Learnings from previous health technology assessments of disease-modifying therapies in neurodegenerative diseases

Sosa J[1], Stan D[2], Perez L[3]

[1]Parexel International, Stockholm, Sweden;
[2]Parexel International, Bucharest, Romania;
[3]Parexel International, Sevilla, Spain

Background

Neurodegenerative diseases (NDs) have lagged behind in terms of therapeutic innovation compared to other chronic diseases. However, recent successful launches have allowed the commercialization of a few disease-modifying therapies (DMTs) targeting NDs [1]. Considering that promising therapies (e.g., sodium phenylbutyrate and taurursodiol, lecanemab) are launching in North America, this study aims to review Health Technology Assessments (HTA) on previous DMTs on NDs in Canada and provide learnings for upcoming DMTs.

Methods

We followed the National Institutes of Health's (NIH) definition of NDs and considered DMTs as all treatments that delay or slow the progression of a disease by targeting its underlying cause, rather than just the symptoms [3, 4]. Subsequently, we retrieved all HTA reports evaluating DMTs on NDs published by the Canadian Agency for Drugs and Technologies in Health (CADTH) in the past ten years [2,3]. Finally, we conducted a descriptive analysis on the reports to identify areas of transferable learning (**Figure 1**).

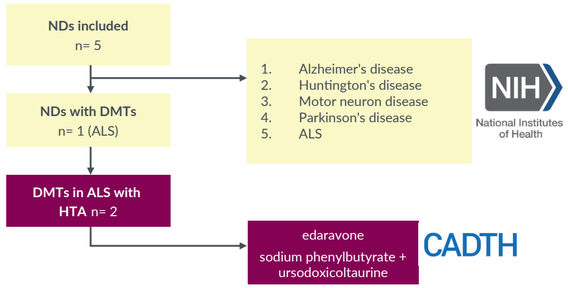
Results

We identified five diseases classified as NDs by the NIH. Among these, only amyotrophic lateral sclerosis (ALS) was associated with licensed DMTs. Within ALS, only two DMTs were identified as launched and assessed in Canada: edaravone and sodium phenylbutyrate + ursodoxicoltaurine (**Table 1**). For both DMTs, reimbursement was granted only for early stages of the disease and tied to a 95% price reduction to meet the willingness-to-pay thresholds (WTPT) for cost-effectiveness. In the HTA reports, both DMTs + standard of care (SoC) were compared against placebo + SoC, as no DMTs were available (**Figure 2**). The efficacy of both DMTs was assessed using a clinically validated disease-specific instrument to measure disease progression and neurologic functionality. The relatively short time in the clinical trials length and follow-up was aligned with the fast disease progression.

Conclusions

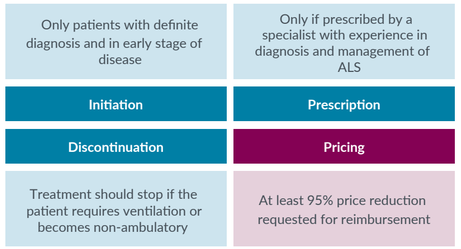
Novel DMTs launching in the in NDs space (e.g., lecanemab) can expect to be compared against symptomatic treatments due to the lack of DMTs for these disease areas. In cases where the prices of symptomatic treatments threaten the willingness-to-pay for DMTs despite their value, manufacturers may need to explore innovative mechanisms for financing and reimbursement, including outcomes-based entry agreements. In contrast, the appropriateness of short clinical trial and follow-up times observed for NDs related to fast disease progression and expected short survival time will likely support manufacturers' evidence package, lowering expectations on long-term value demonstration from the financing authorities.

Figure 1: Flow chart diagram of methodology



Abbreviations: ALS: Amyotrophic lateral sclerosis, DMT: Disease-modifying therapy; HTA: Health Technology Assessment, ND: Neurodegenerative diseases

Figure 2: CADTH's conditions for reimbursement in the analyzed NDs



Abbreviations: ALS: Amyotrophic lateral sclerosis; CADTH: Canadian Agency for Drugs and Technologies in Health

Table 1: Table showing names of some of the instruments selected under each disease area

Drug	Decision Date	Decision	Comparator	Endpoints	Follow up	Safety warnings	Cost effectiveness	Price reduction
Edaravone	March 2019	Reimbursed, conditioned	Placebo + SoC	Overall Survival Disease-specific PRO tools – ALSFRS-R total score – Norris Scale total score – ALSAQ-40	24 weeks	No	– Not cost-effective, price perceived as too high – ICUR of $1,957,200	95% required to meet WTPT of $200,000 per QALY gained in patients with ALS stage 1
Sodium Phenylbutyrate + Ursodoxicoltaurine	August 2022	Reimbursed, conditioned	Riluzole + SoC	Disease-specific PRO tool – ALSFRS-R total score	24 weeks	No	– Not cost-effective, price perceived as too high – ICER of $2,086,658	98% required to meet WTPT of $50,000 per QALY gained

*All efficacy outcomes had missing data, including the ALSFRS-R total score at Week 24 due to patients discontinuing from the study (23% of the randomized population) leading to uncertainty in the results
Abbreviations: AE: Adverse event; ALS: Amyotrophic Lateral Sclerosis Functional Rating Scale - revised; ALSAQ-40: ALS Assessment Questionnaire-40; DMT: Disease-modifying therapy; ICER: Incremental cost-effectiveness ratio; ICUR: Incremental cost utility ratio; ND: Neurodegenerative disease; PRO: Patient-reported outcomes; SoC: Standard of care, QALY: Quality-adjusted life-year, WTPT: Willingness to pay threshold

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Parexel International
2520 Meridian Pkwy
Durham, NC 27713, USA
+1 919 544-3170
www.parexel.com