Strategies to overcome common hurdles of patient access to AAT augmentation therapy

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i.v. AAT augmentation therapy – reimbursement status in Europe

as of Dec 2016

# does not include reimbursement under exceptional circumstances, e.g. individual funding requests (IFRs), compassionate use, clinical trial extensions, or for off-label indications
Common misconceptions about reasons for negative reimbursement recommendations
Overview

- The journey from medicine development to patient access
  - Clinical development and regulatory approval
  - Health technology assessment
- Common hurdles to widespread patient access
- Possible solutions
- Implementation via multi-stakeholder collaboration
The journey from medicine development to patient access
From bench to bedside – the clinical development, approval and reimbursement processes are lengthy, complex, and costly.

**Drug research / Preclinical development**

**Clinical development**

- **Phase I:**
- **Phase II:**
- **Phase III:**

**Evaluation / Drug licensing / Reimbursement**

**Patient access**

**Regulatory agencies:**

- **European Medicines Agency**
- **FDA**

**Health technology appraisal (HTA) agencies:**

- **NICE** National Institute for Health and Care Excellence
- **Gemeinsamer Bundesausschuss**
- **AIFA** Agencia Italiana del Farmaco
- **HAS** Haute Autorité de Santé
- **CADTH** Canadian Agency for Drugs and Technologies in Health
- **pCODR** Pan-Canadian Ovarian Drug Review

**Payers / Providers:**

- Clinicians
- Prescribers
- Pharmacists

> 1 billion EUR
Regulatory approval → marketing authorization / licence

- Evaluation of medicine’s safety-efficacy profile, based on detailed review and critical appraisal of all clinical trials data, incl. pivotal trial

- Potential request for continuous post-licensing data collection (e.g. Phase IV study, patient registries) and periodic review

- Safety monitoring of medicines across their lifecycle
Regulatory approval → marketing authorization / licence

- Evaluation of medicine’s safety-efficacy profile, based on detailed review and critical appraisal of all clinical trials data, incl. pivotal trial

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Assessment of new treatment only in **absolute** terms

- Usually vs placebo
- Not in broader context of treatment alternatives, price, value for money etc.
Health technology appraisal (HTA) → reimbursement

- HTA aims to assist policy makers, payers and health care providers in making informed decisions on allocation of restricted health care budgets

- Systematic, evidence-based, broad-ranging evaluation of the implications of using technologies within a particular health-care system

- Objectives:
  - Optimal utilisation of available resources for safe, efficacious and effective health technologies that are patient-focused, increase population health and provide best value
  - Consideration of infrastructural, organisational, societal, ethical and equity issues

- Priorities and processes differ across countries and jurisdictions
The two main components of HTA: assessment and appraisal

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- Minimal uncertainty!
HTA: assessment and appraisal of technology within broad context

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- Clinical studies data
- Economic data

**APPRAISAL**

- Evidence review and synthesis
- Framing key questions
- Evidence-based decision making

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**ASSESSMENT**

Assessment of new treatment in relative terms

- Usually vs standard of care
- In broader context of treatment alternatives, price, value for money etc.
HTA: assessment and appraisal of technology within broad context

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**CHALLENGES FOR PATIENT ACCESS**

Opportunities for effective engagement (provide expertise, data, perspective, input):

- Patients
- Clinicians and other healthcare professionals
- Industry
- Other stakeholders

Δ Cost

Δ Effectiveness

Assessment in relative terms:

- Usually vs standard of care
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Common hurdles to widespread patient access to AAT augmentation therapy and possible solutions
Positive reimbursement recommendation – strictly a function of incremental cost and effect?

\[ \Delta \text{Cost} \over \Delta \text{Effectiveness} \]

A ... Augmentation therapy
B ... Standard of care

Cost-effectiveness threshold
Positive reimbursement recommendation – strictly a function of incremental cost and effect?

\[
\frac{\Delta \text{Cost}}{\Delta \text{Effectiveness}}
\]

A ... Augmentation therapy  
B ... Standard of care

Cost-effectiveness threshold

Treatment A more costly and less effective (Treatment B dominates)

Treatment A less costly but less effective

Treatment A less costly and more effective (Treatment A dominates)

Difference in costs \((C_A - C_B)\)

Difference in effectiveness \((E_A - E_B)\)
### Challenges - industry

High acquisition costs for AAT augmentation therapy:
- Limited availability of human plasma
- Lengthy, complex manufacturing process
- Pathogen safety

Limited market size:
- Need for return of investment
- Rare disease

### Possible solutions

**Lower production costs:**
- Recombinant AAT
- More effective manufacturing; higher yields

Reduce profit margin

**Expand market size:**
- Targeted detection (rarity bonus, total budget impact?)
- New indications
### Challenges – all stakeholders

- **AATD-related emphysema is a difficult condition to study:**
  - Complex
  - Slowly progressing
  - Asymptomatic during early stage
  - Heterogenous

- **CT densitometry is not an ideal primary clinical trial endpoint:**
  - Surrogate outcome
  - Not well understood by payers
  - Not suitable for regular monitoring

- **No effect on “hard” endpoints (e.g. mortality), and “clinically relevant treatment benefits” (e.g. measurable physiological functional improvements) have been demonstrated in RCTs**

- **No robust quality-of-life data available from RCTs**

### Possible solutions

- **Longitudinal data, including early disease stage:**
  - Targeted, early detection & prospective long-term observational studies
  - Improve utilisation and synthesis of existing data in retrospective registry studies

- **Novel outcome measures for AATD-related emphysema (specific & sensitive):**
  - Develop new outcomes
  - Adapt existing outcomes

- **Extrapolation/modelling of outcomes

- **Real-world evidence**
  - Retrospective / prospective
  - Matched cohort comparisons
  - Outcomes-based reimbursement

- **Real-world evidence (see above)**
Evidence review and synthesis

Evidence-based decision making

Framing key questions

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Assessment in relative terms
Strengthening the patient voice  
→ effective engagement throughout HTA process to help shape context of decision-making

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<th>Challenges - patients</th>
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<td>Seek information and become experts:</td>
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<tr>
<td>▪ Timelines</td>
<td>▪ Relevant official bodies</td>
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<td>▪ Engagement opportunities</td>
<td>▪ Patient umbrella groups</td>
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<td>▪ Effective messaging</td>
<td>▪ Experts and advisors</td>
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<td>Little data on burden of disease and specific unmet need:</td>
<td>Systematic information gathering:</td>
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<td>▪ Access to expert care</td>
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Implementation via multi-stakeholder collaboration
Clinician-driven actions:

- Identify payer requirements and data gaps
- Define research questions based on specific data needs to support reimbursement efforts
- Identify optimal data sources and tools with a view to achieving most robust outcome
- Remove barriers to enable broad access to registry data to health care providers, researchers, payers, industry, etc.
- Work collaboratively, across all stakeholder groups – multi-stakeholder steering committees

Different requirements for health economics outcomes research (HEOR) and real-world data generation vs. traditional clinical research

Close collaboration with HE/HEOR experts is essential from the outset
Industry-driven actions:

- Collaborate with competitors – enable broad data access and sharing
- Better utilise patients as valuable and effective resource beyond clinical research
- Optimise balance between commercial considerations and patient needs
- Develop better national/regional market access strategies and implementation tools
- Generate relevant data

→ Think beyond regulatory approval early during R&D
→ Evidence generation strategy focussed on demonstrating value
→ Consider outcomes-based pricing strategies
Patient advocacy

Patient-driven actions:

- Understand the HTA and reimbursement processes in your country/region
- Share knowledge and resources with other AATD patient groups
- Strengthen your public profile and make your voice heard
- Collaborate with other rare disease patient groups and umbrella groups
- Challenge industry, clinicians, policy makers, HTA bodies and payers to adopt a more patient-centric view and strategies aimed at patient access to augmentation therapy

- Grow national patient network
- Be proactive
- Utilise and adapt existing resources to meet your needs
Collaboration of all stakeholders is key to improve patient access
Thank you!