EE327

Cost-Effectiveness of Teduglutide in Adult and Pediatric Patients with Short Bowel Syndrome in Argentina. A Markov Model Analysis

Carlos Boissonnet [1], Mariano Giorgi [1,2], Laura Brion [3], Laura Ungar [3], Federico Ussher [3], Claudio Covini [4] and Jeannette Rodger [4]

1 Health Economics and Technology Assessment Unit. Centro de Educación Médica e Investigaciones Clínicas "Norberto Quirno" (CEMIC), Instituto Universitario CEMIC (IUC), Buenos Aires, Argentina, Cardiology Section, Department of Internal Medicine, Centro de Educación Médica e Investigaciones Clínicas "Norberto Quirno" CEMIC, Buenos Aires, Argentina; 2 Department of Pharmacology, Instituto Universitario CEMIC, Buenos Aires, Argentina; 3 Medical Affairs, Takeda Argentina S.A., Buenos Aires, Argentina; 4 Access, Takeda Argentina S.A., Buenos Aires, Argentina.

Background

- Teduglutide (orphan drug designation), an analogue of glucagon-like peptide 2, has been licensed for the treatment of short bowel syndrome (SBS) in patients 1 year of age and older following intestinal adaptation after surgery (1,2).
- SBS is an ultra-rare, long-term and potentially life-threatening condition requiring parenteral nutrition (PN). Patients on PN suffer severe complications like intestinal failure liver disease, catheter-related sepsis, liver and intestinal transplant or death (3-5).
- Several studies demonstrated that teduglutide reduces volume and/or days on PN which led to a reduction in severe complications in children and adults (5-9). Recent real-world data on teduglutide show meaningful rates of PN autonomy beyond the 24 weeks evaluated in the STEPS trials (Study of Teduglutide Effectiveness in PN-Dependent SBS Subjects), suggesting significant benefits on longer treatment durations (10-14).
- In Argentina, the most frequent intestinal anatomy in patients with SBS is colon in continuity (type III) (12-15). Interestingly, accumulating evidence suggests that type III patients have higher chances of PN autonomy and complete recovery of their quality of life, even still on teduglutide every other day or after its discontinuation (10-12).
- Teduglutide is a high-cost medication, with an estimated cost of ~300,000 USD per patient per year in Argentina. Comparatively, the cost of PN dependence is estimated to be ~121,000 USD per year for nutritional support alone.

Objective

- To determine the cost-effectiveness of teduglutide in adult and pediatric patients with SBS in Argentina using a Markov Model Analysis

Methods

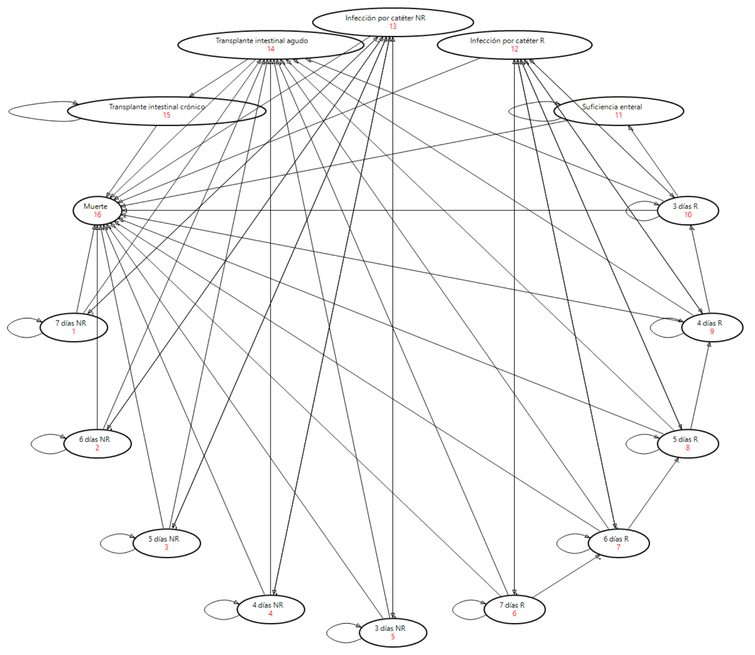
- We developed independent Markov models for adults and children comparing teduglutide (TED) versus standard of care (SoC). Base-case analysis was performed using TreeAge Pro Healthcare 2022.
- The base case was presumed at age 40 (adults) and 12 (children) and to have short bowel syndrome requiring PN for 7 days/week. The time horizon used was lifelong (adults) and 5 years (children). A third-party payer perspective was taken, evaluating only direct costs to the healthcare system.
- Transition states were days in PN (from 7 to 0), catheter-related sepsis, intestinal transplant, and death **(Figure 1).** The model was informed with data from the STEPS trials and observational studies published up to June 2022. Utilities were obtained from published data and costs from local sources (in US dollars). Parameter values are listed in **Table 1**.
- Effectiveness was expressed in Quality-Adjusted Life Years (QALYs). The willingness-to-pay threshold considered was 1 GDP per QALY (8,810 USD).

Table 1: Parameter Values Used in the Models

	Adult Model		Pediatric Model	
	Base case	Range	Base case	Range
Patient initial distribution				
7 days PN / week	0.3	NA	0.375	NA
6 days PN / week	0.1	NA	0.375	NA
5 days PN / week	0.1	NA	0.1	NA
4 days PN / week	0.4	NA	0.1	NA
3 days PN / week	0.1	NA	0.05	NA
6-month significant improvement* rate				
SoC	0.26	0.15 - 0.40	0.11	0.03 - 0.48
TED	0.91	0.76 - 0.98	0.82	0.48 - 0.98
Catheter-related sepsis rate, per month**				
7 days PN / week	0.072	By equation	0.145	By equation
6 days PN / week	0.060	By equation	0.120	By equation
5 days PN / week	0.050	By equation	0.099	By equation
4 days PN / week	0.041	By equation	0.082	By equation
3 days PN / week	0.034	By equation	0.068	By equation
0 days PN / week	0	By equation	0	By equation
Case fatality, catheter-related sepsis	0.017	0.006 - 0.039	0.014	0.005 - 0.037
Catheter thrombosis rate, per month	0.005	0.002 - 0.008	0.0063	0.004 - 0.009
Significant IFALD rate, per month	0.003	0.002 - 0.004	0.0006	0.0004 - 0.0009
Transplant mortality, per month	0.009	0.007 - 0.011	0.007	0.005 - 0.008
Utilities				
0 days PN / week	0.74	0.56 - 0.93	Idem	Idem
3 days PN / week	0.61	0.46 - 0.76	Idem	Idem
4 days PN / week	0.57	0.43 - 0.71	Idem	Idem
5 days PN / week	0.52	0.39 - 0.65	Idem	Idem
6 days PN / week	0.48	0.36 - 0.60	Idem	Idem
7 days PN / week	0.39	0.29 - 0.49	Idem	Idem
Transplantation (month 1)	0.39	0.29 - 0.49	Idem	Idem
Transplantation (later)	0.74	0.56 - 0.93	Idem	Idem

SoC, standard of care; TED, teduglutide; PN, parenteral nutrition; IFALD, intestinal failure-associated liver disease.
* Defined as a reduction of ≥20% of daily PN volume from baseline.
** Estimated by equation (Poisson regression of association between days PN/week and risk of catheter-related sepsis).

Figure 1. Transition States Diagram



R: Responder; NR: Non-responder.
Transition states 1-5: 7-3 days NR; 6-10: 7-3 days R; 11: PN autonomy; 12: catheter-related sepsis in R; 13: catheter-related sepsis in NR; 14-15: acute and chronic intestinal transplant; 16: death.

Results

Adult Model

- In adults, our model predicted that teduglutide reduced mortality (-46.9%), sepsis (-81.5%), intestinal transplant (-84.5%) and increased PN weaning (+251%) **(Table 2).**
- Incremental effectiveness of teduglutide was 4.39 QALY (1.52 times vs. SoC) at 574,773 USD (3.96 times vs. SoC). ICER was 130,891 USD/QALY **(Table 3). Figure 2** shows the cost-effectiveness relationship between teduglutide and SoC.

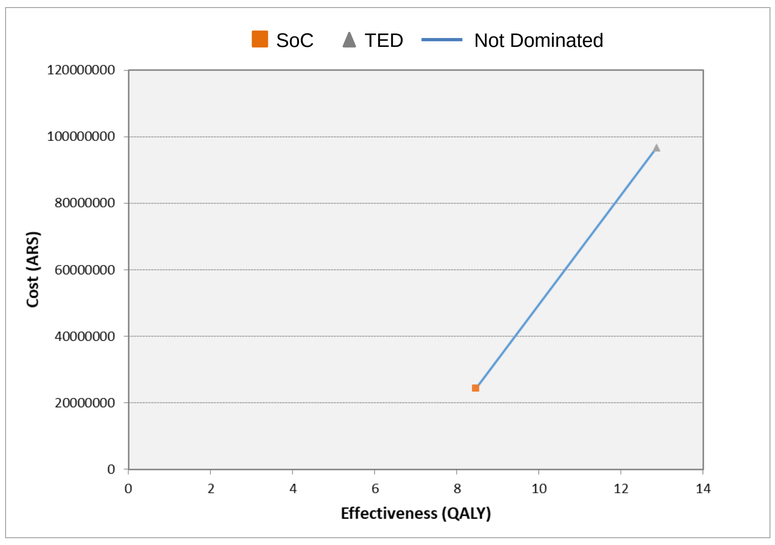
Table 2. Clinical Results in Adults

Month	PN Weaning (%)	Catheter Sepsis (%)	Transplant (%)	Death (%)
		SoC		
6	21.6	7.3	5.0	1.1
12	23.6	6.5	9.3	2.3
24	24.3	5.9	11.0	5.2
60	23.9	4.9	13.0	13.9
120	23.0	4.1	8.3	27.2
240	19.2	2.7	3.3	50.2
		TED		
6	75.6	2.6	0.8	0.8
12	82.6	1.4	1.3	1.2
24	85.2	1.1	1.5	2.1
60	83.9	0.9	1.8	4.9
120	80.6	0.8	1.2	10.2
240	67.4	0.5	0.5	26.8

Table 3. Cost-Effectiveness Results in Adults

Strategies	Cost (USD)	Incremental Cost (USD)	Effectiveness (QALY)	Incremental Effectiveness	ICER (USD/QALY)
SoC	193,754		8.46		
TED	768,527	574,773	12.85	4.39	130,891

Figure 2. Cost-Effectiveness Plane in Adults



Pediatric Model

- In children, our model predicted that teduglutide reduced mortality (-67.7%), sepsis (-61.4%), intestinal transplant (-78.8%) and increased PN weaning (+637.5%) **(Table 4).**
- Incremental effectiveness was 0.67 QALY (1.27 times vs. SoC) at 418,597 USD (2.98 times vs. SoC). ICER was 624,793 USD/QALY **(Table 5). Figure 3** shows the cost-effectiveness relationship between teduglutide and SoC.

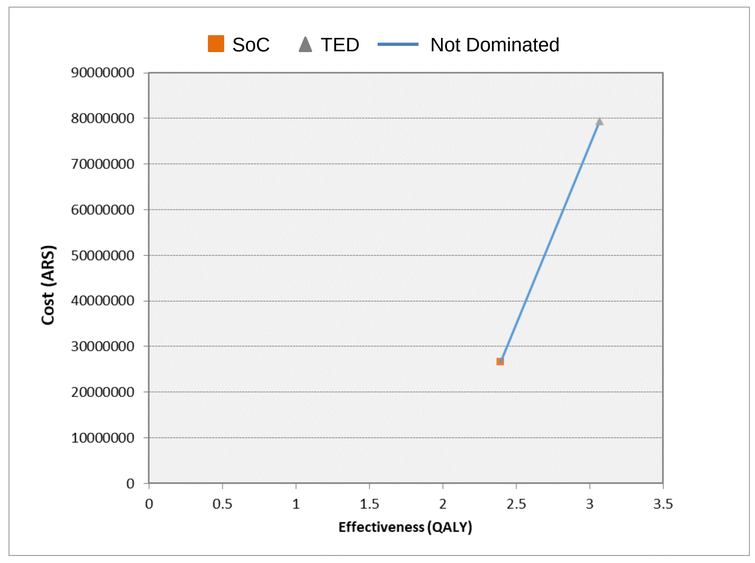
Table 4. Clinical Results in Children

Month	PN Weaning (%)	Catheter Sepsis (%)	Transplant (%)	Death (%)
		SoC		
6	7.8	12.6	6.5	1.1
12	9.0	11.4	12.0	2.5
24	9.6	9.5	20.9	5.7
60	9.6	5.7	35.8	16.7
		TED		
6	57.6	5.9	1.5	0.9
12	66.5	4.0	2.4	1.4
24	70.8	3.1	4.5	2.3
60	70.8	2.2	7.6	5.4

Table 5. Cost-Effectiveness Results in Children

Strategies	Cost (USD)	Incremental Cost (USD)	Effectiveness (QALY)	Incremental Effectiveness	ICER (USD/QALY)
SoC	211,896		2.4		
TED	630,492	418,597	3.07	0.67	624,793

Figure 3. Cost-Effectiveness Plane in Children



Limitations

- Limited published data on real-world safety and efficacy before June 2022.
- Indirect costs associated with SBS were not included in this model.
- The pediatric vial is not available in Argentina; thus, the pediatric model assumed utilization of the adult vial.
- A highly fragmented healthcare system and financial and economic volatility hampered accurate costs and discount estimations; thus, reference prices were considered.

Conclusions and Discussion

- SBS poses a challenge for health technology assessment due to limited published data, as well as the impact SBS etiology and intestinal anatomy, have on such evaluations.
- This model evaluated the clinical benefit of teduglutide in adult and pediatric patients with SBS based on available evidence considering clinical endpoints beyond those related to PN requirements.
- In this model, teduglutide is an effective intervention with significant benefits on relevant clinical endpoints (PN weaning, mortality, catheter-related sepsis and intestinal transplant). However, at the current price, teduglutide is beyond the cost-effectiveness threshold considered in Argentina. Of note, this model only considered teduglutide dosing as per manufacturer´s instructions.
- Remarkably, real-world evidence in Argentina showed sustained clinical benefits in selected patients after PN weaning with teduglutide every other day dosing (12). This topic is addressed in local expert SBS clinical recommendations (16).
- The implementation of value-based contracting methodologies and multidisciplinary approaches aimed at improving treatment outcomes may enhance patient access in Argentina considering the high-cost burden to treat this debilitating disease.

References

1. Shire-NPS Pharmaceuticals Inc. GATTEX® (teduglutide) prescribing information. Lexington, MA, USA. 2021; **2.** Shire Pharmaceuticals Ireland Limited. Revestive® (teduglutide) summary of product characteristics. Dublin, Ireland. 2019; **3.** O'Keefe SJ et al. Clin Gastroenterol Hepatol 2006;4:6–10; **4.** Pironi L et al. Clin Nutr 2016;36:247–307; **5.** Jeppesen PB. JPEN J Parenter Enteral Nutr 2014;38(Suppl):8S–13S; **6.** Jeppesen PB et al. Gastroenterology 2012;143:1473–81 e3; **7.** Kocoshis SA et al. JPEN J Parenter Enteral Nutr. 2020 May;44(4):621-631; **8.** Jeppesen PB et al. Gut 2005;54(9):1224–31; **9.** Schwartz LK et al. Clin Transl Gastroenterol 2016;7:e142; **10.** Harpain F et al. JPEN J Parenter Enteral Nutr. 2022;46:300–309; **11**. Bioletto F et al. Nutrients 2022, 14, 796; **12.** Solar H et al. JPEN J Parenter Enteral Nutr. 2021 Jul;45(5):1072-1082; 13. Gondolesi G et al. JPEN J Parenter Enteral Nutr. 2020 May;44(4): 703-713; **14.** Solar H et al. Clinical Nutrition ESPEN, Volume 54, 2023:552; **15.** Gondolesi G et al. J Parenter Enteral Nutr. 2022;1–9; **16.** Solar H et al. Acta Gastroenterol Latinoam 2022;52(1):47-56

Disclosures and Funding

Boissonnet C and Giorgi M have nothing to declare. Brion L, Ussher F, Ungar L, Covini C and Rodger J are employees of Takeda Argentina S.A.
This study was funded by Takeda Argentina S.A.