RESEARCH PAPER

Zolgensma in Spinal Muscular Atrophy: Clinical Value, Economic Challenges and Indian Access Case Studies

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Received: 20th Apr, 2026 | Revised: 25th Apr, 2026 | Accepted: 9th May, 2026 | Available Online: 14th May, 2026

ABSTRACT

Spinal Muscular Atrophy (SMA) is a rare, progressive, autosomal recessive neuromuscular disorder characterized by degeneration of alpha motor neurons in the spinal cord, resulting in muscle weakness, respiratory compromise, and severe disability. The condition is primarily caused by mutations or deletions in the SMN1 gene, leading to insufficient production of survival motor neuron (SMN) protein. Without timely intervention, severe forms such as SMA Type 1 are associated with significant morbidity and early mortality. Recent therapeutic advancements have revolutionized SMA management, particularly the development of onasemnogene abeparvovec (Zolgensma), a one-time intravenous gene replacement therapy designed to deliver a functional copy of the SMN1 gene using an adeno-associated viral vector. Clinical studies have demonstrated substantial improvements in survival, ventilator-free outcomes, and motor milestone achievement, including sitting, standing, and walking in selected patients. Early treatment, especially during the presymptomatic stage, has been associated with the most favorable outcomes. Despite its remarkable therapeutic value, Zolgensma remains one of the most expensive medicines globally, creating substantial economic and ethical challenges related to affordability, reimbursement, and equitable access. In many low- and middle-income countries, families often depend on crowdfunding, charitable donations, or compassionate access programs to obtain treatment. This review summarizes the pathophysiology of SMA, mechanism of action, clinical efficacy, safety profile, economic burden, and policy implications of Zolgensma. In addition, anonymized Indian case studies (X1–X5) are presented to highlight real-world barriers and innovative funding approaches. While Zolgensma represents a landmark achievement in precision medicine, coordinated healthcare policies and sustainable financing strategies are essential to ensure broader access for eligible patients worldwide.

Keywords: Spinal Muscular Atrophy, Zolgensma, Gene Therapy, SMN1 Gene, Rare Disease Access

How to cite this article: Begum SA, Kumar PR, Tanweer SAS, Phalgun RHS, Teja MR, Nath BJ, Singh RS., Zolgensma in Spinal Muscular Atrophy: Clinical Value, Economic Challenges and Indian Access Case Studies. Int J Drug Deliv Technol. 2026;16(44s): 532-536; DOI: 10.25258/ijddt.16.44s.57

1. Introduction

Spinal Muscular Atrophy (SMA) is a rare, inherited neuromuscular disorder characterized by progressive degeneration of lower motor neurons located in the anterior horn cells of the spinal cord. These motor neurons are responsible for transmitting signals from the central nervous system to skeletal muscles, enabling voluntary movement. Degeneration of these neurons results in progressive muscle weakness, hypotonia, loss of motor milestones, respiratory insufficiency, and, in severe forms, premature death. SMA is recognized as one of the leading genetic causes of infant mortality worldwide [1].

The clinical presentation of SMA varies widely depending on the severity of the disease and the number of copies of the modifier gene SMN2. Infants with severe forms often present with poor head control, feeding difficulty, weak cry, respiratory distress, and inability to sit independently. In contrast, milder forms may appear later in childhood or adulthood with progressive proximal muscle weakness and impaired mobility[2,3].

Historically, management of SMA was limited to supportive care measures such as respiratory assistance, nutritional support, orthopedic management, and physiotherapy. While these

interventions improved quality of life and survival, they did not address the underlying genetic cause of the disorder. Over the last decade, the development of disease-modifying therapies has transformed the prognosis of SMA, making it one of the most notable success stories in precision medicine[4,5].

Among these therapeutic advances, onasemnogene abeparvovec (Zolgensma) has attracted significant attention due to its one-time gene replacement strategy aimed at correcting the primary molecular defect. Despite its remarkable efficacy, its exceptionally high cost and limited accessibility have generated considerable economic and ethical debate. This review discusses the pathophysiology of SMA, available therapies, clinical benefits of Zolgensma, and the challenges associated with equitable access.

1.1 Epidemiology of SMA

SMA affects approximately 1 in 6,000 to 1 in 10,000 live births globally, with carrier frequency estimated at around 1 in 40 to 1 in 60 individuals depending on population background [2]. Because it is inherited in an autosomal recessive pattern, both parents are usually asymptomatic carriers of a defective SMN1 gene[6].

Although SMA is considered a rare disease, its cumulative healthcare burden is substantial due to chronic disability, repeated hospitalizations, need for ventilatory support, and lifelong rehabilitation in untreated patients. Early diagnosis is critical, as therapeutic outcomes are significantly better when treatment is initiated before irreversible motor neuron loss occurs.

1.2 Clinical Burden and Natural History

The natural history of untreated SMA, particularly Type 1 disease, is severe. Infants with SMA Type 1 often fail to achieve the ability to sit independently and may require ventilatory support within the first two years of life. Feeding problems, recurrent respiratory infections, and progressive muscle weakness are common complications[7,8].

Patients with intermediate forms (Type 2) may achieve sitting ability but generally do not walk independently. They often develop scoliosis, joint contractures, and progressive respiratory compromise. Type 3 and Type 4 patients have relatively milder disease, though mobility limitations and muscle weakness may worsen over time.

The psychosocial burden on families is also profound, involving emotional distress, caregiving challenges, and financial strain.

1.3 Evolution of Treatment Strategies

For many decades, treatment options were purely supportive. Standard care included respiratory management, nutritional supplementation, physical therapy, and orthopedic interventions. Although these approaches prolonged survival, they could not halt disease progression[9].

The emergence of targeted molecular therapies changed the SMA treatment paradigm. Nusinersen enhances SMN2 splicing to increase functional SMN protein production, while risdiplam is an oral SMN2 splicing modifier. Zolgensma, however, offers a unique approach by delivering a functional copy of the SMN1 gene through viral-vector-mediated gene therapy, potentially after a single intravenous infusion [10].

1.4 Importance of Early Diagnosis

Motor neuron loss in SMA begins early, often before symptoms become clinically apparent. Therefore, newborn screening programs have become increasingly important. Presymptomatic treatment has been associated with near-normal motor development in some infants receiving early intervention. This has led to growing advocacy for universal newborn screening for SMA, especially in countries where gene therapy is available[12].

1.5 Scope of the Present Review

Given the transformative potential of Zolgensma and the controversies surrounding its affordability, this review aims to examine the scientific rationale, therapeutic effectiveness, safety profile, economic implications, and real-world access challenges associated with this landmark therapy. Particular emphasis is placed on experiences from developing countries, where access to high-cost rare disease treatments remains limited[13,14].

2. Ethical and Policy Issues

The exceptionally high price of Zolgensma has raised major ethical and policy concerns worldwide. Although the therapy offers life-changing benefits for children with Spinal Muscular Atrophy (SMA), its cost places it beyond the reach of many families and healthcare systems, particularly in low- and middle-income countries. This creates significant disparities in access between nations, institutions, and socioeconomic groups[15]. Children born in resource-rich settings may receive timely treatment, while equally eligible patients elsewhere may face delayed care or no access at all.

In many cases, families are compelled to rely on crowdfunding campaigns, charitable donations, corporate social responsibility initiatives, or legal appeals to secure treatment. Such dependence on public sympathy and fundraising can be emotionally distressing, socially inequitable, and uncertain. Access to life-saving therapy should ideally be based on

medical need rather than financial capability or media attention[16].

Another important concern is the sustainability of healthcare budgets. Funding one ultra-expensive therapy may strain public resources and create difficult decisions regarding allocation of limited funds across broader population health needs. Policymakers must therefore balance innovation incentives with fairness and affordability[17].

Several strategies have been proposed to improve access. These include transparent pricing mechanisms, where manufacturers justify costs based on research, production, and therapeutic value; risk-sharing or outcome-based payment models, in which reimbursement is linked to patient outcomes; pooled procurement systems, where governments or regions negotiate collectively for better pricing; and establishment of public rare-disease funds dedicated to high-cost treatments.

Long-term solutions also include strengthening newborn screening, early diagnosis programs, insurance coverage, and encouraging local biotechnology innovation. Ensuring equitable access to transformative gene therapies remains one of the most pressing challenges in modern healthcare policy [8].

3. Case Briefs: SMA Treatment in India

India has witnessed several remarkable cases in which children diagnosed with Spinal Muscular Atrophy (SMA) successfully received **Zolgensma**, one of the world's most expensive gene therapies. These cases highlight the clinical importance of early intervention, as well as the social, financial, and policy challenges associated with accessing rare disease treatment in developing countries. Due to the high cost of therapy, most families relied on crowdfunding campaigns, charitable assistance, public support, and institutional intervention. The following anonymized and educationally adapted case briefs illustrate the evolving landscape of SMA treatment access in India.

3.1 Case X1: Eastern India – Large-Scale Crowdfunding Success

A female infant from eastern India was diagnosed with SMA Type 1, the most severe infantile form of the disorder. Following diagnosis, the family initiated a nationwide crowdfunding campaign through a digital fundraising platform. The campaign generated extraordinary public response, with support from more than 529,000 individual donors, raising approximately ₹8.41 crore[18].

The treatment was successfully administered at a tertiary care hospital in Kolkata in June 2025. This case became notable for setting a record in terms of the highest number of donors contributing to a single medical fundraising campaign on that platform at the time. It demonstrated the growing role of digital philanthropy and social media in financing rare disease treatment.

3.2 Case X2: Northern India – Combined Public and Manufacturer Support

A child from northern India was diagnosed with SMA and evaluated at a premier national institute in New Delhi. The family launched a crowdfunding effort after learning about the urgent need for Zolgensma therapy. The campaign received widespread public support, including assistance from influential community and spiritual leaders. In addition to donations, the manufacturer reportedly extended a concession of approximately ₹5 crore, significantly reducing the total financial burden. The therapy was administered in February 2025 at a specialized pediatric neurology center. This case highlights the importance of combined funding models involving community support and corporate assistance[19].

3.3 Case X3: Western India – Civic Mobilization and Institutional Support

A child diagnosed with SMA Type 2 from western India required urgent treatment access. The child's family initiated a fundraising campaign that attracted extensive support from law enforcement personnel, charitable groups, local businesses, and the general public. More than 160,000 donors reportedly contributed over ₹7.9 crore, with the final amount nearing ₹9 crore.

The treatment was administered in May 2024 at a government-affiliated pediatric specialty hospital in Jaipur. The case received additional visibility through support from public personalities and community leaders. It represents the power of civic solidarity in responding to rare disease emergencies[20].

3.4 Case X4: Southern India – Compassionate Access Program

A child from southern India with SMA Type 1 was unable to raise the complete treatment amount through crowdfunding, despite substantial public support. The family had simultaneously enrolled in the manufacturer's global managed access program, designed to support selected patients unable to afford treatment. The child was ultimately chosen as a beneficiary and received Zolgensma free of cost through the compassionate access route. The infusion was administered in August 2022 at a pediatric super-specialty hospital in Hyderabad. This case

demonstrates the significance of humanitarian access programs for families with limited resources[21].

3.5 Case X5: Andhra Pradesh – Public Donations and Government Intervention

An 11-month-old infant from Andhra Pradesh was diagnosed with SMA Type 1, requiring urgent treatment with Zolgensma at an estimated cost of ₹16 crore. The family initiated a crowdfunding campaign in November 2025, which rapidly gained attention under a viral social media movement. Donations were received from local youth groups, schoolchildren, auto drivers, non-resident Indians, and supporters from abroad. Public contributions reportedly crossed ₹10 crore. Additional government assistance was then secured through the National Policy for Rare Diseases (NPRD-2021) and state-level support, helping complete the required amount. By February 27, 2026, the total funds had been mobilized, enabling treatment planning. This case is especially important because it illustrates a hybrid financing model involving public generosity and government participation, offering a potential framework for future rare disease funding in India[22,23].

3.6 Key Insights from Indian Cases

These Indian cases collectively reveal several important trends:

- Crowdfunding has emerged as a major access route for ultra-expensive therapies.
- Social media campaigns significantly influence fundraising success.
- Manufacturer concessions and compassionate programs remain important.
- Government rare disease policies can bridge financial gaps.
- Timely diagnosis and rapid funding are essential, as treatment outcomes are best when therapy is administered early.

4. Conclusion

Zolgensma represents a landmark achievement in the field of precision medicine and has significantly transformed the therapeutic outlook for patients with Spinal Muscular Atrophy (SMA). As a one-time gene replacement therapy targeting the underlying genetic defect, it has redefined expectations regarding survival, motor milestone attainment, and long-term quality of life in affected children. Clinical studies and real-world experiences have demonstrated that early treatment, particularly in presymptomatic or newly diagnosed infants, can produce remarkable functional outcomes that were previously considered unattainable.

Despite these scientific advancements, equitable access to Zolgensma remains a major unresolved global challenge. Its exceptionally high cost places the therapy beyond the reach of many families, especially in low- and middle-income countries where healthcare financing systems may not adequately support rare disease treatment. As observed in the Indian case studies, families frequently depend on crowdfunding campaigns, philanthropic contributions, compassionate access programs, and government intervention to secure treatment. While these mechanisms have saved lives, they are not sustainable substitutes for structured healthcare policy.

The anonymized case studies (X1–X5) collectively demonstrate multiple pathways through which access has been achieved. **X1** highlighted the impact of large-scale digital philanthropy, where a nationwide campaign generated substantial public support. **X2** illustrated the effectiveness of combined fundraising and manufacturer concessions. **X3** showed the strength of civic solidarity and institutional advocacy. **X4** emphasized the importance of compassionate access programs for financially constrained families. **X5** demonstrated how coordinated public donations and governmental rare-disease funding can bridge critical financial gaps.

These examples underscore the urgent need for comprehensive policy innovation to complement clinical innovation. Strategies such as transparent pricing, insurance inclusion, newborn screening programs, public rare-disease funds, and international collaboration are essential to ensure that life-saving therapies reach all eligible children, regardless of geography or economic status.

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