Restrictions and Real-World Evidence Requirements in the Health Technology Assessment of Gene Therapy Medicinal Products in Europe, Canada, Australia, and the United States

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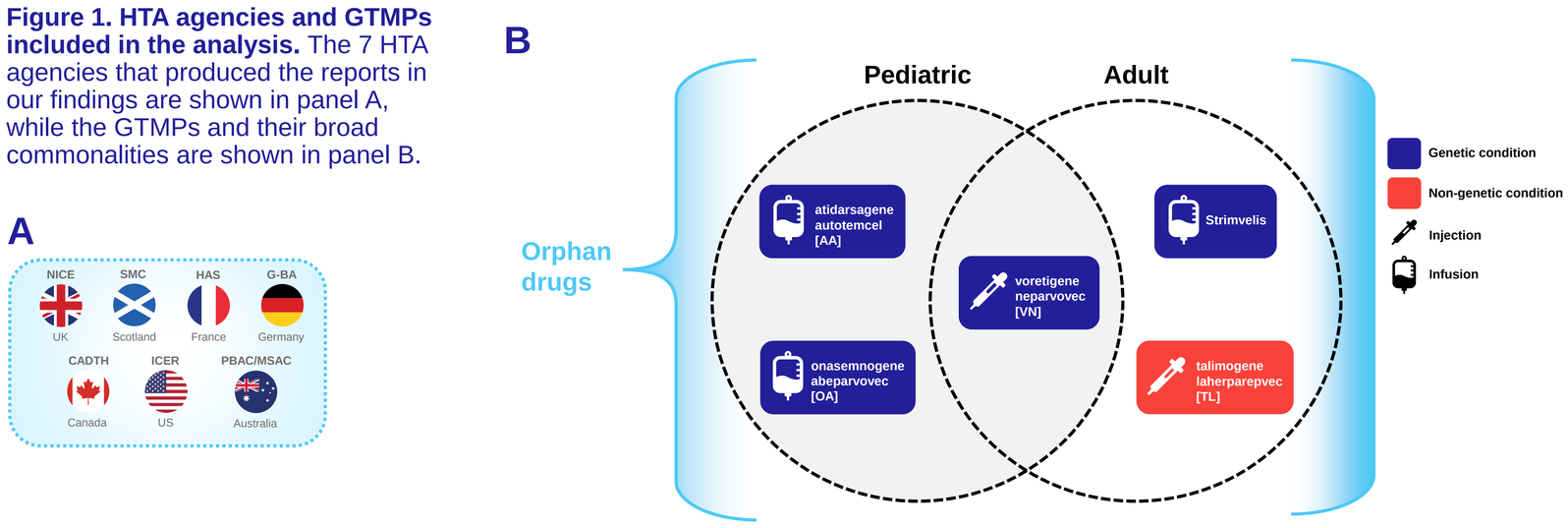
HTA23

Introduction

BACKGROUND

Increasingly, gene therapy medicinal products (GTMPs) are being used to treat patients with rare diseases. GTMPs often demonstrate significant therapeutic benefits within clinical trials for patients with few other options, and some GTMPs are considered curative. Yet there is a high price for developing new GTMPs. It is unclear how the value of GTMPs is interpreted by health technology assessment (HTA) agencies that more commonly evaluate pharmaceutical drugs and medical devices. In some cases, real-world evidence (RWE) may be required for reimbursement, to demonstrate the safety and efficacy of a GTMP outside of clinical trials.

Figure 1. HTA agencies and GTMPs included in the analysis. The 7 HTA agencies that produced the reports in our findings are shown in panel A, while the GTMPs and their broad commonalities are shown in panel B.



Objective

We had two primary objectives:

1. To characterize the restrictions included in HTAs of GTMPs

2. To describe the RWE requirements included in HTAs of GTMPs

Methods

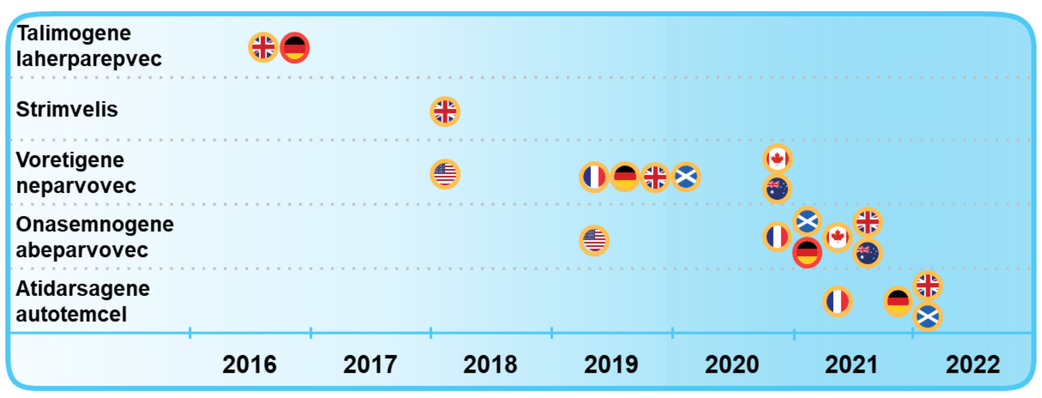
We searched the websites of 7 HTA agencies (NICE [UK], G-BA [Germany], HAS [France], SMC [Scotland], PBAC/MSAC [Australia], CADTH [Canada], and ICER [US]) for published reports of the assessment of 5 GTMPs (atidarsagene autotemcel (AA), onasemnogene abeparvovec [OA], voretigene neparvovec [VN], Strimvelis, and talimogene laherparepvec [TL]) (Figure 1). The reports were analyzed and restrictions for reimbursement were broadly categorized as relating to clinical practice (such as specialist prescribing and administration conditions), price reduction, RWE requirements, reevaluation time limits, and risk sharing agreements. ICER policy recommendations for manufacturers were considered restrictions for the purpose of this analysis.

Results

HTA approvals of GTMPs

A total of 21 HTA reports were reviewed. All were published between 2016 to 2022, and all contained positive reimbursement outcomes (with restrictions), except for G-BA's evaluation of TL in 2016 and OA in 2021 (Figure 2). OA and VN were reviewed by all 7 HTA agencies. NICE reviewed all 5 GTMPs.

Figure 2. Timeline of HTA approvals for GTMPs

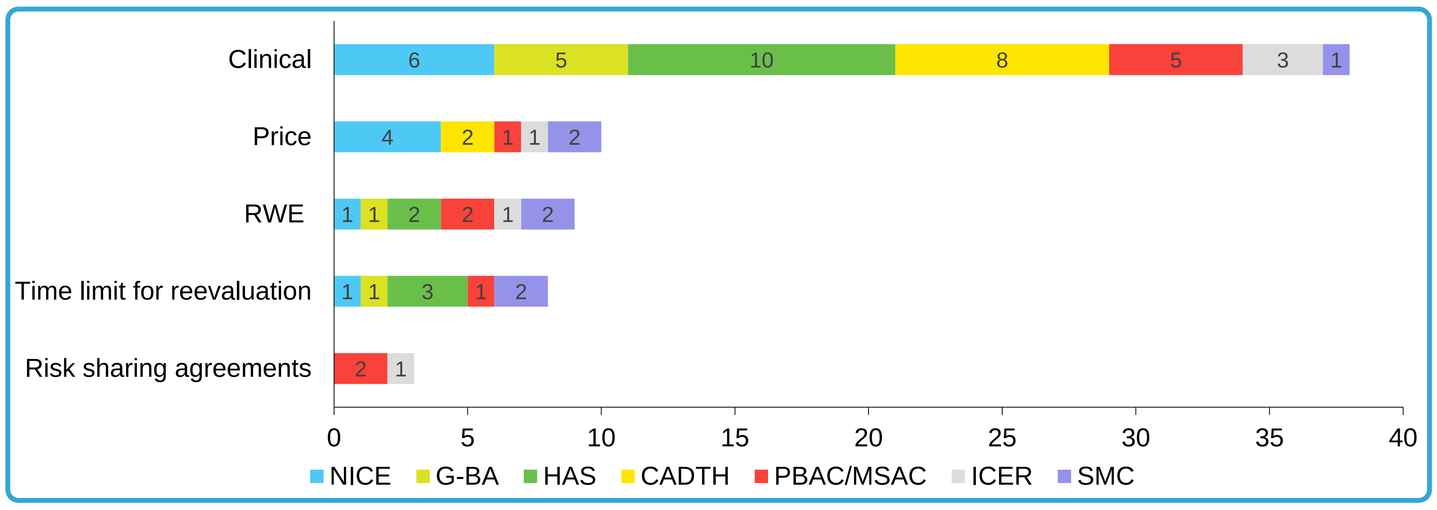


Key: reimbursed with restrictions; not reimbursed

1. The restrictions included in HTAs of GTMPs

Restrictions were common, but not universal across HTAs; the number of restrictions per GTMP ranged from 1 to 8. A total of 67 restrictions across 5 categories were identified: 38 relating to clinical specialist prescribing and administration conditions, 10 requiring a price reduction, 9 requiring RWE, 8 specifying a time limit for reevaluation, and 3 requiring risk sharing agreements. Figure 3 shows the number of restrictions required by each HTA agency for reimbursement across all GTMPs.

Figure 3. Number of HTA restrictions required for reimbursement of GTMPs



2. The RWE requirements included in HTAs of GTMPs

Of the 9 RWE requirements, 5 were for OA, 3 were for VN, and 1 was for AA (Table 1). The utilization of registry data for reevaluation was common; G-BA required RWE generation with the concept prepared by IQWIG. All HTA agencies except for CADTH had at least one RWE requirement.

Table 1. Summary of RWE requirements

Voretigene neparvovec	
HAS (France)	Committee to reassess evidence in 5 years, including European registry data
MSAC (Australia)	Data for the use of VN to be recorded in an international registry to track long term efficacy and safety and be made available for review in 3 years
SMC (Scotland)	As part of the Ultra-orphan pathway data collection is required for 3 years, including RWE
Onasemnogene abeparvovec	
HAS (France)	Committee to reassess evidence, including registry data, after 1 year from date of opinion
G-BA (Germany)	RWE generation requirements and concept to be prepared by IQWIG
NICE (UK)	Data to be collected routinely from all patients who receive treatment during managed access agreement through NHS Blueteq system
PBAC (Australia)	RWE from registry and approvals documentation required as part of the risk sharing agreement
ICER (US)	Registry data should be utilized to answer uncertainties in the evidence base (*policy recommendation)
Atidarsagene autotemcel	
SMC (Scotland)	As part of the Ultra-orphan pathway data collection is required for 3 years, including RWE

Conclusions

- **For indications that lacked effective disease modifying treatment options, GTMPs were recommended for restricted reimbursement in almost all cases.**
- **Requirements for price reductions and future reassessment after RWE collection were common; however, they were not requested by all HTA agencies possibly due to the differing aims and methodologies of HTA bodies.**
- **As more GTMPs enter the market, HTA bodies may maintain disparate evaluation strategies, resulting in a heterogeneous treatment access landscape.**

Disclosures: None

Abbreviations: CADTH, Canadian Agency for Drugs and Technologies in Health; G-BA, Gemeinsamer Bundesausschuss; GTMP, gene therapy medicinal products; HAS, Haute Autorité de Santé; HTA, health technology assessment; ICER, Institute for Clinical and Economic Review; IQWIG, Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen; MSAC, Medical Services Advisory Committee; OA, onasemnogene abeparvovec; PBAC, Pharmaceutical Benefits Advisory Committee; RWE, real-world evidence; SMC, Scottish Medicines Consortium; TL, talimogene laherparepvec; VN, voretigene neparvovec

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