



# ABOUT SPINAL MUSCULAR ATROPHY

**Spinal muscular atrophy (SMA) is a genetic disorder that affects the motor nerve cells in the spinal cord. Depending on the age of onset, SMA can lead to:**

- Debilitating muscle weakness
- Inability to perform basic functions, such as walking, eating or breathing
- Death

There are four primary types of SMA—I, II, III, and IV—based on age of onset and highest physical milestone achieved. Type I is the most severe and most common, typically diagnosed during an infant's first six months. It is often fatal at this early stage in life, and is the number one genetic cause of death for infants.

SMA affects approximately one in 11,000 babies, and can affect any race or gender. About one in every 50 people is a genetic carrier for SMA. Because it is an autosomal recessive condition, generally both parents must be carriers for a child to inherit the condition.

## How It's Treated

Currently, SPINRAZA™ is only drug approved to treat SMA. Early results from ongoing studies of pre-symptomatic treatment with SPINRAZA have found that treating infants with SPINRAZA before they show symptoms leads to greater attainment of motor milestones—such as the ability to sit, stand and walk—compared to infants who did not receive treatment until their symptoms began.

Ongoing research into other treatment options for those with SMA includes treatments that, like Spinraza, can address the underlying genetics of the disorder, as well as treatments that help protect the muscles and nerves.

## Types of SMA

**SMA Type I** (Werdnig-Hoffmann Disease) is the most severe and most common type. It is usually diagnosed during an infant's first six months, and is often fatal early on in life. Babies with SMA type I face many physical challenges, including muscle weakness, as well as trouble breathing, coughing and swallowing.

**SMA Type II** is usually diagnosed between six months and two years of age. The first sign is often a delay or failure in meeting motor milestones. Those with type II can typically sit up without help but are unable to walk.

**SMA Type III** (Kugelberg-Welander Disease / Juvenile SMA) is usually diagnosed between 18 months and three years of age, but can be diagnosed as late as the teenage years. Those with SMA type III are initially able to walk, but have increasingly limited mobility as they grow.

**SMA Type IV** is very rare. It usually surfaces in adulthood and leads to mild motor impairment. While symptoms can begin as early as age 18, they usually begin after age 35.



# IMPORTANCE OF NEWBORN SCREENING FOR SMA

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Occurring in one in every 11,000 births, and with one in 50 people in the general population being SMA gene carriers, SMA is one of the most common lethal genetic disorders. SMA is classified into types based on the age of onset of symptoms and clinical severity; approximately 60 percent of affected children suffer from SMA type I, the most severe form.

Infants with this type of SMA typically begin to experience symptoms between birth and six months of age. Historically, more than 95 percent of these children die in infancy or require extensive respiratory support by their second birthday. Evidence suggests that **newborn screening holds great promise for ensuring access to treatment and helping to move toward a cure for this deadly disorder.**

## Supportive Clinical Evidence

Over the last decade, there have been significant advances in the development and approval of a treatment for SMA. On December 23, 2016, the U.S. Food and Drug Administration approved the first-ever therapy for SMA, called SPINRAZA™. While this therapy represents important progress, diagnosis timing is critical to treatment efficacy.

Infants with SMA type I show normal motor neuron activity early in life but begin losing neurons rapidly around three months of age; by six months of age, 90 percent of motor units have died. A systematic literature review indicates diagnostic delays of nearly four months for SMA type I. These delays can result in missed opportunities for early intervention. For parents and caregivers, they can also involve expensive and, ultimately, unnecessary testing until a correct SMA diagnosis is identified.

Given SMA's rapid progression, an SMA treatment would be most effective if administered early in the disorder's progression—before motor neuron loss. Screening for **SMA and early intervention is the most efficient way for babies with the disorder to have the chance to live their best life.**

**Findings from clinical trials support** both the effectiveness of treatment and that earlier treatment is better. According to research from Biogen:

- Infants treated with SPINRAZA achieved and sustained meaningful improvement in motor function compared to untreated babies.
- 51 percent of infants with SMA symptoms who received SPINRAZA achieved new motor milestones compared to 0 percent who did not receive SPINRAZA.
- SPINRAZA also decreased the risk for death or permanent respiratory support by 47 percent.
- Babies screened for SMA and treated with SPINRAZA before experiencing SMA symptoms achieved even more significant improvement in motor function than babies treated with SPINRAZA after showing symptoms.
- To date, no pre-symptomatic baby with SMA who was treated with SPINRAZA has died or required permanent respiratory support.
- Infants treated for up to one year achieved motor milestones such as the ability to sit, stand, and walk in timelines more consistent with normal development than typical for patients with SMA type I.

## The Overall Case for Newborn Screening

Babies with SMA who receive SPINRAZA after symptom onset appear to achieve more motor milestones and live longer without permanent respiratory support than babies who do not receive SPINRAZA. Babies genetically diagnosed with SMA and treated with SPINRAZA before symptoms appear to do even better. Early diagnosis and treatment can be life-changing for symptomatic or pre-symptomatic infants with SMA, allowing them a greater likelihood of survival and mobility.

Now that a treatment option is available and data indicates that pre-symptomatic treatment improves clinical outcomes, it is imperative that SMA be added to state newborn screening panels as quickly as possible and that additional resources be provided to state public health labs to implement newborn screening for conditions like SMA.



# TALKING POINTS FOR POLICYMAKERS

On most days, lawmakers are in back-to-back meetings. They hear a vast array of information and arguments for their constituents, organizations and colleagues. That's why you must have a story that breaks through. Demonstrate your personal tie to SMA, how it impacts the community and why newborn screening laws are so important to improvement treatment of the disorder. Outlined below are suggested talking points to use in your meetings or phone call with your elected officials.

- Thank you for taking the time to speak with me today. I wanted to talk to you about a genetic disorder known as spinal muscular atrophy (SMA).
- SMA presents severe challenges. For starters, children with SMA have difficulty performing the basic functions of life, like breathing and swallowing.
- And we're impacted by these challenges every day. **[SHARE 30–60-SECOND PERSONAL STORY.]**
- Today, I wanted to share with you why early treatment and diagnosis of the disease is so critical.
- Just last year, there was a significant advancement toward the first-ever treatment for SMA. The FDA recently approved SPINRAZA to treat children and adults with all types of SMA.
- Clinical trials of SPINRAZA showed effectiveness in both pediatric and adult patients, resulting in the FDA's broad label for the drug. Data from the randomized, sham controlled, Phase 3 ENDEAR study showed a statistically significant reduction in the risk of death or permanent ventilation in infants with SMA. In fact, SPINRAZA™ decreased the risk for death or permanent respiratory support by 47 percent compared to the sham treated control group. In addition, 41 percent of treated infants gained motor milestones compared to none in the sham group.
- But, the treatment is most beneficial if delivered early.
- That's why it is of utmost importance that SMA be added to **[STATE/NATIONAL]** screening guidelines to ensure that patients and families are made aware of the disorder. This way, families can act and obtain treatment as early as possible in order to obtain the best outcome.
- Research in animal models and in human clinical trials has demonstrated that beginning therapy as early as possible is of the utmost importance for SMA. Therapy is most effective when it can begin before significant motor neuron loss occurs, typically within the first few months of life. **We know that newborn screening would allow pre-symptomatic therapy, which provides maximum benefit.**
- In infants, motor neuron loss begins in the early perinatal period, with severe denervation occurring in the first 3 months of life, and loss of more than 90 percent of motor units within six months.
  - Research has also shown that, currently, many families face significant diagnostic delays. These delays range from an average of 3.6 months after symptom onset for those with SMA type I, up to an average of 43.6 months (more than 3 ½ years) for those with SMA type III. Newborn screening for SMA would eliminate these delays.
- Taken together, these diagnostic delays and the timeline of motor neuron death suggest that, even in the most severe cases, treatment often would not begin until after substantial motor neuron loss has already occurred. **Newborn screening would prevent this situation, and allow families to receive the maximum impact possible from an approved therapy.**
- I strongly urge the **[STATE LEGISLATURE/CONGRESS/GOVERNOR/NEWBORN SCREENING COMMITTEE]** to consider adding SMA to the state's newborn screening panel, with a focus on the new availability of a life-saving treatment for SMA and the demonstrated benefits of early intervention.