Industry views on current challenges and opportunities on timely approval and access to patients

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Introduction

To deliver innovative new medicines to patients with unmet medical needs in the most efficient way, and in doing so make a real difference to patients’ lives, is a crucially important concept which bridges the regulatory approval process and patient access.

This presentation will discuss:

- Opportunities available to industry within the EU regulatory system to support timely regulatory approval and patient access through increasingly integrated development, focussing on:
  - PRIority MEdicines (PRIME) scheme, and
  - Parallel consultation platform for regulators and Health Technology Assessment bodies (HTA-Bs).

- The possibility to align the development dialogue through these mechanisms and the potential impact of doing so.

- The current challenges that exist with these mechanisms, and with the issue of timely approval and access in general.
Aligning the development dialogue with stakeholders in medicine development

The ultimate target in medicine development should be the availability of these new, innovative treatments to patients, with the marketing authorisation a step in the process towards achieving this.
Why integrating the development dialogue is important

- There is not always agreement between regulators and HTA-Bs in important areas of clinical development plans i.e. clinical trial design, study length, comparators and endpoints.
  - There may also be varying requirements for evidence between different HTA-Bs.
  - Planning to address these gaps in the post-authorisation setting may also lead to challenges in identifying sources of high quality real world data and the design of suitable post-authorisation studies.

### Level of agreement between HTA-Bs vs Regulators (n=31 PSAs)

<table>
<thead>
<tr>
<th>Domain</th>
<th>Full Agreement</th>
<th>Partial Agreement</th>
<th>Disagreement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population (n=112)</td>
<td>9%</td>
<td>30%</td>
<td>23%</td>
</tr>
<tr>
<td>Comparator (n=63)</td>
<td>14%</td>
<td>25%</td>
<td>18%</td>
</tr>
<tr>
<td>Endpoint (n=222)</td>
<td>77%</td>
<td>44%</td>
<td>59%</td>
</tr>
<tr>
<td>Other Study Design Characteristics (n=48)</td>
<td>12%</td>
<td>29%</td>
<td>21%</td>
</tr>
<tr>
<td>Efficacy &amp; Safety Package (n=73)</td>
<td>2%</td>
<td>19%</td>
<td>18%</td>
</tr>
</tbody>
</table>

*n represents the total number of HTA-Bs expressing an opinion for each domain

*Other study characteristics include treatment duration, statistical analysis, dosing and randomization

**PRIME: Potential to address timely approval and patient access?**

### Concept
- Strengthened regulatory toolkit
- Early identification of therapeutic innovation
- Quicker access to treatment
- Faster development of promising medicines

### Eligibility
- Demonstrate potential to address unmet medical need
- Major public health interest
- No satisfactory method of diagnosis, prevention or treatment
- Potential major therapeutic advantage

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**Timely approval/access**
- Enhanced regulatory and scientific support
- Early rapporteur assignment
- EMA kick-off meeting – rapporteur, SAWP, EMA
- Scientific advice at key milestones
- Multi-stakeholder engagement
- Confirm potential accelerated assessment
Potential submission of Aducanumab into the PRIME scheme was first considered by the company in 2015.

EMA launched PRIME in early March 2016:

- European Commission commented that PRIME is a major step forward for patients and their families for unmet medical needs, such as rare cancers, Alzheimer’s disease and other dementias.
- CHMP/SAWP agreed that there is a clear unmet medical need in Alzheimer’s disease and that Aducanumab has the potential to significantly address this unmet need.
PRIME: Potential to address timely approval and patient access?
Kick-off meeting discussion and outcomes

Rapporteur assessment team fully prepared and engaged

Context for discussion and feedback was to facilitate a smooth regulatory pathway

Role of centralised EMA advice; significant value in multi-stakeholder scientific advice

Post authorisation strategy key element of discussion

Reassurance around unanswered questions to be addressed
Further discussion between EMA and patient advocacy groups to ensure best involvement.

EMA proposed to utilise shorter lead in time to centralised advice (40 days rather than 70)
PRIME: Potential to address timely approval and patient access?

- **Potential for accelerated assessment**
  - Reduces the review time within the centralised procedure for medicines designated by EMA to be of major public interest or a therapeutic innovation – saving ~ 4-6 months
  
  - While this is an existing mechanism, early Rapporteur assignment allows continual dialogue to ensure that the development strategy continues to support a package acceptable for an accelerated procedure.
  
  - The opportunity for centralised advice within PRIME means that CHMP and the Rapporteur are engaged from an earlier stage, which increases the likelihood of keeping to an accelerated timetable.
Multi-stakeholder advice and the opportunity for continued dialogue is critical:

- While the mechanism for multi-stakeholder advice already exists in Europe, the ability to bring these groups together with the Rapporteur, earlier in development is a critical component of the PRIME scheme.

PRIME: Potential to address timely approval and patient access?

- Incorporate patients' perspective into clinical development
- Alignment of evidence requirements for regulators, HTA-Bs, and payers
- Early engagement on post-authorisation planning and real world data generation plans
Parallel consultation with regulators and HTA-Bs

- In the context of patient access, the opportunity for multi-stakeholder advice through the mechanism of parallel consultation with regulators and HTA-Bs is particularly important.
  - Discrepancies in data requirements between the HTA-Bs and regulators can lead to delays in reimbursement decisions and ultimately availability of medicines.

- May be particularly relevant to programs that require new regulatory and access approaches:
  - novel target population or new clinical pathway,
  - novel clinical endpoints,
  - lack of a clear comparator,
  - no clear value metrics or thresholds.

**Leads to:**

- Limited/no prior successful examples in demonstrating safety, efficacy, value.
- High uncertainty in regulatory and/or payer requirements.
- High risks exist in market authorization, payer value perception, evidence expectations and ability to demonstrate value.
Could early engagement of regulators and HTA-Bs through parallel consultation help with patient access?

**WHAT:** Potential to reduce uncertainty of response to reimbursement submissions at time of medicine launch

**HOW:**
- Understand how HTA-Bs consider the proposed patient population e.g. as it relates to comparator used in the clinical studies, and their views on use in the broader patient population.
  - Opportunity to work to address the concerns whilst the product is under regulatory review.
- Discuss specific details around the study e.g. trial duration and potential long-term extension plans. Collect feedback on the primary analysis method, mapping of endpoints etc.

**WHAT:** Ensure HTA-B perspectives collected are included in the development strategy

**HOW:**
- Flexibility to adapt plans, so early engagement is important.
Could early engagement of regulators and HTA-Bs through parallel consultation help with patient access?

**WHAT:** Opportunity to proactively engage external stakeholders on the product's value proposition

**HOW:**
- Opportunity for direct dialogue with HTA-Bs and regulators in an open collaborative setting
- Utilize HTA-B feedback to shape subsequent payer engagement plans

**WHAT:** Achieve accelerated approval and reimbursement

**HOW:**
- e.g. Obtain EMA and HTA-B feedback on the acceptability of proposed analysis plan for technology appraisal / benefit assessment
- Identify specific opportunities for expedited HTA-B review
Challenges: timely approval and patient access

- **We welcome the introduction of the new joint platform for parallel advice**
  - However, the capacity for future engagement is likely to be limited, particularly whilst reimbursement format is to be agreed
  - Prioritisation for future requests from companies?
  
  - Opportunity for dialogue later in development e.g. during phase III development or post-authorisation?
    - Flexibility in this would be helpful.

  - Consistency of approach between individual HTA-Bs
    - Discrepancy still exists between marketing authorisation (centralised approval) compared to HTA-Bs.
    - Increasing harmonisation across HTA-Bs is welcomed.

- **Operation of the parallel-HTA meetings**
  - Scope of discussions and number of points to address face-to-face may require increased meeting duration
    - Possibility to address discussion points in writing may help with this
    - Opportunity for further follow-up after initial meeting would also be helpful.

- **Involvement of payers in multi-stakeholder discussions**
  - How do we ensure involvement of payers and co-ordination of their input?
Challenges: timely approval and patient access

• **Internal requirements**
  – Schemes e.g. PRIME can be resource intensive for companies, particularly smaller medicine developers
  – Often parallel request for information and meetings if medicine is within an enhanced regulatory pathways in another jurisdiction e.g. US
  – Alignment of the development dialogue in a more integrated way with multiple stakeholders also requires similar approach within companies
  – Can lead to change in overall approach to development for some companies.

• **Medicine development is a global activity**
  – Welcome any efforts to harmonise requirements across different jurisdictions.
  – Mechanisms exist for regulatory approach, however increased harmonisation across HTA-Bs and reimbursement bodies in other jurisdictions would be helpful.

• **We welcome the increasing involvement in patient representatives in discussions with regulators, industry and HTA-Bs**
  – Their views help to shape the discussion around prioritisation of evidence requirements
  – Key that patients are able to represent the broad view,
  – at a stage when they can influence development discussions or evidence requirements.
Conclusions: timely approval and patient access

• We support initiatives that facilitate multi-stakeholder engagement and alignment of the development dialogue.

• **PRIME**
  – Voluntary scheme that ensures early, coordinated and continuous partnering and interactions between stakeholders to optimise development plans

• **Parallel regulatory HTA advice**
  – Provides a clear pathway and forum for discussion with HTA-Bs to align on key evidence requirements

• **It is important to ensure scientific rigour to meet all stakeholders needs**
  – patients, regulators and HTA-Bs

• With the ultimate aim of providing earlier access for innovative products that encompass robust data collection. These approaches together have the potential to speed up the evaluation of new medicines so that they can reach patients earlier.