AMWINS®
GROUP BENEFITS

Gene Therapy Solutions: Medical Breakthroughs Shouldn't have to Break the Bank

The cost-to-benefit analysis of gene therapy coverage is undoubtedly complex. As more treatments are approved, benefits brokers and employer groups are asking questions about these programs. Staying informed about the state of the industry—and tapping into a trusted partner that is well-versed in this evolving field—is the best way to navigate coverage for these promising new treatments.

CONTACT

To learn more about how Amwins can help you place coverage for your clients, reach out to your local Amwins broker.

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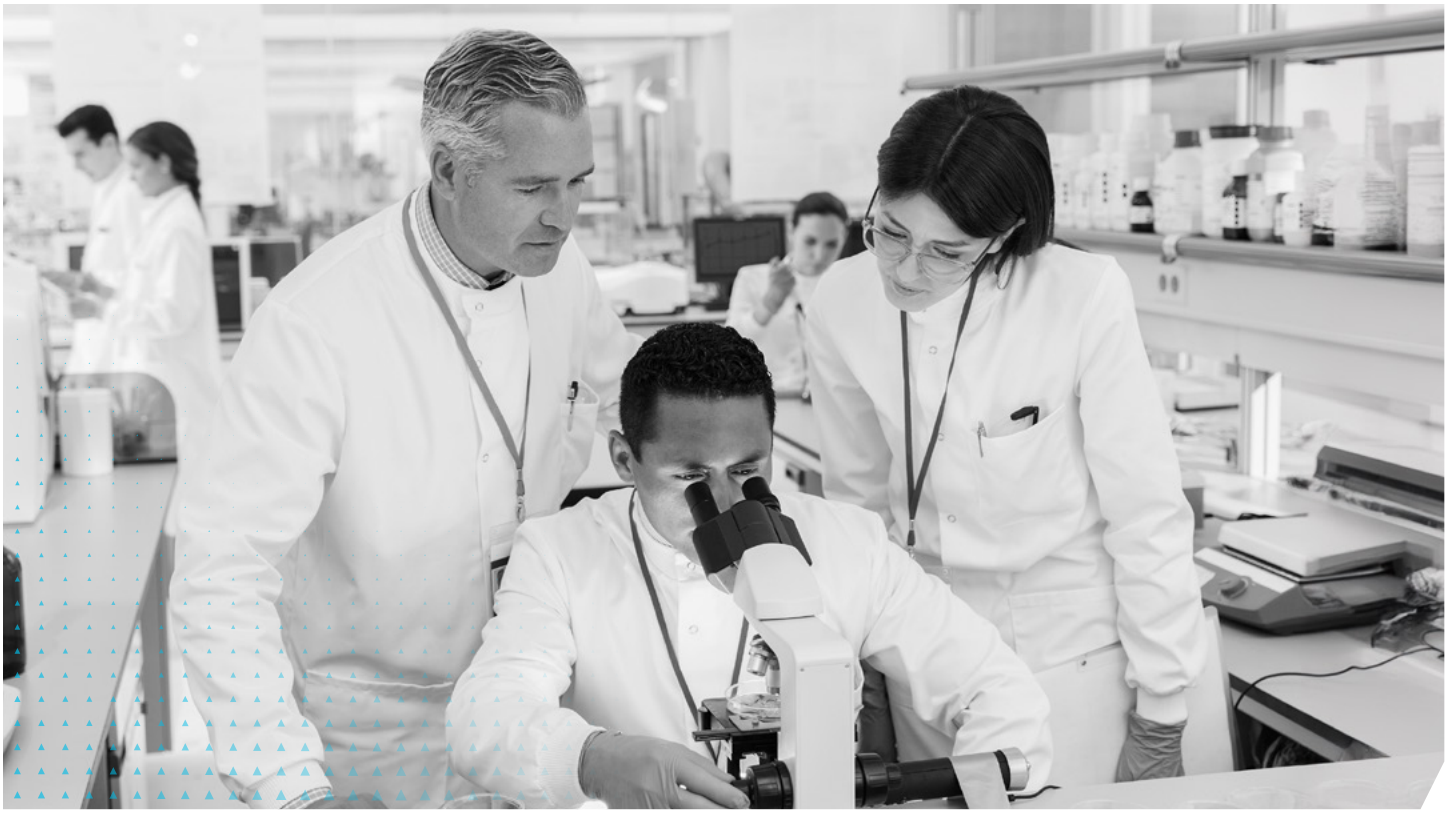


What is Gene Therapy?

Understanding gene therapy begins with appreciating the complex functionality of a single human cell. Trillions of cells receive information from genes and work together to form the tissues and organs driving our bodies to function. In some cases, abnormalities like defective, mutated or missing genes can lead to severe disorders and debilitating diseases. Common genetic disorders include hemophilia, cystic fibrosis, sickle cell anemia, spinal muscular atrophy and hereditary blindness.

As scientific and technological advancements continue to evolve, new and alternative treatment methods have emerged. These treatments are targeting, modifying, and even replacing genes for individuals with specific genetic conditions. Commonly known as gene therapy, these treatments are often curative and provide patients with improved quality and longevity of life. Coverage for these life-changing treatments remains a challenge, leaving employers to choose between excluding these classes of treatment from their benefit packages or risking going bankrupt.

What is Cell Therapy?

Cell therapy is a method used to treat disease by introducing stem cells into the patient. These therapies include cellular immunotherapies, cancer vaccines, and other types of both autologous and allogeneic cells for certain therapeutic indications, including hematopoietic stem cells and adult and embryonic stem cells.

There are two types of cell therapy:
- **Autologus**: Using Patient Cells
- **Allogenic**: Using Donor Cells

Cell therapy extracts cells from a patient or donor, edits the cell to create a healthy viable cell, injects it into the patient for it to multiply and attack the unhealthy cells.

Gene Therapy Solutions with Cost-Containment in Mind

Your benefits strategy relies on cost-containment solutions to provide financial protection. Still, the importance of supporting your employees and their families with today's health and wellness complexities cannot be understated. Amwins Gene Therapy Solutions supplements your current strategy and allows you to face unexpected costs with confidence.

There are currently 32 FDA-approved cell and gene therapy treatments. While prevalence and incidence rates are low today, experts are indicating the treatable population is expected to increase 11.5 times over the next five years reaching nearly 50,000 patients in the US alone*. The driving forces behind this increase are not only related to the increased pace of FDA approvals and approvals for treatments with more prevalent disease states but also more efficient distribution and greater access to qualified providers and facilities.

With each new approval, we are witnessing the expense of these treatments stretch beyond fathom causing the payer community to swiftly act, creating solutions to manage the expense of these therapies without interfering with access to care. Today, these therapies range in cost from **$338,000** to **$4,250,000**.

The value of these therapies should not go unmentioned. These treatments, in some cases, are the only option for these patients and their families. Furthermore, these disease states are debilitating and torturous for the patients who must endure it. When faced with the decision of whether or not to administer these life-changing and life-saving treatments, payers should not be burdened with restricting access due to the insurmountable impact of the cost to treat these patients.

While covering the cost of cell and gene therapy treatments is expensive, the costs of not treating the patient are financially, physically and emotionally significant. Patients left untreated will, in many cases, develop co-morbidities that will lead to increased medical expenditures and decreased lifespan. One must also consider costs for:

- medical equipment
- living-space modifications
- caregiver expenses
- extensive time off work
- lost productivity for parents
- long term disability for the patient

Note: Total number of therapies consistent with FDA recent recommendations to consider HPC cord blood treatments as a single therapy. American Society of Gene + Cell Therapy Cell, Gene, & RNA Therapy Landscape (asgct.org)

"Developments in gene and cell therapies have the potential to provide life-changing treatments but also present significant financial risk to self-funded plan sponsors. Our mission is to support our broker partners by providing meaningful solutions that protect employers as they face the ever-evolving and complex gene therapy landscape."
– Meredith Hunter, Senior Vice President, Stealth Partner Group

Gene Therapy Solutions with Cost-Containment in Mind (cont.)

Amwins Gene Therapy Solutions provides first-dollar reimbursement for 11 of the 15 approved therapies. In addition, this program offers reimbursement for three cell therapies and one maintenance drug, totaling 15 FDA-approved treatments.

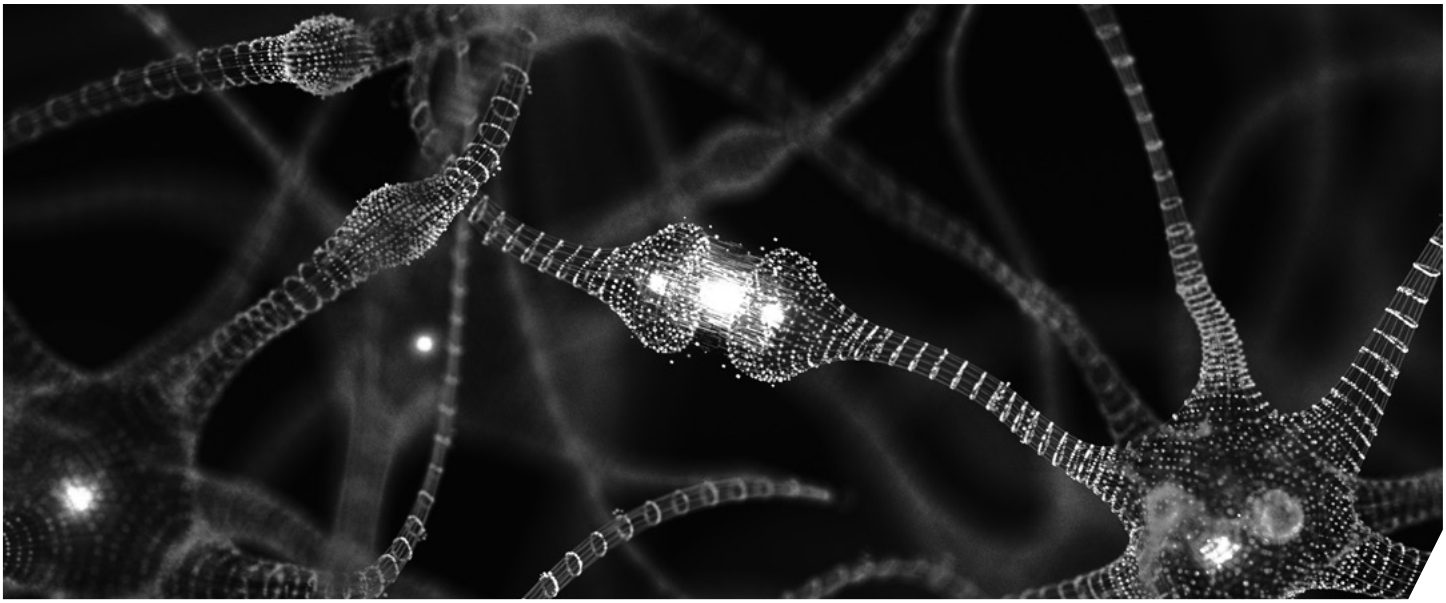
When evaluating therapies to include in our program we focus on the treatable disease states to better understand impact as it relates to a population within a Group Health Plan (GHP). As an example, there is an FDA-approved therapy, Adstiladrin, used to treat patients in advanced stages of Bacillus Calmette Guerin (BCG) - unresponsive non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS). The median age at diagnosis is 73, therefore we did not find value in including this therapy in a GHP program.

Below you will find disease state overviews with treatable therapies that are included in Amwins Gene Therapy Solutions:

1. **Leber Congenital Amaurosis (LCA)**, referred to as hereditary or inherited blindness, impacts one in 80,000 people. It is a progressive disease, and a person can have impaired vision at an early age and later be classified as completely blind. LCA is triggered by a single gene mutation inhibiting the retina's functionality. Impressively, a one-time treatment with Luxturna can repair this mutation and improve vision. **Gene Therapy Solutions covers Luxturna treatment for hereditary blindness up to $913,750 through GTS-5 and GTS-15.**

2. **Spinal Muscular Atrophy (SMA)** is a neuromuscular disease affecting one in 11,000 U.S.-born children. Nearly one in 40 people (6.6 million Americans) may carry the disease. SMA impacts the skeletal and muscular system, driving loss of voluntary muscle movement. Persons with SMA are often unable to perform routine activities of daily living and have a shortened lifespan. There are five types of SMA. Gene Therapy Solutions provides coverage for types 1 and 2. Type 1 is the most common, accounting for 60% of diagnoses in children. Symptoms often develop before six months of age. SMA is serious and life-threatening. However, early treatment slows progression, helps individuals reach milestones and gives hope for greater independence and a more positive prognosis. Type 2 accounts for 27% of cases, and symptoms begin to show within six to eighteen months. Untreated individuals will eventually be unable to walk without assistance. **Gene Therapy Solutions covers Sprinraza and Zolgensma up to $2,344,044 for SMA Types 1 and 2 through GTS-5 and GTS-15.**

Note: Clinical evidence for gene therapy for SMA types 3, 4, and 5 has limited data on clinical efficacy. These types could be covered in the future if more robust clinical data demonstrate appropriate clinical outcomes.



Gene Therapy Solutions with Cost-Containment in Mind (cont.)

3. **Transfusion Dependent Beta Thalassemia (TDT)** is a rare blood disorder that results from defective or missing genes that impact the production of hemoglobin. Hemoglobin is a protein in the blood that allows red blood cells to carry oxygen throughout the body. TDT is severe and requires patients to be dependent on blood transfusions for survival. It's estimated that there are 80-90 million TBT carriers (1.5% of the global population) and that there 60,000 symptomatic individuals born annually[1,2]. Patients living with TDT often have long-term care needs and face significant health complications. While regular infusions may temporarily improve the condition, it will not deliver the gene that would enable the body to produce adequate hemoglobin on its own. **Gene Therapy Solutions covers Zynteglo treatment for Transfusion Dependent Beta Thalassemia up to $2,800,000 through GTS-5 and GTS-15. Amwins Gene Therapy Solutions covers Casgevy up to $2,200,000 for the treatment of Transfusion Dependent Beta Thalassemia through GTS-15.**

4. **Cerebral Adrenoleukodystrophy (CALD)** is a rare genetic disorder caused by a mutation in the ABCD1 gene. This mutation leads to a dangerous buildup of a very long chain of fatty acids causing significant damage to the brain. Adrenoleukodystrophy is estimated to affect approximately 1 in 20,000 to 1 in 30,000 newborn males. CALD is the most severe and neurodegenerative form of this condition and affects about 40% of diagnosed males. Damage caused by CALD may lead to seizures, difficulty walking, intellectual disabilities, and difficulty performing activities of daily living[4]. Without treatment, 50% of CALD patients die within 5 years of their first symptoms. While there is no known cure for CALD, Skysona offers the opportunity for disease stabilization for boys ages 4-17 with early, active CALD. Skysona was clinically shown to prevent further damage to the nerves and death in clinical trial patients[5]. **Gene therapy Solutions covers Skysona treatment for Celebral Adrenoleukodystrophy up to $3,000,000 through GTS-5 and GTS-15.**

5. **Hemophilia A:** is an inherited blood disorder that occurs in one in 5,000 live male births. Abnormalities in the development of coagulation factor VIII impact blood's ability to clot. The disorder is classified based on the amount of factor VIII the body can produce. More than half of the 20,000 living with hemophilia A in the United States are classified as having the severe form of the condition. Individuals with hemophilia A have historically been reliant on factor replacement therapy to receive factor VIII through an infusion as an interim solution. Hemophilia A can pose a life-threatening risk based on the severity of the condition in situations of injury and trauma. The condition can result in long-term joint and organ damage due to prolonged bleeding episodes. In the most severe cases, prolonged bleeding episodes can be fatal. **Amwins Gene Therapy Solutions covers Roctavian for the treatment of hemophilia A up to $ 2,900,000 through GTS-15.**

Gene Therapy Solutions with Cost-Containment in Mind (cont.)

6. **Hemophilia B:** Hemophilia B is an inherited blood disorder caused by a gene mutation that creates an inability to produce coagulation factor IX. Factor IX is required for the blood's ability to clot. Hemophilia B incidence rate is one in 19,283 live male births. The prevalence rates are 3 males per 100,000. Similarly, to hemophilia A, the condition is classified as mild, moderate or severe. Only 30-50% of the hemophilia B population is classified as severe. **Amwins Gene Therapy Solutions covers Hemgenix and Beqvez for the treatment of hemophilia B up to $3,500,000 through GTS-15**. Hemgenix elevated and created sustained factor IX levels for 94% of clinical trial participants, reducing the rate of annual bleeds and reliance on prophylactic treatments[1]. Beqvez clinical trial results report a median of zero bleeds post-treatment for up to three years[2].

7. **Duchenne Muscular Dystrophy (DMD):** Duchenne Muscular Dystrophy (DMD) is a progressive form of muscular dystrophy. DMD is rare and mostly impacts males with symptoms presenting by the age of three, marked by delays in muscular development and ability. DMD affects one in every 3,300 boys[3]. Mutations with the DMD gene impact dystrophin. Dystrophin is a structural protein required for the normal development of muscles and therein the loss of proper function of skeletal muscles and the heart. Early symptoms present as a lack of physical motor function or muscular control with weakness worsening with age. Most individuals with DMD require wheelchairs by the age of 13. The lifespan of individuals with DMD is also negatively impacted by the long-term impacts of the damage to their heart and respiratory symptoms. **Amwins Gene Therapy Solutions covers Elevidys for the treatment of Duchenne muscular dystrophy up to $3,200,000 through GTS-15**. The manufacturer of Elevidys received approval through the FDA's Accelerated Approval pathway for the treatment of pediatric patients ages four to five based on initial clinical trial results and the increased production of the Elevidys micro-dystrophin protein[3].

8. **Sickle Cell Disease:** Sickle Cell Disease (SCD) is characterized by abnormally shaped red blood cells (RBCs). The disease is caused by a mutation in the HBB gene, affecting hemoglobin which is a protein important to the transportation of oxygen in the bloodstream. When this protein is abnormal, it changes the shape of the RBC from disc-shaped to "sickle" or c-shaped. This can lead to blockages within the vessels. SCD can cause complications such as infection, multi-organ failure, heart attacks, strokes, and vaso-occlusive crises (VOCs), which are characterized by debilitating pain. It's estimated that there are 100,000 living with SCD and that it affects one in every 365 live births. **Amwins Gene Therapy Solutions provides coverage for Casgevy up to $2,200,000 and Lyfgenia up to $3,100,000 for the treatment of Sickle cell disease through GTS-15**. None of the thirty Casgevy clinical trial participants rejected their treated cells or were hospitalized for pain crises within the first 12 months of treatment. Twenty-nine participants have remained pain-free and have not required hospitalization for an average of 22.2 months[4].Twenty-eight of the thirty-two Lyfgenia clinical trial participants didn't experience any vaso-occlusive events (VOEs) and thirty of the thirty-two participants didn't experience any severe VOEs. The participants experienced the VOEs more than 18 months after treatment[5].

9. **Metachromatic leukodystrophy (MLD):** Metachromatic Leukodystrophy (MLD) is a genetic condition that impacts the brain, spinal cord, and peripheral nervous. MLD is caused by a mutation in the ARSA gene, which typically produces an enzyme that breaks down sulfatides. This buildup of sulfatides inhibits the successful production of myelin, which protects nerves. These nerves send signals throughout the body. The condition is marked by developmental delays, speech impairment, seizures, and loss of motor function. More than half of those diagnosed with MLD have a late infantile form and typically do not survive past childhood. **Amwins Gene Therapy Solutions covers Lenmeldy up to $4,250,000 for the treatment of MLD through GTS-15**. All 39 children participating in the Lenmeldy gene therapy clinical trial were alive at age six, compared to the 58% survival rate of the children not treated with the drug. 71% of children treated with Lenmeldy could walk by age five unassisted, as well[6].

Gene Therapy Solutions with Cost-Containment in Mind (cont.)

10. **Multiple Myeloma:** Multiple Myeloma is cancer of the plasma cells within the bone marrow. Plasma cells are a type of white blood cell, responsible for making the antibodies that fight infection and disease in the body. The cancerous myeloma cells multiply rapidly, adversely impacting the number of healthy blood cells in the body. As the risk of infection spreads, so do the myeloma cells. Myeloma cells break down bone tissues, weakening the structure overall. They can form tumors called plasmacytomas within the bone marrow, as well. Myeloma cells also release proteins to further alter kidney function7. It's estimated that there will be 35,780 newly diagnosed myeloma cases in the United States this year, accounting for 1.8% of total cancer cases[8]. **Amwins Gene Therapy Solutions covers Abecma up to $498,408 and Carvykti up to $522,055 for the treatment of Multiple myeloma through GTS-15**.

11. **Congenital Athymia:** Congenital Athymia is a condition where a child is born without a thymus. The thymus, a gland located at the top of the heart, is responsible for the production of T-cells. T-cells are a specialized type of white blood cell that aids the body in fighting infection and disease[9]. Children with Congenital Athymia are immune-compromised, unable to produce the necessary cells necessary to fight infection and more likely to develop inflammatory autoimmune conditions. Due to the high risk of infection, most children with this condition live two to three years. The only known treatment for Congenital Athymia is Rethymic. Rethymic is a donor-derived processed thymus tissue that is surgically implanted into the recipient. The thymus tissue product aids in immune system reconstruction. **Amwins Gene Therapy Solutions covers Rethymic up to $2,729,500 for the treatment of congenital athymia through GTS-15**.

1 - CSL Behring Announces the First Patient Has Received FDA-Approved HEMGENIX® (etranacogene dezaparvovec-drlb) for Hemophilia B - Jun 20, 2023

2 - U.S. FDA Approves Pfizer's BEQVEZ™ (fidanacogene elaparvovec-dzkt), a One-Time Gene Therapy for Adults with Hemophilia B | Pfizer

3 - FDA approves First Gene Therapy for Treatment of Certain Patients with Duchenne Muscular Dystrophy | FDA

4 - CASGEVY (Exagamglogene Autotemcel) | Boston Children's Hospital (childrenshospital.org)

5 - Clinical Trial Results | LYFGENIA™ (lovotibeglogene autotemcel)

6 - FDA Approves First Gene Therapy for Children with Metachromatic Leukodystrophy | FDA

7 - NCCN Guidelines for Patients: Multiple Myeloma

8 - Myeloma — Cancer Stat Facts

9 - Congenital Athymia - Symptoms, Causes, Treatment | NORD (rarediseases.org)

Program Protection

Amwins Gene Therapy Solutions currently includes 15 available therapies. As new treatments receive FDA approval, we will evaluate those therapies and treatable disease states to determine the value of including in this program.

Here is how Amwins Gene Therapy Solutions works:
Amwins Gene Therapy Solutions (GTS) offers reimbursement to group health plans and their coordinating stop-loss carrier for qualified claims. Qualifying reimbursements extend from the first dollar of group health plan expense up to specified limits for each covered therapy.

Our program distributes the reimbursement according to the stop-loss deductible. Following the adjudication of a qualified claim, our program reimburses the group health plan dollar one of their expenses up to their specific deductible and the balance of the reimbursement is distributed to the associated stop-loss carrier.

The program is transferable if a group health plan elects underlying plan changes to their network, PBM, TPA or other partners. The group health plan does not run the risk of losing the program.

We have two available options:

Program Options	Covered Pharmaceuticals	Treated Diseases	Maximum Payable Per Covered Person Per Benefit Period	Cost of Program
GTS-5	Luxturna	Leber Congenital Amaurosis (LCA)	$913,750	Contact an Amwins representative for additional information.
	Zolgensma	Spinal Muscular Atrophy (SMA) Types 1 & 2 (Children ages 2 and under)	$2,322,044	
	Spinraza*			
	Zynteglo	Beta Thalassemia	$2,800,000	
	Skysona	Cerebral Adrenoleukodystrophy (CALD)	$3,000,000	
GTS-15	Roctavian	Hemophilia A	$2,900,000	Contact an Amwins representative for additional information.
	Hemgenix	Hemophilia B	$3,500,000	
	Beqvez			
	Elevidys	Duchenne Muscular Dystrophy (DMD)	$3,200,000	
	Casgevy	Sickle Cell	$2,200,000	
		Transfusion Dependent Beta Thalassemia		
	Lyfgenia	Sickle Cell	$3,100,000	
	Lenmeldy	Metachromatic Leukodystrphy (MLD)	$4,250,000	
	Abecma**	Multiple Myeloma	$498,408	
	Carvykti**		$522,055	
	Rethymic**	Congenital Athymia	$2,729,500	

*Maintenance drug; Cost in year 1 is ~ $750K and $~375K in subsequent years.
**Cell Therapies.

2023 Case Study: Zolgensma

Gene Therapy Reimbursement Information

$2.2M
Maximum Benefit

$800K
Employer Reimbursement

$1.4M
Stop Loss Carrier Reimbursement

Employer Type: Municipality
Lives: 5,000
Renewal Date: 1/1
Specific Deductible: $800,000
Prior plan year: Stop loss BUCA bundled
Current plan year: Stop loss unbundled, BUCA moved to ASO

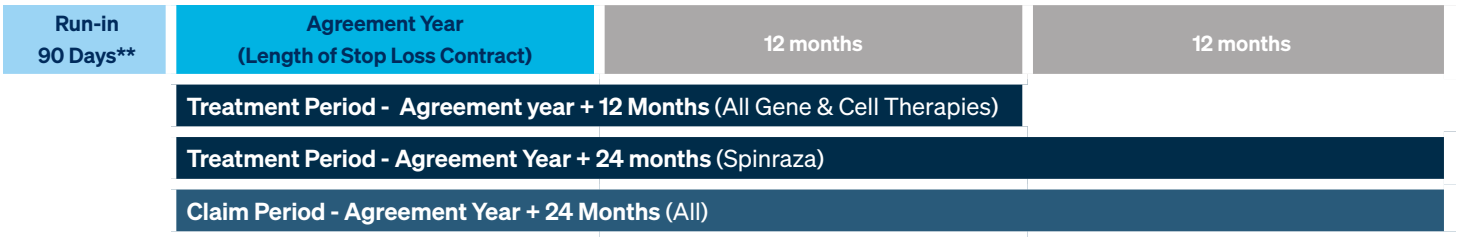
Allowed Charges: $2,254,810
Specific Deductible: $800,000
Stop Loss Paid: $1,454,810
Employer Renewal: 0% increase
Lasers Issued: 0

Zolgensma Reimbursement Timeline

1. Covered infant born on **4/27/2023**. Diagnosis confirmed on **5/6/2023**. Treatment was administered on **5/16/2023**.
2. Facility files the claim on **6/9/2023**.
3. ASO BUCA funds the claim on **6/20/2023**.
4. Stop loss claim begins on **6/22/2023**. Stop loss claim filed **7/17/2023**.
5. Stop loss claim reimbursed **8/15/2023**.
6. Gene therapy claim submitted on **8/24/2023**. Gene therapy claim approved on **9/20/2023.**
7. Gene therapy funds released on **9/22/2023.**

Program Eligibility

The treatment for SMA included in this program are intended for children up to 24 months of age. There is no age limit for Luxturna. Program eligibility is based on a participant meeting the qualifications outlined in the table below.



**Run-in applies to Zolgensma and Spinraza only.

Covered Pharma-ceutical	Disease State	Run-in Period	Coverage Criteria	Treatment Period	Claims Period
Luxturna	Leber Congenital Amaurosis (LCA)	Not applicable.	Covered Person must meet the FDA label guidelines as an eligible recipient of the Covered Pharmaceutical.	Covered Pharmaceutical must be initially administered to Covered Person meeting Coverage Criteria between the first day of the Agreement Period and the 12 months immediately following the last day of the Agreement Period.	Claims for Covered Pharmaceuticals must be filed, approved, and paid by the Named Insured and the Covered Stop Loss Plan within 24 months immediately following the last day of the Agreement Period and are valid for Covered Pharmaceuticals administered during the Treatment Period.
Zynteglo	Beta Thalassemia				
Casgevy					
Skysona	Cerebral Adrenoleukodystrophy (CALD)				
Abecma	Multiple Myeloma		Covered Person must meet the FDA label guidelines in effect May 1, 2025 as an eligible recipient of the Covered Pharmaceutical.		
Carvykti					
Casgevy	Sickle Cell				
Lyfgenia					
Hemgenix	Hemophilia A				
Roctavian	Hemophilia B				
Beqvez					
Elevidys	Duchenne Muscular Dystrophy (DMD)		Covered Person must be between the ages of four and eight years and diagnosed with a Covered Disease during the Agreement Period and meet all other FDA label guidelines as an eligible recipient of the Covered Pharmaceutical.		
Lenmeldy	Metachromatic Leukodystrophy (MLD)		Covered Person must be diagnosed with a Covered Disease during the Agreement Period.		
Rethymic	Congenital Athymia				
Zolgensma	Spinal Muscular Atrophy (SMA) Types 1 & 2 (Children up to age 2)	Covered Person must be born within: – the Agreement Period – 90 days immediately preceding the first day of the Agreement Period or the enrollment start date of Covered Person into the Names Insured's self-funded health care benefits plan within the Agreement Period (the "Run-in Period"), provided in both cases the Covered Person did not receive a diagnosis for the Covered Disease during such 90-day period.	Covered Person must be diagnosed with a Covered Disease between the first day of the Agreement Period and 12 months immediately following the last day of the Agreement Period.		
Spinraza			Covered Person must be diagnosed with a Covered Disease between the first day of the Agreement Period and 24 months immediately following the last day of the Agreement Period.	Covered Person must be diagnosed with a Covered Disease between the first day of the Agreement Period and 24 months immediately following the last day of the Agreement Period.	

Program Advantages

As your trusted partner for cost-containment solutions, we continue to evaluate market needs. Our goal is to identify the most advantageous solutions so administrators can maximize their budget and mitigate unpredictable risk while supporting their workforce through innovative, responsive and robust offerings.

Meaningful Protection
First-dollar protection is given to the plan sponsor

Industry Experts
Our experts monitor the landscape of FDA approvals and make purposeful additions to our program that bring value and positive results to clients

Portability
Changes in the underlying plan does not affect coverage terms

Simplified Billing
Administrative burden is reduced by including the program fee in the stop-loss bill

Next Steps: Find a partner who aligns with your strategy

Offering comprehensive benefits while also being economically efficient is a balancing act. Employers are tasked with designing a benefit strategy around the needs of their employees, while also considering the cost of new treatments in the market. They want financial security that won't compromise access to life-changing and potentially curative gene therapy treatments.

At Amwins, we offer an innovative and sustainable approach that is as evolutionary as the gene therapy treatments themselves. We recognize that employers need more than a program; they need a partner. Amwins Gene Therapy Solutions includes operational oversight, as well as ongoing market cost-benefit analysis. We are committed to offering a solution that allows employers to navigate the everchanging landscape of gene therapy with confidence. From diagnosis to reimbursement, Amwins Gene Therapy Solutions alleviates the administrative and financial burden that can accompany these treatments. Amwins is your trusted partner to navigate the current market and offers peace of mind as you face the future of gene therapy advancements.