Budget Impact Analysis With and Without Performance-Based Managed Entry Agreement of Different Treatments for Spinal Muscular Atrophy (SMA) in the Kingdom of Saudi Arabia

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Background

Spinal Muscular Atrophy

- Spinal Muscular Atrophy (SMA) is an autosomal recessive neuromuscular disorder. It usually occurs due to deleterious mutations in the Survival Motor Neuron-1 (*SMN-1*) gene located on chromosome 5q.[1] The *SMN*-1 gene expresses the SMN protein, which is important for maintaining motor neurons.[2] Lack of the SMN protein can lead to muscle weakness, paralysis, and/or respiratory muscle failure due to degeneration of alpha motor neurons in the spinal cord's ventral grey horn.[1-3]
- There are different types of SMA, ranging from severe to mild, depending on the age of onset and the level of functional impairment (Table 1). Type 1 is the most common, occurring in approximately 60% of cases.[2,4]
- SMA is more common in the Middle East compared to other parts of the world. In the Kingdom of Saudi Arabia (KSA), the carrier frequency of SMA is estimated to be 2.6% with a birth incidence of approximately 32 cases in every 100,000 births.[5]
- Although studies on the economic burden of SMA are available globally,[6] there are no published studies estimating the cost of SMA management in KSA.

SMA Type	Time of Disease Onset
Type 0	In utero
Type 1	Less than 6 months
Type 2	6 to 18 months
Type 3	More than 18 months

Treatment Options for SMA

- Clinically, SMA is primarily managed through **Best Supportive Care (BSC)**, which includes nutritional and respiratory support as well as management of muscle weakness complications.[4] However, the introduction of new treatment options has changed the dynamics around SMA management worldwide in recent times.
- **Nusinersen,** the first disease-modifying therapy for SMA, was approved in 2016.[7] Nusinersen is an antisense oligonucleotide that specifically targets and hybridizes to the intronic splicing silencer N1 (ISS-N1) site in the SMN-2 gene and augments the production of complete SMN2 protein.[8] **It has been approved for all SMA types.**
- **Onasemnogene Abeparvovec**, the first gene replacement therapy for SMA, was approved in 2019. It is an adeno-associated viral vector-based gene therapy designed to deliver a functional copy of the SMN-1 gene. **It has only been approved for SMA type 1 and SMA type 2 patients of less than 2 years of age.[9]**
- **Risdiplam,** the first orally administered drug for SMA, was approved in 2020.[10] It functions as an SMN-2 gene splicing modifier leading to higher levels of SMN protein.[11] **It has been approved for all SMA types patients of more than 2 months of age.**
- All three drugs are registered in the KSA and per unit costs around **SAR 394,762.5 for nusinersen**, **SAR 7,984,675.90 for onasemnogene abeparvovec**, and **SAR 46,543.40 for risdiplam** as per the Saudi Food and Drug Authority (SFDA) database.

Objective

This study evaluated the budgetary impact of first-in-class interventions for the management of SMA from the perspective of the KSA's Ministry of Health (MoH), with the following objectives:

- **To understand the overall cost of treatment of different interventions for the management of SMA**
- **To understand the net budgetary impact of SMA interventions with BSC for treating different types of SMA**
- **To understand the impact on direct medical and other costs**

Methods

Strategy and Base Case Setting for Model Development

- A budget impact model was developed from the MoH perspective to estimate the total cost for the best supportive care (BSC) with and without the first-in-class interventions, over a time horizon of 5 years. The model's overall methodology and base case settings are outlined below.
- The model was developed using the available data on various model inputs collected through an explorative literature review followed by primary market research and validation by expert committees.
- **Model Inputs:** The inputs used in the model were the estimation of the eligible patient population, market share, clinical outcomes, and costs pertaining to drug acquisition, drug administration, disease monitoring, diagnostics, and drug-related adverse events.

Explorative literature search for various model inputs → **Discussion guides** developed to narrow gaps in secondary data → **Validation** by key experts in MoH, KSA → **Model development** for budget impact analysis with specific inputs for KSA

Elements	Input
Perspective	Ministry of Health (MoH) - Kingdom of Saudi Arabia
Patient Population	Patients with SMA: Type 1, Type 2, and Type 3
Comparators	• Nusinersen, Onasemnogene abeparvovec, or Risdiplam • Best supportive care (BSC)
Analytical Tools	Microsoft® Excel
Time Horizon	5 years
Currency	Saudi Riyal (SAR)

Key Considerations for Model Development

- **Median Survival to Estimate Drug Acquisition Cost:** To better compare these three unique interventions with different treatment practices, drug acquisition cost was calculated using median survival data. Median survival data for nusinersen and risdiplam were calculated by extrapolating the Kaplan-Meier curve from the ENDEAR[12] and FIREFISH[13] trial data and were used in all scenario analyses.
- **Managed-Entry Agreement:** Performance-based managed-entry agreement (PBMEA) was introduced for all three interventions to assess its impact on the overall budget and treatment cost per patient.
- **Market Share:** The study evaluated the market share of first-in-class interventions under different scenarios over a 5-year period**. The scenarios included individual interventions, two interventions, and all three interventions with BSC.**
- **Medical cost:** The impact on direct medical costs was estimated based on the performance data as captured in terms of **survival rates, invasive and non-invasive ICU requirements, and improvement in head control as the main clinical outcome.**

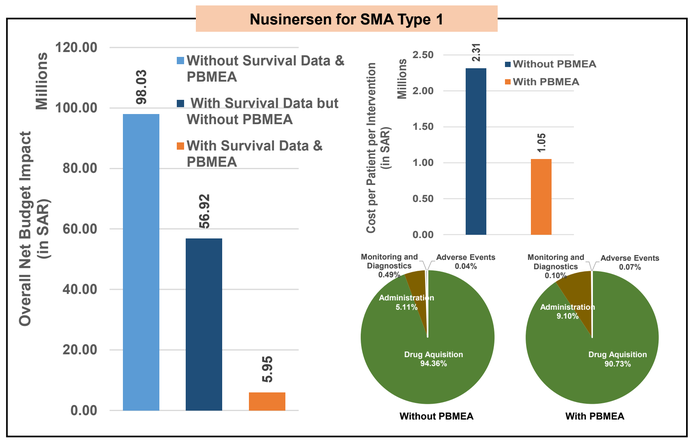
Model Outputs

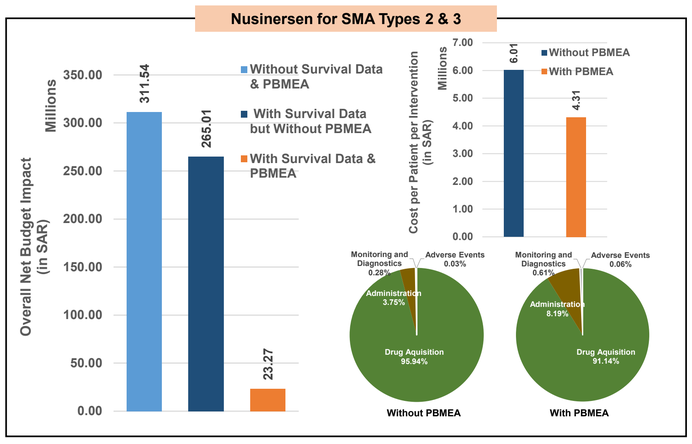
- The model assessed the following two scenarios in the presence and absence of survival data:
  - **World without intervention:** Management of SMA by BSC only.
  - **World with intervention:** Management of SMA by introducing **individual interventions, two interventions, and all three interventions with BSC**. Over time, the market share of BSC decreased and the use of first-in-class interventions increased. The objective is to estimate the net budget impact over a 5-year time horizon with and without PBMEA.

Results

Nusinersen with BSC for SMA Type 1 and SMA Type 2 & 3

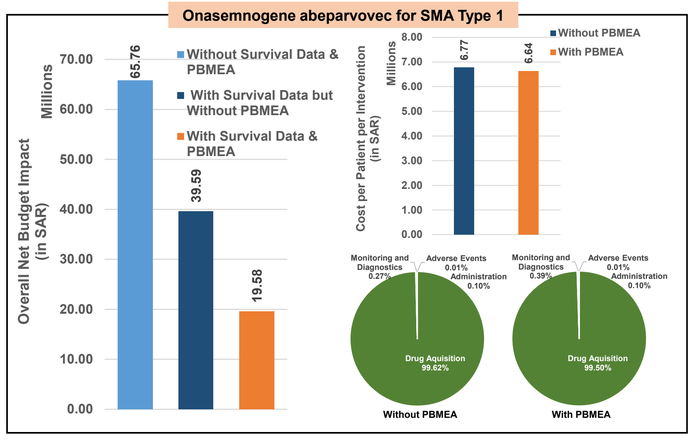
- It is predicted that the market share for nusinersen will rise to 25% for SMA type 1 and 55% for SMA type 2 & 3 within 5 years considering nusinersen with BSC as the only treatment option. However, market shares vary when considering scenarios with multiple interventions.
- The drug acquisition cost constitutes 94-96% of the total cost of nusinersen treatment for all SMA types as estimated over a 5-year time horizon.
- Based on time-to-event data, the estimated median survival rate for nusinersen treatment in patients with SMA type 1 is 1.29 years. SMA type 2 patients have a reported survival rate of 98.5% at 5 years, while for those with SMA type 3, life expectancy is not significantly different from that of a normal population. After including the survival data for both the subpopulations of SMA, the net budget impact was significantly reduced.
- **Further, the introduction of PBMEA can reduce the net budget impact of introducing nusinersen with BSC from 225% to 84% for SMA type 1 and from 283% to 76% for SMA types 2 & 3.** This trend can also be observed for the total cost of the treatment per patient.

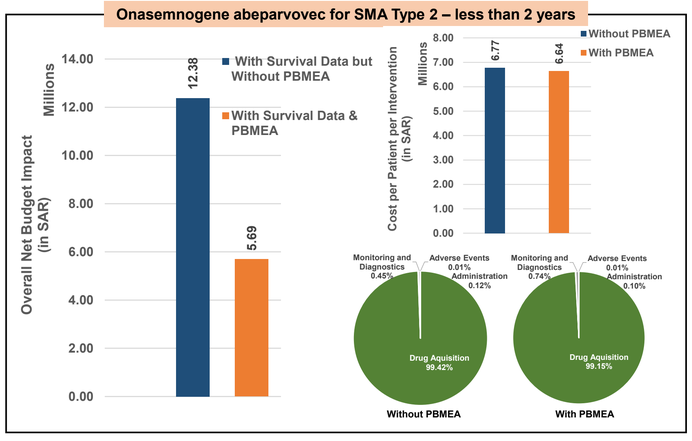




Onasemnogene Abeparvovec with BSC for SMA Type 1 and SMA Type 2 – less than 2 years of age

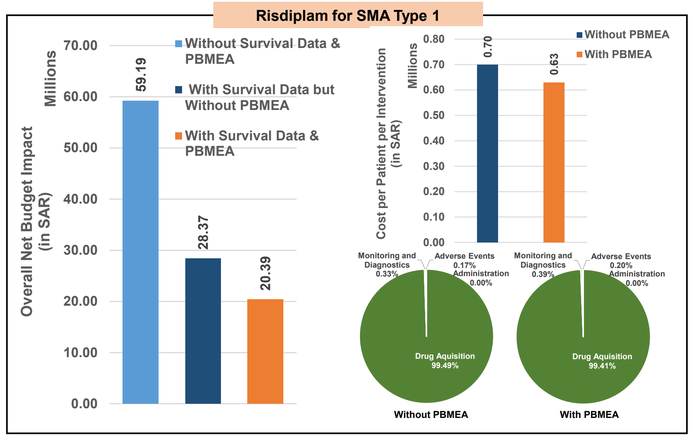
- It is predicted that the market share for onasemnogene abeparvovec will rise to 7% for SMA type 1 and 20% for SMA type 2 – less than 2 years within 5 years considering onasemnogene abeparvovec with BSC as the only treatment option. However, market shares vary when considering scenarios with multiple interventions.
- The drug acquisition cost constitutes more than 99% of the total cost of onasemnogene abeparvovec treatment for both subpopulations as estimated over a 5-year time horizon.
- The median survival data is unnecessary for onasemnogene abeparvovec since it is a one-time gene therapy and does not affect the drug acquisition cost.
- **The introduction of PBMEA can reduce the net budget impact of onasemnogene abeparvovec with BSC for SMA type 1 from 156% to 77%, and for SMA type 2 – less than 2 years from 254% to 117%.** However, the total cost of treatment per patient does not follow a similar trend. This is likely due to the fact that the intervention is a one-time treatment.

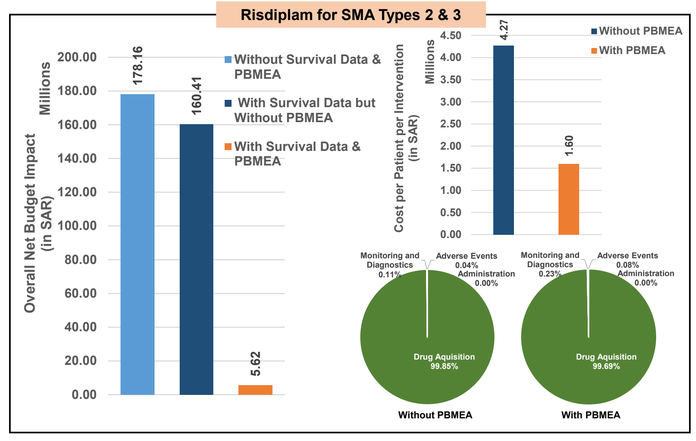




Risdiplam with BSC for SMA Type 1 and SMA Type 2 & 3

- It is predicted that the market share for risdiplam will rise to 62% for SMA type 1 and 55% for SMA type 2 & 3 within 5 years considering risdiplam with BSC as the only treatment option. However, market shares vary when considering scenarios with multiple interventions.
- The drug acquisition cost constitutes 99% of the total cost of risdiplam treatment for all SMA types as estimated over a 5-year time horizon.
- Based on time-to-event data, the estimated median survival rate for risdiplam treatment in patients with SMA type 1 is 3.66 years. SMA type 2 & 3 patients have a similar survival rate as reported for nusinersen above. Therefore, the cost and financial impact of risdiplam were calculated using this information.
- **The introduction of PBMEA can reduce the net budget impact of introducing risdiplam with BSC from 112% to 81% for SMA type 1 and from 171% to 36% for SMA types 2 & 3.** This trend can also be observed for the total cost of the treatment per patient, especially for SMA type 2 & 3. This can be attributed to the difference in the survival rates of the patients in both subpopulations.





Scenario with all three interventions with BSC

- Market shares of all three interventions vary when considering a scenario with all three interventions combined with BSC. **Here, only SMA type 1 and SMA type 2 – less than 2 years are considered as onasemnogene abeparvovec has not yet been approved for SMA type 2& 3.**
- The PBMEA was found to effectively minimize the budget impact in this scenario as well. **The reduction is 6% for SMA type 1 and 92% for SMA type 2 – less than 2 years of age.**

Market Share and Overall Net Budget Impact of Introducing all Three Interventions with BSC for SMA Type 1 and SMA Type 2 – Less than 2 Years

Onasemnogene abeparvovec or Risdiplam with Nusinersen and BSC	Market Share		Overall Net Budget Impact without and with PBMEA			
			Type 1		Type 2 – less than 2 years	
	Type 1	Type 2 – less than 2 years	Without PBMEA	With PBMEA	Without PBMEA	With PBMEA
Nusinersen with BSC	36%	40%	SAR 59,739,123	SAR 33,573,883	SAR 9,494,545	SAR 2,442,373
Onasemnogene abeparvovec with BSC	7%	3%				
Risdiplam with BSC	15%	23%				
BSC only	42%	35%				

Conclusions

- **In this study, survival data, patient eligibility, and efficacy endpoint data from clinical trials were used to estimate the budget impact of introducing these first-in-class interventions, along with BSC, to manage SMA in the Kingdom of Saudi Arabia.**
- **The study also considered PBMEAs that decreased the overall budget impact, maintaining the eligibility characteristics, and linking the resource allocation to health outcomes.**
- **The introduction of the first-in-class interventions will have an impact on the MoH budget with drug acquisition cost being the primary contributor. However, this can be offset by an improvement in clinical management through PBMEAs.**
- **The increase in budget is associated with improved survival rates, contributing to the rise in management costs as a necessary aspect of treatment prioritization taking into consideration SMA's poor prognosis and overall burden of the disease.**
- **This study is the first health economics evaluation to assess all three first-in-class interventions with survival data and PBMEAs.**
- **The Saudi Ministry of Health has also become the first health authority to cover the cost of all three interventions for the treatment and management of SMA.**

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