What has worked well in Fabry disease? A HTA Landscape Assessment Study

HTA364

Raju Gautam[1], Saeed Anwar[2], Ratna Pandey[2], Shilpi Swami[1] , Tushar Srivastava[1]

[1]ConnectHEOR, London, UK; [2]ConnectHEOR, Delhi, India
Email: raju.gautam@connectheor.com

connectHEOR

BACKGROUND

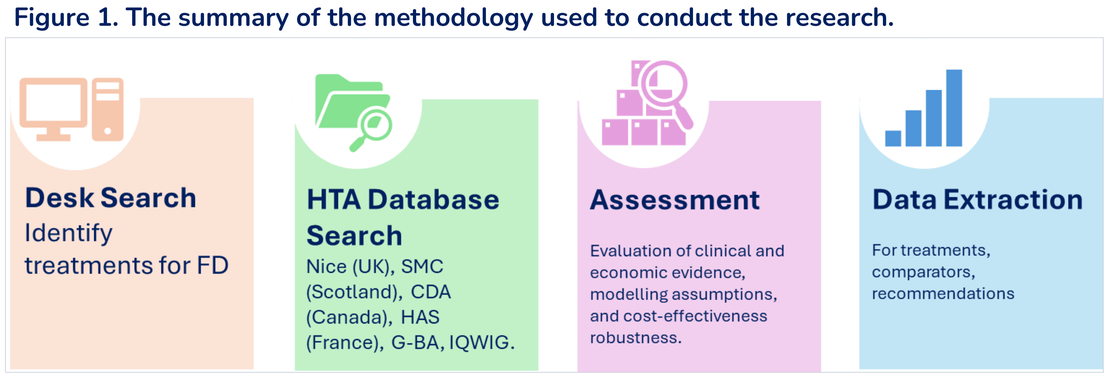
Context: Fabry disease (FD) is an X-linked lysosomal storage disorder caused by deficient α-galactosidase A that leads to accumulation of glycolipid. It is a rare inherited disease impacting multiple organs such as kidneys, heart, skin, and nervous systems.[1,2] Understanding the health technology assessment (HTA) of treatments for rare-disease is imperative to identify the decision drivers, evidence gaps, and critiques to inform the future submissions.[3]

Objective: The objective of this study was to assess the HTA landscape of treatments for FD.

METHODS

- A desk research was conducted to identify the treatments approved and available for FD.
- The HTA reports of treatments were searched on following websites: NICE (UK), SMC (Scotland), CDA (Canada), HAS (France), G-BA, IQWiG (Germany), and European Network of HTA (EUnetHTA).
- The reports were assessed for clinical and economic evidence, reimbursement recommendations, and key issues/critiques (**Fig. 1**).

Figure 1. The summary of the methodology used to conduct the research.



RESULTS

- The desk research revealed four treatments approved and available for FD (**Table 1**).

Class	Treatment	Brand name
Enzyme replacement therapy (ERT)	Agalsidase-α	Replagal®
	Agalsidase-β	Fabrazyme®
	Pegunigalsidase-α	Elfabrio®
Pharmacologic chaperone therapy	Migalastat	Galafold®

- The website searches identified **14 HTA reports** in total published between 2004 and March 2025; their distribution and landscape is presented in **Figure 2** and **Figure 3**.
- **Half of the submitted HTAs were recommended with conditions**, whereas **~30% were not recommended** (**Figure 4**). The recommendations by HTA agencies and by years are presented in **Figure 5** and **Figure 6**.

Figure 2. Distribution of identified HTA reports

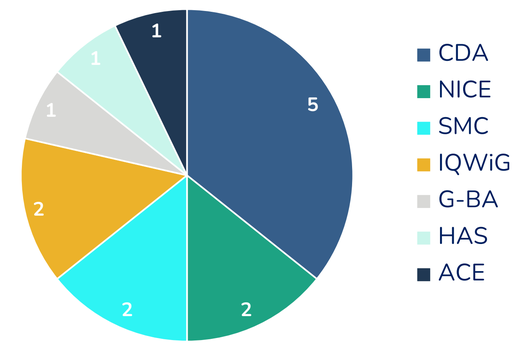


Figure 3. HTA landscape journey of treatments for FD

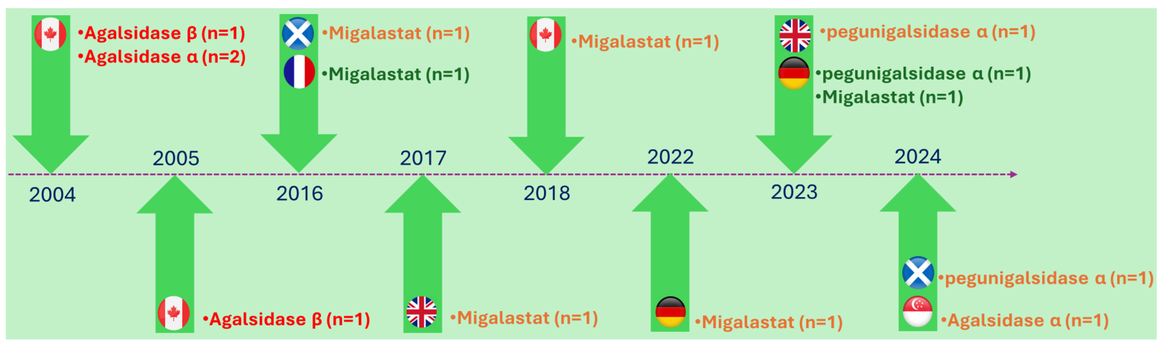
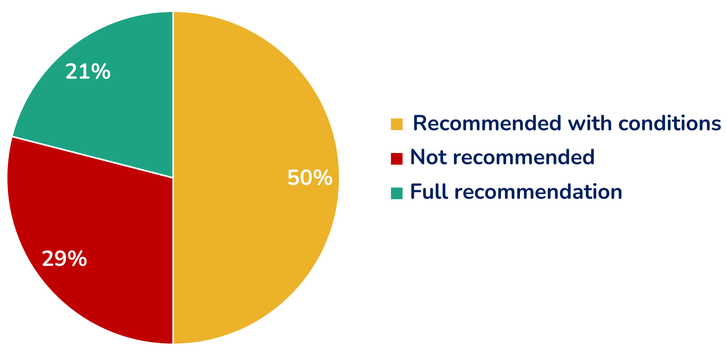


Figure 4. Distribution of identified HTAs by recommendations



This analysis suggests that HTA journey of treatments in FD has been challenging and inconsistent, with most HTA receiving conditional recommendations. While orphan medications address medical needs for a small number of patients and their development should be encouraged, HTA agencies mainly assess it from economic value in addition to the clinical benefits over the existing standard care.

Figure 5. Distribution of the recommendations by HTA body

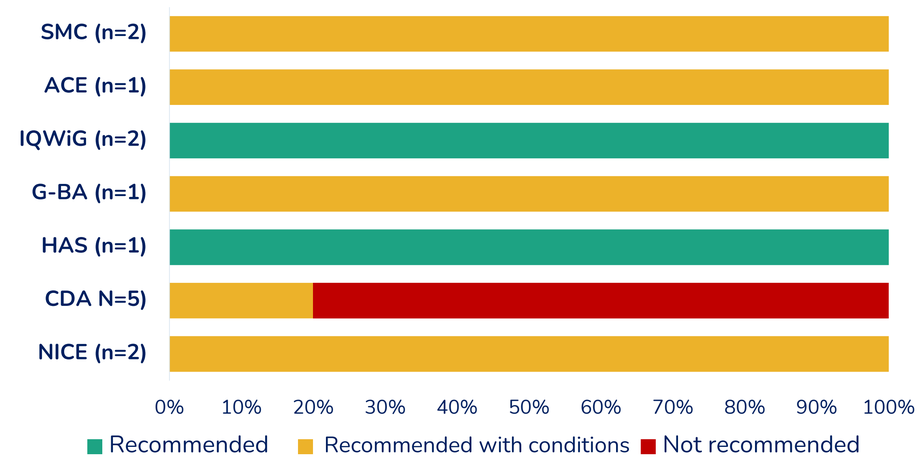
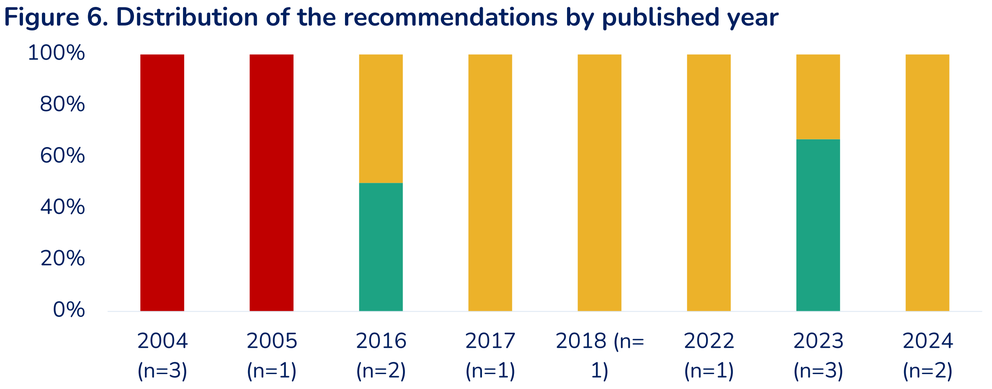
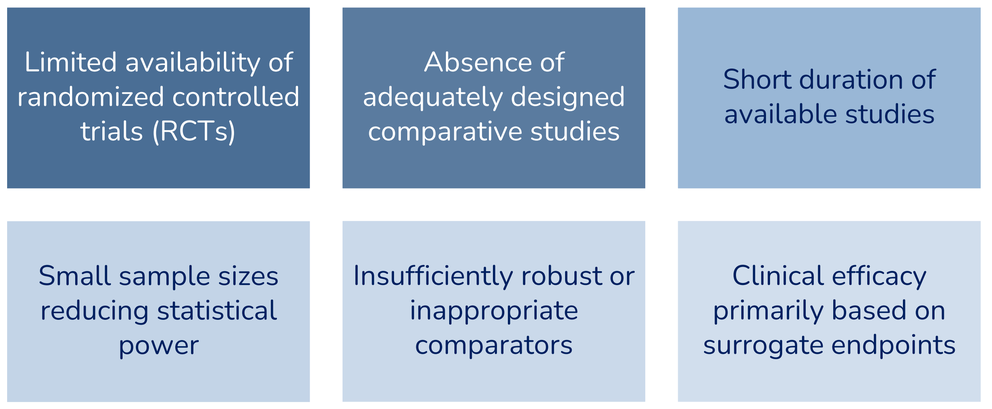


Figure 6. Distribution of the recommendations by published year



- **Three HTAs** with **full recommendations** comprised of **IQWiG Germany** (Pegunigalsidase-α, Migalastat) and **HAS France** (Migalastat; actual benefit substantial only in FD patients with amenable mutation; Clinical Added Value [CAV] level IV, minor). **Four** with **no recommendations** were mainly from **CDA Canada** (Agalsidase-α, Agalsidase-β).
- For HTAs with conditional recommendations, it was often linked to **clinical restrictions** (e.g., patients with amenable mutations, no high clinical need, lack of response to existing therapy) or **commercial considerations** (e.g., managed entry agreements, discount-based patient access schemes).
- Key limitations consistently identified across appraisals included short trial duration, small sample sizes, and insufficiently robust comparative designs (**Figure 7**). Although these treatments demonstrated effects on surrogate endpoints, their impact on clinically meaningful outcomes remains uncertain.

Figure 7. Key issues Highlighted by HTA agencies during appraisals



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