neuromuscular clinics. If you wish to receive Spinraza, please contact the appropriate (adult or pediatric) Stanford Neuromuscular Clinic to schedule an appointment, which is the first step toward receiving this medication.

To be contacted for SMA research studies you can enroll in the Stanford Neuromuscular Research Database, from which all research subjects are recruited. Contact information is listed below.

***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 drug treatments will be provided by an outpatient procedure. The entire visit should last no more than 2 hours, though might take slightly longer if general anesthesia (only commonly used for children 2-12 years of age) 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 21 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 can accommodate them earlier and more easily. If desired, patients aged 16-21 years who receive their ongoing care in the LPCH Neuromuscular, can receive their Spinraza injections at SNHC if that is a better option, and would be expected to continue receiving their clinical care at LPCH.

***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 would help us

adjust the on-going management, treatment and therapy plans to optimize benefits of Spinraza and maximize functional capabilities. Patients can transfer their drug administration to Stanford as those who can only receive care at Stanford are accommodated and a treatment appointment is available. **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 21 years of age or older are welcome to receive comprehensive care in the Stanford Adult Neuroscience Health Center (SNHC) Neuromuscular Clinic. Patients aged 16-21 years of age who want to receive Spinraza treatment at SNHC, even though they are receiving their on-going care at LPCH, are also welcome to schedule an appointment in the SNHC Neuromuscular Clinic. 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.