



Assessing the Value of Nusinersen for SMA: A Comparative Analysis of Reimbursement Submission and Appraisal in European Countries

Blonda A^{1*}, Barcina T¹, Simoens S¹

¹KU Leuven, Department of Pharmaceutical and Pharmacological Sciences, Leuven

*Contact: alessandra.blonda@kuleuven.be

Introduction

- Nusinersen is an orphan drug intended for the treatment of spinal muscular atrophy (SMA), a severe neuromuscular disorder
- Considering the very high costs of orphan drugs and the expected market entry of cell and gene therapies, there is increased interest in the use of health technology assessment (HTA)
- This study explored the role of the economic evaluation and budget impact analysis on the reimbursement of nusinersen

Methods

- Analysis of HTA reports for nusinersen in 12 European countries
- Extraction of information on economic evaluation and budget impact
- Literature search on overall reimbursement decision and managed entry agreements (MEA)

Results

I. Cost-effectiveness

- None of the countries considered nusinersen to be cost-effective
- Many remaining uncertainties such as utility values, Biogen's assumptions on long-term effectiveness and discrepancies between the clinical trial and real-world patient group

II. Budget impact

- Limited public data on the scope and outcome of the budget impact analysis

III. Contextual Determinants

- Indications of several implicit, context-dependent determinants in favor of reimbursement
- No transparency regarding the extent to which these determinants influenced the decision

IV. Overall reimbursement decision

- All countries reimbursed nusinersen despite uncertain or unfavorable cost-effectiveness and budget impact
- No correlation between nusinersen's cost-effectiveness and reimbursed SMA subtypes

V. Managed entry agreements

- Lack of public data on how MEAs improve cost-effectiveness or manage uncertainties

Conclusion

- An HTA based on economic criteria alone is insufficient to value orphan drugs
- The economic evaluation loses its value as a tool to rank orphan drugs and allocate resources due to the lack of transparency on arguments in favor of reimbursement
- Decision-makers should formally incorporate all determinants into a reimbursement process that is transparent, inclusive and impartial

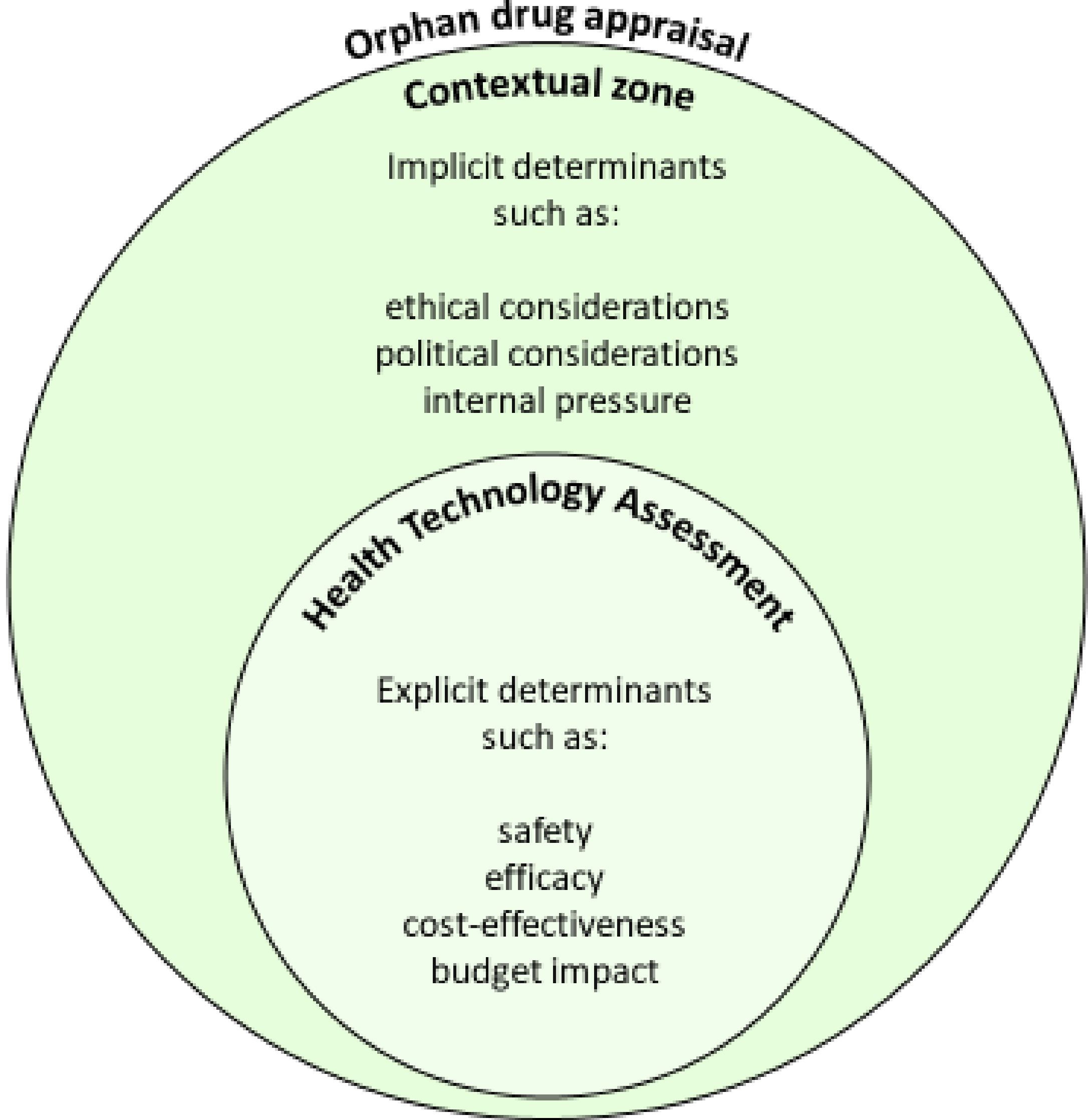


Fig 1. Visualization of the appraisal process of an orphan drug such as nusinersen

Table 1. Cost-effectiveness of nusinersen for SMA*

	EO (SMA I)		EO (SMA I) incl. caregiver		LO (SMA II and III)		LO (SMA II and III) incl. caregiver	
	ICER (€/QALY)		ICER (€/QALY)		ICER (€/QALY)		ICER (€/QALY)	
	Biogen	HTA agency	Biogen	HTA agency	Biogen	HTA agency	Biogen	HTA agency
Canada	464,891	6,399,097	-	-	SMA II: 2,153,470 SMA III: 1,994,746	SMA II: 17,034,246 SMA III: 4,189,627	-	-
France	-	-	-	-	2,719,821	-	-	-
England and Wales	492,350	508,896	486,015	762,895	1,513,499	493,756	1,084,900	764,425
Ireland	512,844	-	253,502	-	2,156,624	-	1,061,372	-
Scotland	508,537	-	503,247	-	1,926,381	-	1,365,539	-
Sweden	-	Between 583,036 and 779,435	-	-	-	Between 736,298 and 1,297,144 ¹	-	-
The Netherlands	529,749	632,802	-	-	1,117,179	1,792,939	-	-
US	1,037,257	-	-	755,556 ² 1,048,450 ³	7,607,792	-	7,607,792	-

Table 2. Budget impact of nusinersen for SMA

	Total cost per patient	Total budget impact
Belgium	-	For SMA type I, II, III and pre-symptomatic patients: - €40,000,000 in year 1 - €25,000,000 in year 2 - €28,000,000 in year 3
Canada	\$708,000 in year 1 \$354,000 for each subsequent year	-
France	Only data on estimated number of patients	-
England and Wales	No data	-
Germany	€621,354 in year 1 €310,878 – €310,943 for each subsequent year	-
Italy	-	-
Ireland	-	€37,880,000 for five years
Scotland	-	Data kept confidential under conditions of a patient access scheme
Sweden	€467,973 in year 1 €233,987 in following years	Data kept confidential under conditions of a MEA
The Netherlands	€499,800 in year 1 for SMA I, II or III €249,900 in following years for SMA I, II or III	For patients in whom therapeutic added value is demonstrated: - €29,738,100 - €30,084,334 incl. drug administration costs
The US	\$573,900 per year for pre-symptomatic SMA	-

* Costs were adjusted for inflation and currency. ¹ Only for SMA II. ² healthcare sector perspective. ³ modified societal perspective.

Abbreviations: EO, early onset; LO, later onset; MEA, managed entry agreement; QALY, quality-adjusted life year; SMA, spinal muscular atrophy