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Towards Market Access of Advanced Therapy Medicinal Products in the Netherlands: Reimbursement Routes and Past Practices

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KEY FINDINGS

- **The reimbursement routes consists of two parallel processes: (i) entitlement to reimbursement and (ii) reimbursement in practice.**
- **Past practices for our cohort showed:**
  - Most MA-ATMPs were first put on a temporary negative list, warranting them to undergo an HTA and negotiations to exit this list.
  - While HE-ATMPs could obtain reimbursement in practice, no HE-ATMP had obtained an add-on title.

BACKGROUND

Obtaining reimbursement for **Advanced Therapy Medicinal Products (ATMPs)** is one of the challenges towards market access.[1] Academic developers in particular struggle to navigate the different reimbursement routes across Member States.[2]

This research aimed to identify reimbursement routes for ATMPs in the Netherlands and to assess past utilization of these routes for ATMPs.

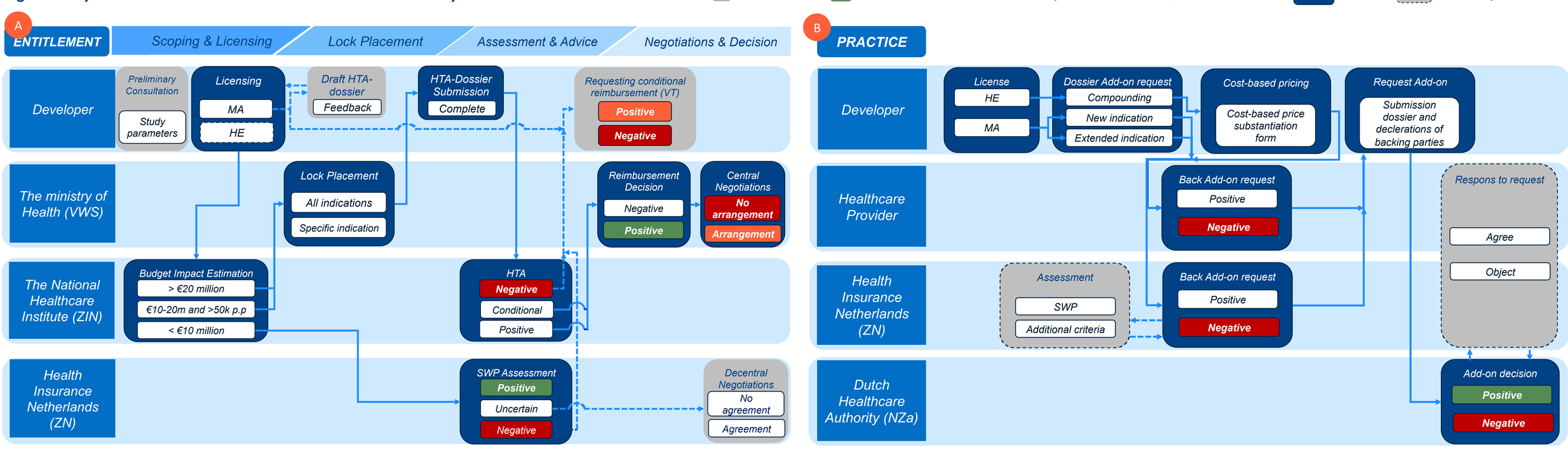
METHODS

Considering routes from moment of obtaining marketing authorization (MA) or exceptional availability through hospital exemption (HE) to reimbursement by health insurance companies.

Identification of reimbursement routes:
- Review of legal and policy documents – summarized in a roadmap.
- Roadmap reviewed by a focus group of developers to assess usability and relevance.

Past practices for cohort:
- Cohort (January 2008 - March 2024) considering MA-ATMPs and HE-ATMPs.

Figure 1: **A) Route for Entitlement to Reimbursement** and **B) Reimbursement in Practice**



MA, Central Marketing Authorisation; HE, Hospital Exemption; HTA, Health Technology Assessment; VT, Conditional reimbursement program; SWP, added therapeutic benefit assessment.

RESULTS

We found that the reimbursement pathway consists of (i) **entitlement** to reimbursement and (ii) reimbursement in **practice** (Figure 1). These routes are partially parallel, as both routes can be initiated following marketing authorisation or obtaining HE.

Inpatient care in the Netherlands is generally reimbursed via the **open system**; a set of criteria to comply to rather than a positive or negative list. These criteria include 'to be according established science and practice' (i.e., **added therapeutic value**, SWP). However, if there is a high macro budget impact (>€10m and >€50k per patient), the Minister of Health can temporarily put indications of ATMPs on a negative list (i.e., "**the lock**"), until a detailed assessment indicates added value, sometimes warranting a **financial arrangement**.

Past utilization is indicated by Table 1. The cohort consisted of 27 ATMPs considering 34 indications. Thirteen indications were reimbursed in March 2024.

We found that **MA-ATMPs** do not follow different routes than other (expensive) medicinal products. Often, they are not reimbursed via the open system but put in the lock. They then need to undergo an HTA, and negotiations for entitlement to reimbursement, and obtain an Add-on title for reimbursement in practice.

For **HE-ATMPS** we found that they need to comply with the criteria for entitlement to reimbursement, yet lack a dedicated route for assessment, because they are not 'authorized medicinal products'. While they have the option to obtain an add-on title for practical reimbursement, no HE-ATMP has obtained one so far.

Table 1: Utilization of Routes by Cohort

No longer Authorized | Pending | Negative | Positive | No data

Product	Indication	Lock placement*	Recommendation HTA body	Add-on title	Financial arrangement	Reimbursed
Chondrocelect	Cartilage defect in knee					
Glybera	Lipoprotein Lipase Deficiency					
MACI	Cartilage defects in knee					
Provenge	Metastatic prostate cancer					
Holoclar	Corneal damage with LSCD					
Imlygic	Metastatic melanoma					
Strimvelis	ADA-SCID					
Zalmoxis	Adjuvant to HSCT					
Spherox	Cartilage defects in knee					
Alofisel	Perianal fistulas					
Yescarta	DLBCL and PMBCL					
	DLBCL and HGBL					
	Follicular Lymphoma					
Kymriah	B-cell ALL					
	DLBCL					
	Follicular Lymphoma					
Luxturna	Hereditary retinal dystrophy					
Zynteglo	ß-thalassemia					
Zolgensma	SMA type 1					
Libmeldy	Metachromatic leukodystrophy					
Tecartus	Mantle cell lymphoma					
	B-cell ALL					
Skysona	Adrenoleukodystrophy					
Abecma	Multiple myeloma					
Breyanzi	DLBCL, PMBCL, FL3B					
	DLBCL, PMBCL, FL3B					
Carvykti	Multiple myeloma					
Upstaza	AADC deficiency					
Roctavian	Severe hemophilia A					
Ebvallo	EBV+ PTLD					
Hemgenix	Hemophilia B					
Casgevy	ß-thalassemia					
	SCD					
TM001**	Metastatic melanoma					

**Lock introduced in 2015 – fully implemented in 2018. **Did not obtain marketing Authorization but available through the Hospital Exemption. LSCD, Limbal Stem Cell Deficiency; ADA-SCID, Adenosine Deaminase Deficiency – Severe Combined Immunodeficiency; HSCT, Hematopoietic Stem Cell Transplantation; DLBCL, Diffuse Large B-Cell Lymphoma; HGBCL, High-Grade B-Cell Lymphoma; PMBCL, Primary Mediastinal Large B-Cell Lymphoma; ALL, Acute Lymphoblastic Leukemia; SMA, Spinal Muscular Atrophy; FL3B, Follicular Lymphoma Grade 3B; AADC, Aromatic L-amino acid decarboxylase ; EBV, Epstein-Barr-Virus ; PTLD, Post-transplant lymphoproliferative disorder.*

DISCUSSION

This researched showed that reimbursement for ATMPs is not a clear linear process and that it differs between MA-ATMPs and HE-ATMPs. Some aspects that have a large impact on the route available:

- **HE-ATMPs** are not considered 'authorized medicinal products' and can therefore not be put in the lock. Moreover, they lack a dedicated route to be assessed for entitlement to reimbursement.
- The **macro budget impact estimation** influences whether the ATMP can be reimbursed via the open system or the lock. However, no final prices are yet available this early in the process.
- **Legislative and policy changes** are expected to affect the reimbursement routes, including the new European Union Health Technology Regulation (mandatory for ATMPs starting January 2025) and recently announced plans of the new Dutch Minister of Health. How these will affect the reimbursement routes is not yet known.

CONCLUSION

This research provides a current overview of the reimbursement routes for ATMPs in the Netherlands and shows how ATMPs have utilized these routes. As MA-ATMPs do not follow an exceptional route, the roadmap is also applicable to other (expensive) medicinal products.
This could help (academic) developers gain insight in the reimbursement process. As the regulatory landscape evolves, this research can serve as a benchmark for future research.

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