HTA body (HTAb) experience on joint scientific advice/early dialogues EMA/HTA with ATMPs

Chantal Guilhaume
Scientific Project Manager, EUnetHTA JA3
Medical, Economic and Public Health Assessment Division
Haute Autorité de Santé (HAS)
France
### EUnetHTA Organisational and governance structure

#### Work Package 1 Network Coordination - Dutch Health Care Institute

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Spain</td>
<td>Sweden</td>
<td>Norway</td>
<td>Austria</td>
<td>Czech Republic</td>
<td>Germany</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>Belgium</td>
<td>Croatia</td>
<td>Cyprus</td>
<td>Ireland</td>
<td>Denmark</td>
</tr>
<tr>
<td>Finland</td>
<td>France</td>
<td>Greece</td>
<td>Hungary</td>
<td>Slovakia</td>
<td>Latvia</td>
</tr>
<tr>
<td>Malta</td>
<td>Poland</td>
<td>Portugal</td>
<td>Romania</td>
<td>Slovenia</td>
<td>Estonia</td>
</tr>
<tr>
<td>Italy</td>
<td>Estonia</td>
<td>Lithuania</td>
<td>Bulgaria</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Lead: AETS-ISCIII**

**Lead: TLV**

**Lead: NIPHNO**

**Lead: HAS**

**Lead: IQWiG**

**Lead: NICE**

**Lead: Agenas**
Work packages EUnetHTA JA3

**Work package 1 Network Coordination**

**Work package 2 Dissemination**

**Work package 3 Evaluation**

**Work package 4 Joint production**
- Pharmaceuticals
- Other Health Technologies

**Work package 5 Evidence generation**

**Work package 6 Quality management**
- Scientific guidance
- Tools

**Work package 7 National implementation**
WP5 partners

- 38 organisations
- 22 countries

HAS (Lead Partner)
G-BA (Co-Lead Partner)
ZIN (A, B1)
HVB (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)
DGFDM IT (B1)
Veneto/CRUF (A, B1)
RER (A, B1)
UCSC GEMELLI (B1)
Hdir (A, B1)
NOMA (B1)
AETSA (A, B1)
AETS ISCIII (A)
MPA (A)
TLV (A, Strand B1 AC Lead)
NICE (A, Strand B2 AC Lead)
SNHTA (A, B1)
JAZMP (A, B1)
NIJZ (B2)
AQUAS (A, B1)
AEMPS (A)
AVALIA-T (A, Strand B1 AC Lead)
OSTEBA (B1)
AETS ANS (A, B1)
AETS ISCIII (A)
NICE (A, Strand B2 AC Lead)
SNHTA (A, B1)
EUnetHTA early dialogues
Pharma

- A coordinated process,
- Launch 2017, Start July 2017
- One stop-shop (HAS)
- One secretariat (HAS)
- A rapporteur and a scientific coordinator per ED
- An ED working party (most experienced agencies)
- Still Voluntary basis, so prioritization.
- A consolidated recommendation from HTAbs
- Patients involvement
- Conflict of interests and confidentiality management

2 EUnetHTA coordinated procedures

Multi HTA procedure

Parallel consultation procedure

For high priority request
One Gateway for all ED procedures involving HTAbs

Simultaneous request to EUnetHTA and EMA

Parallel Consultation EUnetHTA + EMA

EDWP Prioritization

Low priority
- EMA + voluntary HTABs

EMA / HTA Individual Parallel Consultation (PCI) Procedure

EMA + EUnetHTA EDWP + 3 voluntary HTABs

EMA / EUnetHTA Consolidated Parallel Consultation (PCC) Procedure

EMA + EUnetHTA EDWP + 3 voluntary HTABs

Coordination by ED Secretariat

High priority

EDWP + 3 voluntary HTABs

EUnetHTA multi-HTA procedure

Request to EUnetHTA only

Multi-HTA Early Dialogue EUnetHTA

EDWP Prioritization

EMA / EUnetHTA ED working party: EDWP

Legend:
- EUnetHTA Procedure
- Non-EUnetHTA procedure

CIRS/HAS/sept 2018
The Early Dialogue Working Party (EDWP) Reasoning

- **Non “high priority” Parallel Consultation requests may lead to PCI pathway**
- **Why?**
  - Mode of action not new;
  - Product not targeting, a life-threatening or debilitating disease;
  - Alternative treatment available (i.e. no unmet need);
  - Products not under remit of many HTAs (“lifestyle” drugs, vaccine products, etc.);
  - Lack of data in submission file to justify PCC;
  - Ongoing pivotal trial.
From July 2017 through Nov 2018

45 Letters of Intent

12 Orphans
4 ATMP

Majority in cancer indication (17/45)

22 Individual Parallel Consultations

3 Orphan drugs
0 ATMP

17 EUnetHTA EDs
(3 Multi-HTA + 14 Consolidated Parallel Consultations (PCC))

9 Orphans
4 ATMP

6 Cancer
2 Neurodegenerative disorder
1 Viral disease
8 Other

4 withdrawn (by the Applicant)
2 declined (procedure not followed; did not meet eligibility criteria for multi-HTA)
HTAb participation in “EUnetHTA” EDs / PCI

PCC/Multi-HTA: Max 9; Min 5; Avg. 7.3

Scientific Coordinators:
HAS, G-BA, NICE, NOMA, AEMPS

Rapporteurs:
G-BA, HAS, NICE

PCI: Max 5; Min 1; Avg. 2.8

Scientific Coordinators:
G-BA, AEMPS, NICE, NOMA
Description of 4 ED ATMP

- 3 Orphan designations
- 2 SMEs
- Various therapeutic indications
- All ED were Parallel Consolidated Consultation
- HTAb participation: Max 9; Min 5; Avg. 7.5
- Patients involved in 2/4 EDs
- Discussion on Ph3 clinical trial and economic questions
# ATMP Case Study

Topics covered by questions from applicant

<table>
<thead>
<tr>
<th>ATMP 1</th>
<th></th>
<th></th>
<th></th>
<th>Economic</th>
<th>Others</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
<td>Intervention</td>
<td>Comparator</td>
<td>Outcomes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ATMP 1</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>6</td>
<td>2</td>
<td>13</td>
</tr>
<tr>
<td>ATMP 2</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>ATMP 3</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>2</td>
<td>11</td>
</tr>
<tr>
<td>ATMP 4</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>4</td>
<td>17</td>
</tr>
</tbody>
</table>

Long-term data collection plan/Post-launch evidence generation (PLEG) partially addressed as no detailed proposal from the applicants.
Ideal Timing for EUnetHTA ED on pivotal trial and PLEG

- Start Pivotal trials
- End Pivotal trials
- EMA Submission
- CHMP Decision
- MAA

- EUnetHTA ED
- Advice to the company
- EUnetHTA PLEG pilot
- HTAb involvement ONLY
### ATMP Case Study
#### Alignment of HTAb recommendations

<table>
<thead>
<tr>
<th></th>
<th>Full agreement</th>
<th>Partial agreement</th>
<th>Disagreement</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Population</strong></td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Comparator</strong></td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td><strong>Outcome</strong></td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**Full agreement**
- HTABs provide a common response. Does not prevent supplementary national specifications.

**Partial agreement**
- > 50% of HTA bodies agree on a common response.

**Disagreement**
- < 50% of HTA bodies agree on a common response.
Opportunity to anticipate future Joint Assessment

**EU Regulatory Process**
- EMA Process
- CHMP opinion
- Positive decision of EC
- EPAR

**WP4 HTA Process**
- Expression of interest from pMAH - initiate discussions
- Letter of Intent
- Information/Data Requests
- Authoring team develop PICO
- Scoping meeting with pMAH
- Finalisation of project plan
- Submission file
- Co-production of 1st version of REA
- 2nd version of REA *Including editorial review*
- Fact check
- Final version of REA

**Stakeholder involvement**
- Identification of clinical experts and patients
- Review project plan by clinical experts
- Involvement of patients
- pMAH provides submission file
- Review by external experts and fact check by MAH
- Local REA’s (e.g. national, regional)
Thank you
Any Questions?
eunethta-has@has-sante.fr