



Minutes of EMA/EUnetHTA meeting

Diemen, 4 July 2019

Role	Name	
Co-chairs:	Hans-Georg Eichler and Giovanni Tafuri	
Present:	<p><u>EUnetHTA</u>: Nick Crabb – NICE, Ines Costa – INFARMED (via TC), Sara Couto – INFARMED (via TC), Jadwiga Czczot – AOTMiT, Rudy Dupree – ZIN, Claudia Furtado – INFARMED (via TC), Wim Goettsch - ZIN , Marcus Guardian – ZIN, Chantal Guilhaume – HAS (via TC), Ali Hussein – ZIN, Krystyna Hviding – NOMA, Chaienna Schreuder – ZIN, Ad Schuurman- ZIN, Regina Skavron - G-BA, Anna Stromgren – TLV, Giovanni Tafuri - ZIN, Tove Ringerike – NIPHNO, Anne Willemssen – ZIN</p> <p><u>European Commission</u>: Orsolya Nagy</p> <p><u>EMA</u>: Michael Berntgen, Pierre Demolis (via TC), Hans-Georg Eichler, Harald Enzmann, Juan Garcia Burgos, Ralf Herold, Kristina Larsson, Jordi Llinares Garcia, Jane Moseley, Francesco Pignatti (via TC), Bruno Sepodes, Spiros Vamvakas.</p>	
Item	Draft agenda	Name
1.	Introduction to the day and adoption of the draft agenda	Hans-Georg Eichler and Giovanni Tafuri
2.	Update on Joint Action 3	Marcus Guardian
3.	Update from the European Commission	Orsolya Nagy
4.	Feedback from the EMA/payer meeting	Hans-Georg Eichler
5.	<p>Information exchange and mechanism for reciprocal learning opportunities:</p> <ul style="list-style-type: none"> • Histology independent developments • Webinar on an ATMP • Feedback from the CHMP Strategic Review and Learning Meeting • Update on availability of EMA information to facilitate REA preparation 	<p>EMA: Michael Berntgen, Jordi Llinares Garcia, Francesco Pignatti, Spiros Vamvakas</p> <p>EUnetHTA: Anna Stromgren, Regina Skavron, Anne Willemssen</p>

6.	Sharing respective practices and experiences related to the involvement of patients in activities: the new EUnetHTA document on patient inputs in REAs	EMA: Juan Garcia Burgos EUnetHTA: Anne Willemsen, Giovanni Tafuri
7.	Compliance with post-marketing commitments: recent reviews	EMA: Jordi Llinares Garcia
8.	Updates on co-authored research papers: <ul style="list-style-type: none"> • Post-Launch Evidence Generation plans • Unmet Medical Need concept: • Comparison between significant benefit and added value 	EMA: Jane Moseley, Jordi Llinares Garcia, Kristina Larsson EUnetHTA: Wim Goettsch, Chantal Guilhaume
9.	Progress of the EMA/EUnetHTA work plan activities	EMA: Michael Berntgen EUnetHTA: Giovanni Tafuri
10.	Closing remarks	Hans-Georg Eichler and Giovanni Tafuri

This was the 17th meeting between the European Medicines Agency (EMA) and representatives from the European Network for Health Technology Assessment (EUnetHTA) and attended by the European Commission. The draft agenda was adopted without changes.

Update on Joint Action 3

An update on the current Joint Action was provided. Key achievements were the changes in the governance structure and a new prioritisation approach to identify eligible compounds for the production of REAs, the EUnetHTA Prioritisation List (EPL). As a result of the EPL the number of REAs has been increasing over time (10th assessment being conducted) and a positive trend for implementation at the national level has been observed compared to previous Joint Action 2. The activity of Early Dialogues (ED) is successfully proceeding and analyses on ED experiences are due to be published shortly. Furthermore, Post-Launch Evidence Generation (PLEG) projects are being developed with three pilots.

EUnetHTA has also been intensively investing in the engagement with external stakeholders, in particular with patients and health care providers. A common EUnetHTA policy on conflict of interest (Col) with transparent criteria and an *ad hoc* Col Committee has recently been established.

The current JA3 will be extended until May 2021 with no additional financial resources than the original budget of the European Commission. In view of the extension, general consensus was expressed to extend the current EMA EUnetHTA work plan to 2021.

Decision: EMA and EUnetHTA agree to extend the duration of the current EMA/EUnetHTA work plan to 2021, in view of the extension of Joint Action 3 by one year.

Update from the European Commission

The state of play on the HTA proposal at the European Parliament and at the Council was presented, with a description of key amendments.

Following the entry into force, a three-year period before the date of application is planned, which will allow for the development and adoption of all tertiary legislation provided for in the proposal as well as the preparatory steps necessary for the joint work. This process will take into account tools and guidelines developed by EUnetHTA during its Joint Actions.

A further three-year transitional period is envisaged after the date of application to allow for a phase-in approach in terms of the work undertaken and to allow Member States to fully adapt to the new system.

The current Finnish Presidency (July-December 2019) has committed to progress with the negotiations and the subsequent Croatian Presidency (January-June 2020) has expressed willingness to bring forward the file.

Feedback from the EMA/payer meeting

On 18 June 2019, the second meeting between EMA and healthcare payers in the European Union - namely representatives from the *Association Internationale de la Mutualité* (AIM), the European Social Insurance Platform (ESIP), the Medicine Evaluation Committee (MEDEV) and the multi-stakeholder platform Mechanism of Coordinated Access to Orphan Medicinal Products (MoCA) - was held at the Zorginstituut Nederland in Diemen, with the participation of EUnetHTA observers. The objective was to explore synergies and foster mutual understanding and cooperation to help improve timely and affordable access of patients to new medicinal products.

EMA provided an update on the content of the meeting, which covered collaboration between EMA and payers on prospective planning of evidence generation for orphan medicinal products as well as on the concept of unmet medical need, the wording of therapeutic indications, horizon scanning initiatives and post licensing evidence generation. It was noted that the meeting report will be published shortly.

Information exchange and mechanism for reciprocal learning opportunities

The first part of the discussion focussed on histology independent developments. In February 2019 a webinar involving both EMA and EUnetHTA was organised in order to explore the various perspectives on histology independent indications and the (expected) challenges in relation to the assessment of these products. HTA bodies highlighted the challenge of conducting comparative safety and effectiveness exercises and in general to apply consolidated HTA methodologies (e.g. the definition of an ICER) under such new paradigm. The discussion further expanded on such challenges with presentations from both the HTA and the regulatory perspective on the topic. In a wish list to EMA, HTA bodies expressed the need to have an EPAR that best addresses such uncertainties. Continued collaboration on this topic was supported by both parties, including product-specific exchanges once the regulatory assessment is completed.

The second part of the meeting focussed on the webinar following the recent authorisation of an advanced therapy medicinal product. The webinar was held by rapporteurs of the Committee for Advanced Therapies of EMA and was attended by participants from 13 different EUnetHTA partner organisations.

The aim was to ensure that the scientific rationale for the CHMP positive opinion was clear for subsequent decision makers, including the explanation of the specifics of this ATMP; to provide the opportunity to provide clarifications on elements of the assessment or the labelling and to stimulate an early exchange on the post-licensing evidence need.

The third point covered during this session was a feedback from the CHMP Strategic Review and Learning Meeting held in Budapest in May 2019. In particular, EMA and EUnetHTA representatives presented the summary of discussions and key learnings on the topic of "Exchange between CHMP, HTAs and payers on labelling principles". Concrete cases of indication wordings potentially leading to challenges during the HTA process were presented. EMA reported that a reflection paper on the wording of therapeutic indications will be published shortly. This should facilitate the interpretation of the information contained in SmPC section 4.1 for HTA purposes. In general, it was agreed that continuous discussion and exchanges between EUnetHTA partners and CHMP is needed on regular basis and should be focussing on concrete examples, with particular attention to SmPC section 5.1.

The availability of EMA information to facilitate the preparation of REAs was then discussed. Communication between EMA and EUnetHTA Work Package 4 is indeed crucial, respecting confidentiality arrangements. Several uncertainties challenge the timeliness of REAs production, namely the lack of knowledge of the final labelling at time of CHMP opinion, possible changes of timelines of the regulatory review, uncertainty about the date of final CHMP opinion, varying time between EC decision and EPAR publication. Provision of SmPC under the confidentiality framework was also discussed. Also the need for citation of the CHMP AR in the draft Joint Assessment was discussed, as this will facilitate the quality and relevance of Joint Assessments. These issues were acknowledged and it was agreed to optimise the current arrangements to facilitate information exchanges and usability of this information in the production of Joint Assessments.

Action Points:

- EUnetHTA and EMA to continue exchanges on histology independent indications, possibly based on specific products at the time of EPAR publication.
- A follow-up survey on the ATMP webinar to explore participants' feedback and learnings, and follow-up on discussions concerning PLEG for this product and engagement with the sponsor.
- Proactive identification of other potential products of interest for exchanges between EMA and EUnetHTA.
- EMA to publish the reflection paper on the therapeutic indication.
- EUnetHTA to continue sharing concrete experience from using labelling and EPARs for their decision making, including sub-groups of relevance and the importance of section 5.1. Furthermore, considerations regarding a more structured framework for clarification questions on labelling.
- Confidential arrangements between EMA and EUnetHTA to be updated to include information exchange on regulatory timelines, provision of the final adopted SmPC together with the CHMP Assessment Report (AR) as well as the possibility to cite the CHMP AR in the draft REA.

Sharing respective practices and experiences related to the involvement of patients in activities: the new EUnetHTA document on patient inputs in REAs

The discussion focussed on the experience gained by EMA and EUnetHTA on the process of patient engagement.

EMA has now gained long experience in patient interactions with the objective to collect systematic patient input along the medicine lifecycle. In addition, the impact of such interactions is continuously monitored by EMA through surveys to patients and assessors. Recent surveys showed that patients provided substantial inputs on several aspects of clinical development during the process of scientific advice.

The recently published EUnetHTA document on the involvement of patients in the process of REA production was presented. The document stems from the experiences gained by EUnetHTA partners at the national level but also from the several interactions and meetings between European patient and consumer organisations and an *ad hoc* EUnetHTA Task Group on Patients & Consumers and Health Care Providers. The different methods to collect patient inputs reported in the document were presented by EUnetHTA. In line with the EMA process, EUnetHTA makes use of questionnaires to receive feedback from patients or caregivers on the perceived contribution to the REA. EUnetHTA is currently working on a new document describing the process of health care providers' involvement in its activities.

Action Points:

- EUnetHTA and EMA to continue exchanges on the process and documentation of patient and health care providers engagement in output documents.

Compliance with post-marketing commitments: recent reviews

An EMA review on products approved with conditional marketing authorisations (CMA) was presented by EMA. It described the evidence based on which a product is granted a CMA, the average time occurring from CMA granting to a conversion to full MA (about 3 years) and key features of the specific obligations (SOs) imposed by CHMP. Most importantly to note that the analysis of 10-year experience found that SOs did not have any change to their initially agreed scope. The case of a product not fulfilling an SO and failing to confirm clinical benefit, and therefore being revoked a CMA, was also presented.

Updates on co-authored research papers.

In light of the ongoing collaboration between EUnetHTA partners and EMA on scientific publications for peer-reviewed journals, an update was provided by the authors.

Paper on Post-Launch Evidence Generation plans, the Unmet Medical Need concept and a comparative analysis between significant benefit and added value have been finalised.

Progress of the EMA/EUnetHTA work plan activities

On the basis of the EMA/EUnetHTA work plan 2017-2020, a review was conducted focusing on the progress with the various activities. This was to ensure that the work plan will be delivered as expected. Most activity areas are showing progress. Particular attention needs to be given to the REAs, for which collaboration with regulators is crucial. The growing number of REAs will increase the opportunity to further adapt the current processes. The areas of collaboration on Patient Reported Outcomes (PROs) needs to be developed. An update on the activities on combination products/companion diagnostics is considered of interest and will be provided at the next bilateral.

Action Points:

- Reflection on how to further develop the discussion on PROs
- Update on the activities on combination products/companion diagnostics to be provided at the next EMA/EUnetHTA bilateral
- Follow-up review of the work plan activities at the next EMA/EUnetHTA bilateral

Closing remarks

The next meeting will be hosted by EUnetHTA and will be scheduled for end-2019.