Improving Access to Behavioral and Mental Health Therapies in the EU: An Analogue Assessment Deep Dive

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INTRODUCTION

Mental disorders are common and have substantial economic and societal impact across Europe. One in six people in Europe suffers from a mental disorder such as anxiety, depression, and bipolar disorders every day, and without effective treatment and support, mental health problems can have a devastating effect on people's lives, increasing the risk of dying from suicide[1].

Despite the huge burden of mental disorders and high unmet need for novel therapies, access to branded therapies targeting mental disorders has been sparse in Europe. For instance, a recent report by the European Commission noted that around 56% of patients with major depression receive no treatment at all, despite the availability of effective treatment.[2] While some countries have launched policy initiatives to achieve better access to mental health therapies and services in the past[3], there is still a gap in access to these therapies and notable disconnect between evidence requirements for favorable health technology assessments (HTA) and feasibility to deliver from a clinical perspective.

OBJECTIVES

The purpose of this research was to assess the evidence generation strategies performed to optimize HTA outcomes and improve access to therapies with neurological indications, including mental disorders, in Europe.

METHODS

An initial list of therapies approved by the EMA between 2016 and 2021 was extracted from the EMA website. The list of therapies was filtered to prioritize those with neurology indications, identifying a total of 49 therapies, of which 17 had submitted supplemental evidence to the G-BA in Germany, HAS in France and NICE in the UK.

The list of neurological therapies with supplemental evidence was scanned to identify those approved for the treatment of a mental disorder (i.e., associated with cognitive, or behavioral disturbances[4]), including schizophrenia, opioid-related disorders, Parkinson's disease, and depressive disorder, among others. The following therapies were selected for a deep dive analysis due to the amount of additional evidence generated and submitted: AIMOVIG, QUVIVIQ and SPINRAZA with a neurological indication, and BUVIDAL, ZUBSOLV and LIBMELDY with a mental health indication.

RESULTS

- Analogues with a neurological indication generally were able to achieve more favorable HTA outcomes compared to the analogues with a mental disorder (Figure 1).
- AIMOVIG was able to secure favorable HTA outcomes (e.g., Considerable Added Benefit in Germany) in their re-submission with comparative data against the SoC in migraine.
- In the case of SPINRAZA, HTA agencies conducted separate assessments for different subpopulations, resulting in more negative outcomes for the subpopulations where robust data from a randomized Phase 3 clinical trial was missing.
- Amongst the mental health therapies, only LIBMELDY was able to achieve positive HTA outcomes across EU3 due to its statistically significant improvements in motor function in metachromatic leukodystrophy, which were deemed patient relevant. On the contrary, both BUVIDAL and ZUBSOLV faced challenges in securing access, with BUVIDAL ultimately withdrawing from the EU in September 2023.
- The lack of sufficient evidence to demonstrate sustained clinical benefit in the long-term and the lack of a clinically meaningful benefit in QoL emerged as the most commons gaps highlighted by HTA agencies.
- The use of an inappropriate trial comparator was partly driving unfavorable HTA outcomes for most analogues; however, the feasibility of conducting a head-to-head trial with the SoC as an active comparator in mental health conditions remains unclear.
- For example, a non-drug therapy was considered the first line SoC for insomnia (i.e., cognitive behavioral therapy, CBT), and both the G-BA and HAS raised uncertainty in QUVIVIQ's added clinical benefit relative to the SoC, expecting at least the underlying use of CBT in patients enrolled in the clinical trial to reflect real-world practice.

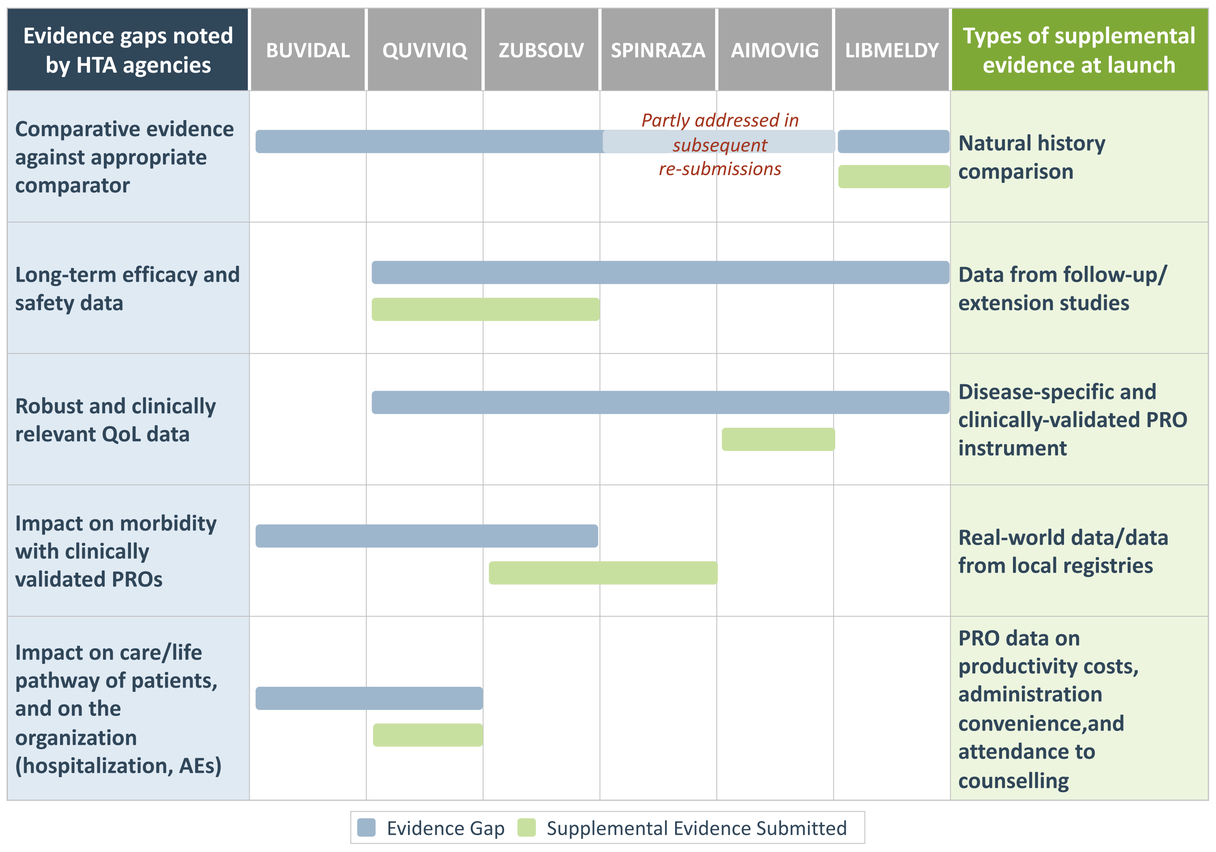
Figure 1. HTA outcomes of prioritized analogues in France, Germany, and the UK

		HTA Outcomes		
Product	**EMA Indication**	🇩🇪	🇫🇷	🇬🇧
AIMOVIG	Prophylaxis of migraine in adults who have at least 4 migraine days per month	Considerable Added Benefit	SMR Important, ASMR V	Recommended with Conditions
QUVIVIQ	Insomnia with symptoms present for at least 3 months and considerable impact on daytime functioning	No Added Benefit	SMR Moderate, ASMR IV	Recommended with Conditions
SPINRAZA	5q Spinal Muscular Atrophy (SMA)	Considerable, Non-quantifiable, No Added Benefit across subpopulations	SMR Important, ASMR III/ V depending on the subpopulation	Recommended with Conditions
BUVIDAL	Opioid dependence within a framework of medical, social and psychological treatment	N/A	SMR Important, ASMR IV	N/A
ZUBSOLV	Opioid dependence within a framework of medical, social and psychological treatment	N/A	SMR Important, ASMR V	Not Assessed/considered in recent NICE guidance
LIBMELDY	Metachromatic leukodystrophy (MLD) with biallelic mutations in the ARSA gene in children with late infantile or early juvenile forms	Considerable and Hint of Non-quantifiable Added Benefit across subpopulations	SMR Important, ASMR III	Recommended without restrictions

Analogues with neurological indication and mental health component — Positive Outcome · Neutral Outcome · Negative Outcome

Despite the challenges and evidence gaps noted by the HTA agencies, these analogues presented other types of supplemental evidence, aiming to enhance their HTA ratings (Figure 2).

Figure 2. Evidence gaps and supplemental evidence generation activities conducted by selected analogues



The use of follow-up studies to assess the long-term efficacy and safety of the product as well as real-world data from clinical practice or local registries were the most common evidence generation activities.

LIBMELDY's use of a natural history comparison successfully showed the severity and progressive nature of the disease and the absence of curative treatments, optimizing its HTA ratings despite the limitations of such comparison.

Lastly, analogues like AIMOVIG invested in the development of a disease-specific patient-reported instrument to demonstrate the disease impact on the patient's ability to function in activities of daily living, which was deemed patient-relevant.

Other therapies such as QUVIVIQ and BUVIDAL leveraged data from PROs to demonstrate benefit in terms of cost-savings, administration convenience, or even attendance to counselling in the case of BUVIDAL. The impact of such evidence on reimbursement was rather limited as the clinical effectiveness shown in their pivotal trials, as well as the cost-effectiveness in the UK, were the primary value drivers.

DISCUSSION AND CONCLUSION

Discussion

Most of the investment in supplemental evidence generation was seen with analogues with a neurological indication. Analogues like AIMOVIG in migraine, SPINRAZA in SMA and QUVIVIQ in insomnia presented multiple different types of supplemental evidence in their assessment (e.g., long-term studies, RWE, development of PRO tools) and were able to achieve relatively favorable HTA outcomes in most cases.

On the contrary, analogues with a behavioral component such as ZUBSOLV and BUVIDAL for the treatment of opioid dependence were quite unsuccessful in achieving favorable access. Their attempts to generate additional evidence consisted of extension studies to prove their sustained benefit in the long-term, including some patient case studies or data on patient convenience, which had limited impact on their HTA ratings given the use of an inappropriate trial comparator.

Conclusion

This research showed that mortality and/or morbidity outcomes shown in randomized clinical trials with an appropriate comparator remain the primary driver for successful HTA outcomes. Despite the difficulty for mental health therapies to show such patient-relevant outcomes in a robust clinical trial, learnings from the neurological analogues explored indicate that additional evidence generation strategies, particularly the development of disease-specific PROs and use of RWE at launch, have the potential to improve access to innovative mental health therapies in Europe.

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