The Impact of Accelerated Regulatory Approval on Health Technology Assessment: an Evaluation of Orphan Drugs in Four Markets

Gomes S[1], Jin G[1], Szende A[1], Uddin J[1]
[1]Fortrea, Product Development & Market Access Consulting, London, United Kingdom

Introduction

- Accelerated regulatory approval (RA) was established to reduce the timeframe to review a marketing-authorization application, if the product is considered to be of major interest for public health and therapeutic innovation.
- Similar processes to accelerate Health Technology Assessments (HTAs) are currently not common.
- Orphan drugs (ODs) are of major interest to public health and therapeutic innovation, as they are considered vital in the treatment, prevention or diagnosis of life-threatening or chronically debilitating rare diseases.
- We set out to understand the impact accelerated RA has on HTA timelines for ODs across four markets: Canada, England, France, and Germany.

Methods

- We reviewed ODs in receipt of accelerated RA in the four markets of interest from May 2018 to May 2023.
  - A targeted search was conducted to identify ODs that had been granted accelerated RA by the Canadian Agency for Drugs and Technologies in Health (CADTH) and European Medicines Agency (EMA).
- A targeted research analysis focusing on time taken to reach a final HTA decision was subsequently conducted.
  - The search was run for Canadian Agency for Drugs and Technologies in Health (Canada), Gemeinsamer Bundesausschuss (Germany), Haute Autorité de Santé (France) and National Institute for Health and Care Excellence (England).
- Median times to HTA resolution reported in literature in the markets of interest (Canada, England, France, Germany) were compared to median times to HTA resolution in our sample, which included: Tegsedi, Verkazia, Onpattro, Evrysdi, and Takhyro.
  - The median time to HTA resolution reported in literature for Canada, England, France and Germany was calculated from HTA submission to final recommendation (Wang, 2020).
  - The median time to HTA resolution for the sample varied slightly, shown below.

Country	Method
Canada	HTA submission to final recommendation
England	HTA evaluation consultation to final recommendation
France	First HTA session to final recommendation
Germany	Start of the HTA procedure to final resolution

- Key outcomes and willingness to pay thresholds applied to assess cost-effectiveness were also analysed.

Products

- When conducting our research, we identified a total of five ODs that had been granted accelerated RA by the CADTH and the EMA**:** Tegsedi, Verkazia, Onpattro, Evrysdi and Takhzyro.
- Tegsedi, Onpattro, Evrysdi and Takhzyro were submitted for HTA in Canada, England, France and Germany.
- Verkazia was submitted for HTA solely in Canada and France.

HTA Resolution Timelines

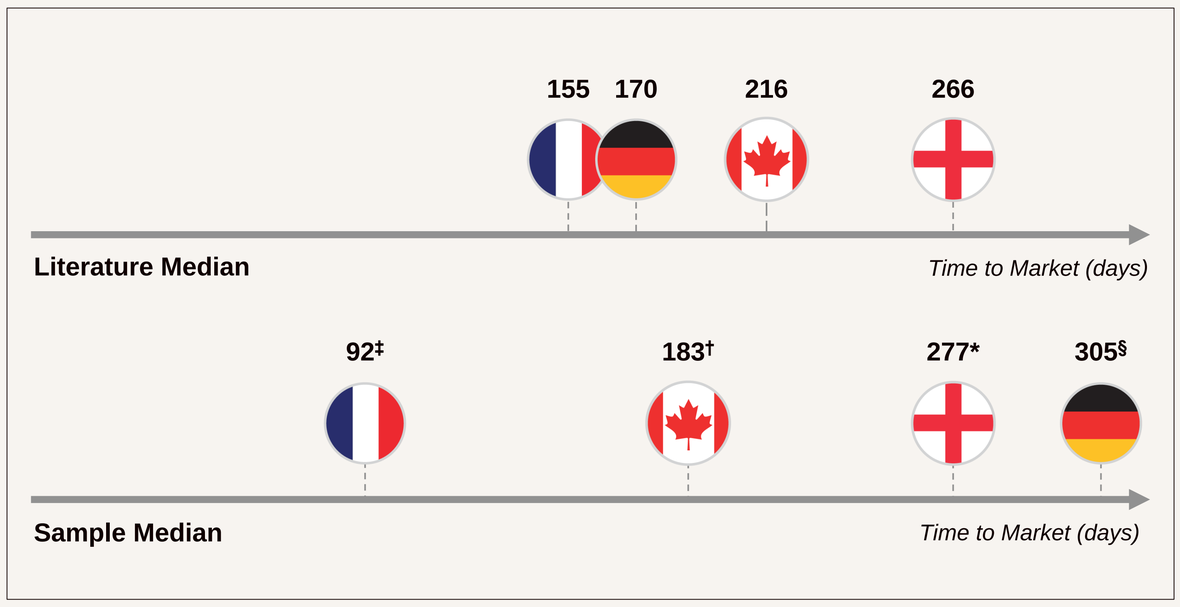
- The median time to final HTA decision differed across markets (**Figure 1**).
  - England was similar to the overall median time reported in literature (277 days* vs 266 days).
  - Canada and France showed shorter timelines (Canada: 183 days† vs 216 days; France: 92 days‡ vs 155 days).
  - Germany showed longer timelines (305 days§ vs 170 days); however, new ODs are immediately reimbursed following RA as long as annual revenue is maintained below threshold (€50M before 2023 and €30M after 2023) (BfArM 2023, Bundesgesetzblatt 2022), possibly impacting HTA resolution timelines.

Reimbursement

- All ODs assessed were reimbursed, some under special appraisals (**Figure 2**).
  - Evrysdi through a managed entry agreement in England, and on a per patient basis in France.
  - Takhzyro in a specific sub-population in France.
- The ICER thresholds for these ODs in Canada and England were in line with other drugs that received RA via the conventional non-accelerated route (**Figure 2**).

Limitations

- The pool of OD granted accelerated RA simultaneously by the CADTH and the EMA within the timeframe we looked at (May 2018 to May 2023) gave us a small sample to analyse with high variability between the HTA resolution timelines for each market, limiting our findings and conclusions.



*From evaluation consultation to recommendation. †From submission to recommendation. ‡From first HTA session to recommendation. §From start of procedure to resolution.

Figure 1. Median time to HTA resolution in the sample (Tegsedi, Verkazia, Onpattro, Evrysdi, Takhyro) and literature across four markets (Canada, England, France and Germany).

	Time to HTA Resolution					Willingness to Pay				
	Tegsedi	Verkazia	Onpattro	Evrysdi	Takhzyro	Tegsedi	Verkazia	Onpattro	Evrysdi	Takhzyro
Canada	– 297.8 days†	✓ 165.1 days†	✓ 182.5 days†	– 280.8 days†	✓ 173.1 days†	= C$50k/ QALY	= C$50k/ QALY	= C$50k/ QALY	= C$50k/ QALY	= C$50k/ QALY
England	✓ 125.7 days*	X No HTA was conducted	✓ 208.5 days*	– 439.1 days* MEA	– 344.6 days*	= £100k/ QALY HST	X NA	= £100k/ QALY HST	= £50k/ QALY EOL	= <£20k/ QALY
France	✓ 99.3 days‡	✓ 92.3 days‡	– 195.5 days‡	✓ 69.8 days‡ Patient basis	✓ 56.4 days‡ Sub-population	X NA	X NA	X NA	X NA	X NA
Germany	– 438.1 days§	X No HTA was conducted	– 438.1 days§	= 172.1 days§	= 172.1 days§	X NA	X NA	X NA	X NA	X NA

✓ Better outcome vs. standard = Similar outcome vs. standard – Worse outcome vs. standard

*From evaluation consultation to recommendation. †From submission to recommendation. ‡From first HTA session to recommendation. §From start of procedure to resolution.

Figure 2. Time to HTA resolution and willingness to pay for Tegsedi, Verkazia, Onpattro, Evrysdi and Takhzyro across four markets (Canada, England, France and Germany).

Conclusions

- Accelerated RA had a different impact on HTA of ODs in different markets.
  - It seems that this status leads to faster HTA outcomes in Canada and France.
  - This status does not seem to impact HTA in England and Germany.
- No relationship was found between accelerated approval and the applied threshold for willingness to pay.

Abbreviations

EOL: End of Life; HST: Highly Specialised Technology; HTA: Health Technology Assessment; MEA: Managed Entry Agreement; NA: Not Applicable, as no appraisal was conducted; OD: Orphan Drug; RA: Regulatory Approval.

References

BfArM. Orphan Medicinal Products. Available at: https://www.bfarm.de/EN/Medicinal-products/Licensing/Medicines-for-rare-diseases/_artikel.html. Accessed May 2023.

Bundesgesetzblatt. Federal Law Gazette Part I, No. 42 November 11, 2022. Law for the Financial Stabilization of Statutory Health Insurance (GKV Financial Stabilization Act). Available at: https://www.bgbl.de/xaver/bgbl/start.xav?startbk=Bundesanzeiger_BGBl. Accessed May 2023.

Wang T, McAuslane N, Liberti L, Gardarsdottir H, Goettsch W, Leufkens H. Companies' Health Technology Assessment Strategies and Practices in Australia, Canada, England, France, Germany, Italy and Spain: An Industry Metrics Study. Front Pharmacol. 2020 Dec 3;11:594549. doi: 10.3389/fphar.2020.594549.

ISPOR Europe 2023