Aligning Evidence Requirements for Drug Authorization and Coverage – Central and Eastern European (CEE) Countries Insights

ISPOR Warsaw 2019
28 March 2019
Aligning Evidence Requirements for Drug Authorization and Coverage – Central and Eastern European (CEE) Countries Insights

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EUnetHTA Early Dialogues

Evidence Generation all along the development life-cycle

ISPOR Warsaw panel session
“Aligning Evidence Requirements for Drug Authorization and Coverage – Central and Eastern European (CEE) Countries Insights”

March 28, 2019

Maggie Galbraith
Project Manager, EUnetHTA JA3
Medical, Economic and Public Health Assessment Department
Haute Autorité de Santé (HAS)
Historical timeline of EUnetHTA

2006

- EUnetHTA Project
  - Inception

2016

- Joint Action 1
  - Putting into practice

- Joint Action 2
  - Strengthening practical application

- Joint Action 3
  - Turning pilots into standard practice
Key benefits of collaboration on HTA

Quality
• Ensuring a quality standard

Consistency
• May also indirect influence decisions and support price negotiations

Timeliness
• Earlier access if added value (and value for money) is proven

Efficiency
• Reduce duplications
Summary of activities in EUnetHTA JA3

- **WP4 Joint Production**
  - To produce 37 REA (Relative Effectiveness Assessment) on pharmaceutical and 43 on other technologies
  - To provide a system for topic selection and prioritization, e.g. horizon scanning

- **WP5 Evidence Generation**
  - To conduct Early Dialogues (joint HTA or parallel/joint with regulators)
  - To link additional data collection to several activities (adaptive pathways, MEA, etc)

- **WP6 Quality Management**
  - To provide quality management for EUnetHTA joint products
  - To further develop methodologies and tools for joint work if necessary

- **WP7 National implementation and impact**
  - To facilitate the reuse and implementation of joint products at the national/local level
  - To measure the impact of joint work in collaboration with other work packages

- **WP1 Coordination**
- **WP2 Dissemination**
  - Transversal work packages
- **WP3 Evaluation**
WP5: Evidence Generation

Lead partner: Haute Autorité de Santé (HAS)

a. Early Dialogues

G-BA Co-Lead

• Based on JA2 and SEED experience, continue and improve the conduct of EDs for drugs and devices, including parallel advice with regulators, with contribution of patients and concerned stakeholders.

• Propose and implement a new financing system based on a fee-for-service approach

b. Post Launch Evidence Generation

Activity centers: AIFA, TLV, avalia-t, NICE

• Improve post-launch evidence generation:
  → Main activity: PLEG pilots (Strand B1), based on JA2 work and partners national experiences.
  → Supporting activity: Standards Tool for Registers in HTA (Strand B2), using results of PARENT Joint action.
WP5A Objectives

• Support developers of medical technologies by providing a collaborative approach among a wide-range of European HTA bodies (HTAB) to provide consolidated advice on their product development plans while also maintaining individual HTAB positions where needed;

• Supply and incorporate patient and clinical expert contributions in the final recommendations provided by HTAB

• Link EDs to subsequent activities on additional data collection, including the use of patient registries.
WP5 Partners

• 38 organisations
• 22 countries

HAS (Lead Partner)
G-BA (Co-Lead Partner)
ZIN (A, B1)
HVBA (A)
KCE (A)
IPH-BE (B1)
RIZIV-INAMI (A)
* NCPHA (A)
* CIPH/HZJZ (A, B1, B2)
MoH Cyprus (A)
* UTA (B1)
FIMEA (B1)
IQWiG (A)
EKAPTY SA (B1, B2)
* NIPN (A)
AIFA (A, Strand B1 AC Lead; B2)
AGE.NA.S (A)
DGFDNM IT (B1)
Veneto/CRRUF (A, B1)
RER (A, B1)
UCSC GEMELLI (B1)
Hdir (A, B1)
NOMA (B1)
* AOTMIT (A)
INFARMED (A, B1)
* NSPHMPDB (A)
* UniBA FOF (B1)

* JAZMP (A, B1)
* NIJZ (B2)
AQUAS (A, B1)
AEMPS (A)
AVALIA-T
(A, Strand B1 AC Lead)
OSTEBA (B1)
AETS (A, B1)
AETS ISCIII (A)
MPA (A)
TLV
(A, Strand B1 AC Lead)
NICE
(A, Strand B2 AC Lead)
SNHTA (A, B1)

* CEE Partners
EUnetHTA Definition of an Early Dialogue

A non-binding scientific advice, before the start of pivotal clinical trials (after feasibility / proof of concept study), in order to improve the quality and appropriateness of the data produced by the developers in view of future HTA assessment / re-assessment.
One Gateway for all ED procedures involving HTAbs

**Simultaneous request to EMA and EUnetHTA**

**ED Secretariat**
eunethta-has@has-sante.fr

**Parallel Consultation**

**EDWP* Prioritization**

**EMA** + voluntary HTABs coordinated by EUnetHTA ED Secretariat

**EMA / HTA**

Individual Parallel Consultation (PCI)

Individual recommendations

**EMA + EUnetHTA EDWP + 3 voluntary HTABs coordinated by EUnetHTA ED Secretariat**

**EMA / EUnetHTA**

Consolidated Parallel Consultation (PCC)

Consolidated EUnetHTA final recommendations

**EMA**

Consolidated Parallel Consultation (PCC)

Consolidated EUnetHTA final recommendations

**EUnetHTA multi-HTA Early Dialogue**

**EDWP Prioritization**

**EMA + voluntary HTABs coordinated by EUnetHTA ED Secretariat**

**EDWP + 3 voluntary HTABs coordinated by EUnetHTA ED Secretariat**

**EDWP + 3 voluntary HTABs coordinated by EUnetHTA ED Secretariat**

**Consolidated EUnetHTA final recommendations**

**Consolidated EUnetHTA final recommendations**

**Request to EUnetHTA only**

Legend: Non-EUnetHTA procedure EUnetHTA Procedure

*EDWP: Early Dialogues Working Party

March 28, 2019

**PCC & multi-HTA = « EUnetHTA » EDs**
The Early Dialogue Working Party (EDWP)

**Members:** AEMPS (ES), AIFA/RER (IT), G-BA (DE), HAS (FR), NICE (UK), NIPN (HU), NOMA/TLV (NO/SE), RIZIV-INAMI/ZIN (BE/NL)

**Selection criteria:**
The product should aim to bring added benefit to patients i.e. by:

- A new mode of action for the indication
- \(AND\) targeting a life-threatening or chronically debilitating disease
- \(AND\) responding to unmet need (no treatment or only unsatisfactory treatment available)
Early Dialogue Requests: July 1, 2017 - March 1, 2019

53 Requests

<table>
<thead>
<tr>
<th>No°</th>
<th>Therapeutic field</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>Auto-immune disease/dysfunction</td>
</tr>
<tr>
<td>17</td>
<td>Cancer</td>
</tr>
<tr>
<td>5</td>
<td>Neurodegenerative disorder</td>
</tr>
<tr>
<td>1</td>
<td>Diabetes</td>
</tr>
<tr>
<td>4</td>
<td>Viral disease</td>
</tr>
<tr>
<td>20</td>
<td>Other</td>
</tr>
<tr>
<td>3</td>
<td>Medical devices</td>
</tr>
</tbody>
</table>

21 Individual Parallel Consultations
Including 1 vaccine
20 Completed
1 On-going

2 SME applicants
3 Orphan drugs
0 ATMP

1 on hold (to be resubmitted in March)
5 withdrawn (by the Applicant, 1 resubmitted and accepted as PCI)
2 declined (procedure not followed; did not meet eligibility criteria for multi-HTA)
1 still under acceptability evaluation (MD)

22 EUnetHTA EDs
(4 Multi-HTA [3 pharma, 1 device + 18 Consolidated Parallel Consultations (PCC))

6 Cancer
3 Neurodegenerative disorder
1 Viral disease
11 Other
1 Medical Device

6 SME applicants
11 Orphan designations
6 ATMP

14 Completed (as of Nov 2018)
Early Dialogue Procedural Timeline

- **D - 60**: Letter of Intent
- **D - 30**: Draft Briefing Document
- **D 0**: Final Briefing Document
- **D + 30**: List of Issues
- **D + 60**: F2F meeting
- **D ~ +75**: EUnetHTA Final Recommendations
Analysis: Topics Covered by EDs

Method: The EUnetHTA ED Secretariat conducted an analysis of the Briefing Book for the 14 completed “EUnetHTA” EDs (3 multi-HTA, 11 PCC)

- Average number of questions per ED: +/- 9 questions
- Number of questions per PICO

<table>
<thead>
<tr>
<th>Topic</th>
<th>Number of questions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
<td>24</td>
</tr>
<tr>
<td>Intervention</td>
<td>2</td>
</tr>
<tr>
<td>Comparator</td>
<td>15</td>
</tr>
<tr>
<td>Outcome</td>
<td>34</td>
</tr>
</tbody>
</table>

⇒ Most of questions on population, outcomes and comparators
⇒ Only 2 questions on intervention. None for ATMP.

- Number of questions on Statistical analysis and Study Design: 16
- Number of Economic questions: 8/14 EDs
- Others topics: 8/14 EDs (~60%) related to Post-launch/long-term data collection
### Analysis: Alignment between HTAB

<table>
<thead>
<tr>
<th></th>
<th>Full agreement</th>
<th>Partial agreement</th>
<th>Disagreement</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HTABs provide a common response</strong></td>
<td>Does not prevent supplementary national specifications</td>
<td>&gt; 50% of HTA bodies agree on a common response</td>
<td>&lt; 50% of HTA bodies agree on a common response</td>
</tr>
</tbody>
</table>

#### Population
- Full
- Partial
- Disagreement

#### Comparator
- Full
- Partial
- Disagreement

#### Intervention
- Full
- Partial
- Disagreement

#### Outcome
- Full
- Partial
- Disagreement

No disagreement

**P = O:**
- full 85.7%
- partial 14.3%

**C:**
- full 78.6%
- partial 21.4%
Impact on the development plan
(based on feedback from 8 “EUnetHTA ED” Applicants)

Were changes made to development plan?
- Yes: 25%
- No: 75%

Where?
- Population: 28%
- Comparator: 9%
- Endpoints: 27%
- Clinical trial design: 22%
- Economic model: 18%
Learnings from a Network Perspective and what it could provide to others

- Batch processing of all requests allows for prioritization and common agreement on future promising innovations
- HTAB are capable of providing consolidated recommendations on key points of the development and mutual understanding of HTAB specificities while leaving room for national specificities
- EUnetHTA EDs improve the quality of development and set of evidence to be used for future HTA assessment
- Allows for fruitful exchanges between HTAB with relevant methodology discussions
Thank you
Any Questions?
eunethta-has@has-sante.fr
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_Pero Draganić_

Agency for Medicinal Products and Medical Devices of Croatia - HALMED
The Ministry of Health of the Republic of Croatia has the task to work on the improvement, protection and promotion of citizens’ health.

Most of its activities the Ministry of health carry out through the institutions involved in the healthcare process, like:

- Croatian Health Insurance Fund – CHIF (HZZO)
- Croatian Institute of Public Health
- Agency for Medicinal Products and Medical Devices – HALMED
- Agency for Quality and Accreditation in Health Care and Social Welfare (AAZ) - HTA Agency
Agency for Quality and Accreditation in Health Care and Social Welfare - HTA Agency

With the entry into force of the Act on Quality of Health Care (Official Gazette No. 118/2018) of January 1, 2019, the Ministry of Health takes over all the activities, the letter of the document and other documentation, the means of work, the rights and obligations and the financial resources of the Agency for Quality and Accreditation in Health Care and Social Welfare.

Does the present status of the Agency change?

The Agency has been moved to the Ministry of Health, will be one of the departments, and professional or scientific activity will remain unchanged.
Decision making process

Ministry of Health:

Agency for Medicinal Products and Medical Devices (HALMED);
1) marketing authorization of drugs
2) regulation of medical devices

Croatian Health Insurance Fund (HZZO);
1) managing the Health Insurance Fund and contracting health care services
2) key role in the definition of basic health services covered under statutory insurance
3) the establishment of performance standards and price setting for services covered by the HZZO
   - pricing and reimbursement decision on drugs and medical devices
Croatian process of decision-making and HTA process

Croatian Health Insurance Fund (CHIF) Drugs Committee and Medical Devices Committee

Recommendation

CHIF Board

DECISION

HTA document with recommendation

Agency (AAZ) - HTA Department

ASSESSMENT

(Currently not mandatory)

National adaptation

HTA document with recommendation

EUnetHTA and HTA Network (Article 15, CBHC Directive) Full Core HTA and Core HTA for Rapid REA of Pharmaceuticals and other health technologies National/regional work produced in another country/region

Request

Active collaborative production

Request

HTA document with recommendation

Industry submission files

Request

HTA document with recommendation

Request

HTA document with recommendation

Hospitals Management

DECISION

Croatian Framework for HTA

2006, Strategy of the development of the Croatian Health care system 2006-2011

2007, Act on Quality of Health Care: The Agency for Quality and Accreditation in Health (as legal, public, independent, non-profit institution), should provide the procedure for and database on HTA

Health technologies: pharmaceuticals, medical devices, diagnostic and screening techniques, surgical procedures, other therapeutic technologies and procedures, and health promotion activities

2009, Ordinance regarding reimbursement on drugs (Official gazette No. 155/09) and Ordinance regarding reimbursement on medical devices (Official gazette No. 138/09): not mentioned HTA process and role of HTA Department

2011, Act on Quality of Health Care and Social Welfare (AAZ - HTA and database on HTA at national level; Proposes Ordinance on HTA to the Minister of Health; Provides continuous education in the field of HTA; National and international collaboration in the field of HTA)

Department for Development, Research and HTA: formal activities in the field on HTA actually began in October 2009

Source: http://www.aaz.hr/
And it continued like this ...

International Projects

- PaSQ Joint Action (2012-2015)
- EUnetHTA Joint Action 1 (2010-2012)
- EUnetHTA Joint Action 2 (2012-2015)
- EQUIPT (2013-2016)
- EUnetHTA Joint Action 3 (2016-2020)

International collaboration

- HTA Network
- HTAi, ISPOR, ISPOR HTA Roundtable Europe, ISPOR HTA Council
- WHO National Contact Point on HTA
- TAIEX Project (2010), 2 days Workshop - “Health Technology Assessment; main principles, HTA process and report”
- ISPOR HTA Training Programe (2015)

Production of HTA Reports (national, international)

And at the end...

The „Agency” has arrived under the jurisdiction of the Ministry of Health

For „the Agency”, professional or scientific activity will remain unchanged.

But „Agency” is not allowed to make recommendations now, only scientific conclusions.
...but, in the future the activity continues with...

**Added value of joint work and use**
- Sharing the expertise: ↓ time for the production of national HTA reports, ↑ the number and quality of national reports, ↑ local competence and capacity in HTA
- ↑ international and scientific visibility through joint work and publishing of scientific papers; national awareness and political recognition of the concrete benefits of joint HTA

**Challenges and key solutions**
- HTA in Croatia is not currently mandatory within decision-making process and AAZ does not select the topics that it assesses at the national level - no certainty that a topic AAZ will be asked to assess will be one that EUnetHTA also assesses
- lack of mandatory HTA in Croatia - the key barrier preventing the immediate use of EUnetHTA assessments in the Croatian national setting
- translation any information taken from an existing report into Croatian (the language of assessment must legally be Croatian)
- until 31/12/2018 AAZ included recommendations in their report – from 01/01/2019 scientific conclusions only

**Systematic and sustainable use of HTA at national level**
- 2014, 67th World Health Assembly Resolution: Health intervention and technology assessment in support of universal health coverage

Source: Mirjana.Huic@miz.hr
...and, also... **sustainable HTA collaboration**!

"If you want to go fast, go alone. If you want to go far, go together."


Source: Mirjana.Huic@miz.hr
Thank you!
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Tomas Tesar

Union Health Insurance Fund, Bratislava, Slovakia
Expectation: the Early Dialogue can improve access for patients

- collaboration supports evidence generation
- cooperation can ensure greater alignment in concepts such as unmet medical need and therapeutic innovation
- regulators and HTA agencies can jointly discuss with developers a plan how to generate further levels of evidence
- cooperation on selection of comparators, validation and selection of endpoints and scientific guidelines
<table>
<thead>
<tr>
<th>Member State</th>
<th>Number of Reimbursement Requests (related to 25 pharmaceuticals)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bulgaria</td>
<td>6</td>
</tr>
<tr>
<td>Croatia</td>
<td>7</td>
</tr>
<tr>
<td>Estonia</td>
<td>1</td>
</tr>
<tr>
<td>Hungary</td>
<td>8</td>
</tr>
<tr>
<td>Slovakia</td>
<td>10</td>
</tr>
<tr>
<td>Slovenia</td>
<td>6</td>
</tr>
<tr>
<td>Poland</td>
<td>10</td>
</tr>
</tbody>
</table>

Range 1-10, Mean 6.86

• Early Dialogue / Scientific Advice
  ✓ design and implement a single, common, European procedure for Parallel Consultation (previously known as parallel scientific advice/early dialogue)
  ✓ facilitate learning and understanding of evidence needs
• “Late dialogues” / peri-licensing advice
• Methodologies to identify the treatment eligible population
• Significant benefit vs. added therapeutic value for orphan medicines
• Unmet medical need and therapeutic innovation for priority setting
• Shared understanding of methodological approaches for design, analysis and interpretation of clinical trials and observational studies
• Population-specific or Intervention-specific areas
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