Pharmacy Focus: Spinal Muscular Atrophy (SMA) Treatment

SMA Overview

Spinal Muscular Atrophy (SMA) is a genetic disorder that affects motor neurons, which are the nerve cells in the spinal column that control voluntary muscle function. The loss of motor neurons, due to a deficiency in the body's ability to produce enough of a protein called survival motor neuron (SMN), causes progressive muscle weakness and loss of movement due to muscle atrophy.

There are several types of SMA. The earlier the age of onset, the greater the severity of the disease. SMA ultimately affects the muscles involved in walking, arm movement, sitting and head control. As the disease progresses and muscles continue to shrink, scoliosis can occur. Breathing and swallowing become difficult and complications like respiratory failure can make SMA fatal.

SMA is caused by mutations in the SMN1 gene and is inherited in an autosomal recessive manner. Diagnosis is made through analysis of suspected symptoms or a family history and confirmed through genetic testing. Supportive treatment may include physical therapy, nutrition support, chest physiotherapy and, in severe cases, ventilatory support. The focus is on improving quality of life and deterring complications.

Pharmaceuticals also have become an option. The first FDA-approved treatment for SMA, Spinraza® (nusinersen), was introduced to the U.S. market in December 2016. It has been shown to slow the progression of the disease and improve muscle function, but the response to the drug varies by individual. Then in May 2019, the FDA approved the gene therapy Zolgensma®. This therapy enables the body to produce the SMN protein by replacing the defective or missing SMN1 gene.

Zolgensma® 2019 Information

- Zolgensma® has been FDA approved for IV infusion in patients with SMA who are less than 2 years of age.
- Zolgensma® has not been FDA approved for use in patients with advanced SMA (ventilator dependent or complete paralysis).
- Zolgensma® has not been FDA approved for more than one administration.

Looking Ahead at Zolgensma® and SMA

By 2020, the manufacturer is expected to request FDA approval to add a new route of administration, Intrathecal (IT). With the FDA approval for IT administration, it is anticipated there will also be a request to lift the age restriction for Zolgensma®.

SMA Treatment Options Comparison

Drug	Use	Method	How It Works	Costs
Spinraza® (nusinersen)	SMA Types 1, 2, 3, 4	Intrathecal injection	Introduces a molecule that works to increase the body's ability to produce the SMN protein	Approximately $850,000 the first year and $400,000 every year thereafter
Zolgensma® (onasemnogene abeparvovec-xioi)	SMA in patients under the age of 2 years who are not ventilated or completely paralyzed	One-time infusion	Gene therapy; works by replacing the defective or missing primary SMN gene, leading to production of the needed SMN protein	$2,125,000 to $5,000,000 (once in a lifetime treatment)

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SMA Treatment Business Considerations

- Zolgensma® is an expensive, life-saving therapy for those with SMA
- When an SMA diagnosis (ICD 10 G12 series) is identified, HM Insurance Group assumes eligible patients will receive Zolgensma® therapy UNLESS detailed information related to ineligibility or administration on a previous plan year has been supported
- HM Insurance Group should be notified if clients exclude gene therapy as a covered benefit
- Policyholders should know their population risk
- Policyholders should know the health plan's criteria for use of pharmaceuticals
  - — Recognize that Spinraza® use in those eligible for Spinraza® has a very high probability of the patient ultimately receiving Zolgensma®
  - — Consider claims for SMA genetic testing procedure codes (before and/or after birth) as an opportunity to identify risk
  - — Ask if the health plan requires Specialty Pharmacy to bill the health plan directly (as opposed to the less predictable provider "Buy and Bill" option)
- Prepare for potential expenditures after therapy

SMA Pharmaceutical Costs Could Reach $5M

- Average cost of Spinraza® is up to $850,000 (first year) and up to $400,000 (every year after for life)
- Estimated cost of Zolgensma® ranges between $2,125,000 and $5,000,000, depending on who is billing the plan

Clinical Therapy Considerations

	Spinraza®	Zolgensma®
FDA Approved Use	The treatment of spinal muscular atrophy (SMA) types 1, 2, 3, 4 in pediatric and adult patients	The treatment of spinal muscular atrophy (SMA) in pediatric patients up to 2 years of age
Population	9,000 individuals in the United States; 400 babies are born with the disease each year	
FDA Approved Dosing	Intrathecal Injection: 12 mg/5 mL (2.4 mg/mL) in a single-dose vial. Year 1 could see 7 claims (4 claims within the first 42 days) Ongoing years should see 3 claims a year	One-time Intravenous Infusion based on weight
Direct Costs	Between $125,000 and $140,000 per dose	Regardless of payment model, CuraScript SD will bill either the health plan or the provider no less than $2.125 million for the one time dose or the provider will mark up and bill the health plan
Adverse Effects, Warnings and Precautions	• Thrombocytopenia and coagulation abnormalities • Renal toxicity • Lower respiratory infection and constipation in patients with infantile-onset SMA (6.1) • Pyrexia, headache, vomiting and back pain in patients with later onset	• Acute serious liver injury • Thrombocytopenia and bleeding problems • Elevated cardiac troponin-I levels • Vomiting
Study Information	260 patients (48% male, 80% Caucasian), including 227 followed for at least 6 months and 181 followed for at least 1 year	44 patients infused; ongoing observational trials indicate that 75% are able to sit without support and ~17% were able to stand and/or walk by 24 months
Payment Structures	Medical claims may include CPT 96450, HCPCS code J2326	Providers may choose to bill the health plan via Specialty Pharmacy OR to "Buy and Bill" as an HCPCS temporary "Q Code" until a permanent HCPCS Code is established
Traditional Therapies	Supportive only	

Pharmacy Focus provides valuable information about pharmaceutical industry developments and their associated costs that can impact the growing claims trend in the self-funded insurance market. Be aware of influences and gain insight into approaches that may help to contain costs. Please share topic suggestions or feedback with **HMPharmacyServices@hmig.com**.

References: U.S. Department of Health & Human Services Genetic and Rare Diseases Information Center (https://rarediseases.info.nih.gov/diseases/7674/spinal-muscular-atrophy), accessed May 30, 2019; "Clinical Development Program for SMA," https://www.avexis.com/research-and-develpoment, accessed May 31, 2019; Spinraza [prescribing information], Biogen, 2016-2018 (https://www.spinrazahcp.com/content/dam/commercial/specialty/spinraza/hcp/en_us/pdf/spinraza-prescribing-information.pdf); Zolgensma [prescribing information], AveXis, 2019 (https://www.avexis.com/content/pdf/prescribing_information.pdf)

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