The Relationship of Conditional Regulatory Approvals to HTA Recommendations — Outcome and Timing

Pharmaceutical Policy
Concurrent Session B3 — Oral Presentation

Monday, April 15, 2019
Special Thanks to: Jesmine Cai, Tina Wang, and Neil McAuslane

Lawrence Liberti
Executive Director
CIRS - Centre for Innovation in Regulatory Science
lliberti@cirsci.org
Background

Over the last decade, there is increasing use of facilitated regulatory pathway (FRP) by regulatory agencies to expedite the review of important new treatments for serious illnesses or addressing unmet medical need.

Facilitated Regulatory Pathways

Regulatory pathway designed to facilitate availability, review and/or approval of medicines where there is an unmet medical need by providing alternatives to standard regulatory review routes.

ARE HTA RECOMMENDATIONS ALIGNED WITH FRPs TO ENABLE TIMELY ACCESS TO MEANINGFUL NEW MEDICINES?
The purpose of the study was to investigate the relationship of conditional approvals (including NOC/cs) to HTA recommendations in terms of the HTA outcomes and timing.
**Study method**

<table>
<thead>
<tr>
<th>Data source</th>
<th>CIRS HTAdock Database</th>
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<tbody>
<tr>
<td></td>
<td>An ongoing programme to monitor regulatory and HTA performance, data collected for new active substances (NASs) appraised by key HTA agencies, analysing synchronisation between the regulatory decision and first HTA recommendation in timing and outcome.</td>
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| Datasets in this study | For this presentation, analyses focused on NASs appraised by key HTA agencies from 2015 to 2017 |

Data collected on internationalised NASs were evaluated in terms of:

- Type of regulatory review pathways (Standard vs. Conditional)
- HTA decisions/recommendations
- Timing of regulatory submission to HTA decisions/recommendations

NASs were identified from the CIRS Regulatory Approval Times Database that had:

- Regulatory approval from both of these agencies: (2012 to 2017)
  - EMA
  - Health Canada

1st HTA recommendation by one of the following HTA agencies: (2015 to 2017)

- CADTH
- HAS
- IQWIG
- SMC
- TLV

The 1st HTA recommendation was then classified into the following categories:

- Positive
- Positive with restrictions
- Negative
- Multiple
### Study method - Trichotomous categorisation of HTA Decisions

<table>
<thead>
<tr>
<th>Decision</th>
<th>Canada</th>
<th>England</th>
<th>France</th>
<th>Germany</th>
<th>Scotland</th>
<th>Sweden</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>List</td>
<td>Recommended</td>
<td>Major benefit</td>
<td>Major added benefit</td>
<td>Accepted</td>
<td>General subsidy</td>
</tr>
<tr>
<td>Positive with restrictions</td>
<td>List with clinical criteria and/or conditions</td>
<td>Managed Access Scheme</td>
<td>Moderate benefit</td>
<td>Considerable added benefit</td>
<td>Accepted with restrictions</td>
<td>Restricted subsidy</td>
</tr>
<tr>
<td>Negative</td>
<td>Do not list at the submitted price</td>
<td>Not recommended</td>
<td>Lesser benefit</td>
<td>No added benefit proven</td>
<td>Not recommended</td>
<td>No subsidy</td>
</tr>
</tbody>
</table>
Conditional vs. standard approvals in Canada

Number of NASs with 1st HTA recommendation in 2015-2017

- Standard (64):
  - Negative: 11
  - Restriction: 49
  - Positive: 4

- Conditional (17):
  - Negative: 6
  - Restriction: 11
HTA recommendation - timelines

Time from HC submission to CADTH recommendation according to procedure

- Median, Box: 25th and 75th percentiles

Number of products submitted through Standard process: 40
Conditional process: 14
Comparison with Europe: 1st HTA Recommendations 2015-2017

Number of NASs with 1st HTA recommendation in 2015-2017

- **Canada**: 49 Standard, 11 Conditional
- **England**: 29 Standard, 5 Conditional
- **France**: 46 Standard, 9 Conditional
- **Germany**: 20 Standard, 17 Conditional
- **Scotland**: 22 Standard, 2 Conditional
- **Sweden**: 18 Standard, 3 Conditional

Legend:
- **Red**: Negative
- **Yellow**: Restriction
- **Green**: Positive
- **Gray**: Multiple
This cohort contained 24 NASs that were approved by
• Health Canada in 2015-2017
• FDA Accelerated process in 2015-2017

Out of 12 FDA Standard Approval in this cohort, 100% were approved as standard approval by HC

Out of 12 FDA Accelerated Approval in this cohort, 52% were approved as conditional approval by HC

- 21% (17/81) NASs were granted a NOC-C by Health Canada
- For NOC-Cs the median time for HC approvals was approximately one month faster than standard approvals.
- Median time to CADTH recommendation was only about 2 weeks longer than for standard, but NOC-Cs were more likely to receive an initial negative recommendation.
- For Conditional Approvals, positive/positive with restriction recommendations were more frequent in Europe than Canada.
- This warrants a better understanding of the factors underlying the initial negative recommendations, to better align expedited access recommendations with NOC-Cs.
Recommendation to align facilitated regulatory and access pathways

Prioritising important therapies—What are the criteria that will be used to determine which products should be considered for these pathways? How should they address evolving unmet clinical needs?

Consolidate, list, adapt

Alignment—What are the elements needed to bridge the barriers and exploit the opportunities to promote convergence to ensure effectiveness and efficiency of the regulatory and HTA approaches?

Consult, discuss, define, recognize, accept

- Conduct earlier joint discussions among companies, regulators, and health technology assessors to develop agreements as to the core package for approval, evidence.
- Involve expected improvements.
- Recognise agreements as an access strategy.

Understanding stakeholder differences on views of outcome and success of flexible regulatory and access pathways: How can stakeholders bring the pathways to life?

Discuss, confide, acknowledge, plan, commit, accept, teach

- Conduct life-cycle spanning, multi-stakeholder dialogue in safe harbour spaces and include data protection and confidentiality. Acknowledge global differences in dialogue processes.
- Address issues in timing and compliance of commitments through earlier discussion, planning and agreement on post-approval commitments, including processes for enforcement and distinctions between commitments for FRPs vs. FARPs.
- Remain open to the use of FRPs/FARPs, while understanding that they are still in the experimental phase. Make FRP experiences publicly available for global learning.

McAuslane et al: The Confluence of Accelerated Regulatory and Health Technology Assessment Access Pathways. CPT Nov 2018
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