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Minutes EMA – Payer Community meeting

19 September 2017, 10.00-16.00 BST

European Medicines Agency, 30 Churchill Place, London, Room 3F

Co-chairs: Payer Community: Ad Schuurman (am) / Menno Aarnout (pm)
EMA: Harald Enzmann (am) / Hans-Georg Eichler (pm)

Role	Name
Present:	Menno Aarnout (AIM), Francis Arickx (RIZIV INAMI), Elina Asola (STM/PPB), Michael Berntgen (EMA), Jacqueline Bouvy (NICE), Laurent Brassart (EMA), Anna Bucsecs (MoCA), Francesca Cerreta (EMA), Irina Cleemput (KCE), Nick Crabb (NICE), Clémence Dancoisne (Federation of French Healthcare Mutuals), Christine Dawson (ESIP), Corinne De Vries (EMA), Ursula Descamps (CNAMTS), Kristina Dunder (MPA/EMA), Hans-Georg Eichler (EMA), Arnaud Emeriau (ESIP), Harald Enzmann (BFarM/EMA), Michael Ermisch (GKV-Spitzenverband), Elisa Ferrer (EURORDIS), Antra Fogeles (NHS Latvia), Jurij Fürst (ZZZZ), Wim Goettsch (ZIN), Aldo Golja (Dutch Ministry of Health, Welfare and Sport (VWS)), Olga Gutierrez Barbadillo (Ministry of Health Spain), Antje Haas (GKV-Spitzenverband), Anne Hendrickx (Socialist Mutuals Belgium), Ana Hidalgo-Simon (EMA), Wills Hughes-Wilson (SOBI), Zoltan Huszti (NEAK), Pontus Johansson (TLV), Thomas Kanga-Tona (AIM), Vasileios Kourafalos (EOPYY), Christina Kvalheim (NOMA), Kristina Larsson (EMA), Yann Le Cam (EURORDIS), Dimitra Lingri (EOPYY), Aneta Lipinska (AOTMiT), Jordi Llinares-Garcia (EMA), Evelyn Macken (Independent Mutuals Belgium), Mercedes Martinez-Vallejo (Ministry of Health Spain), Martin Meissnitzer (HVB), Daniel O'Connor (MHRA/EMA), Hans Ovelgonne (CBG-MEB), Hanneke Parkinson (EMA), Guido Rasi (EMA), Sabine Richard (AOK), Jiri Samek (SUKL), Robert Sauermann (HVB), Ad Schuurman (ZIN), Jana Sipkova (remotely) (VZP), Alexios Skarlatos (EMA), Jocelijn Stokx (Christian Mutuals Belgium), Sarka Studena (remotely) (VZP), Fanny Tissier (REIF), Enrico Tognana (EMA), Spiros Vamvakas (EMA), Marc Van de Castele (RIZIV INAMI), Martin Van der Graaff (ZIN), Kart Veliste (remotely) (Haigekassa Estonia), Rick Vreman (ZIN)

Item	Agenda	Name
1.	Welcome by EMA's Executive Director	Guido Rasi
2.	Introduction and adoption of draft agenda	Payers: Ad Schuurman EMA: Harald Enzmann
3.	Tour de table	All
4.	Multi stakeholder Late & Early dialogue additional participant: MoCA Steering Group	Payers: Ann Bucsecs EMA: Spiros Vamvakas, Daniel

Item	Agenda	Name
		O'Connor
5.	Horizon Scanning for pharmaceuticals Synopsis of KCE report Full KCE report	Payers: Irina Cleemput, Aldo Golja EMA: Michael Berntgen
6.	Indication and Labelling, general aspects	Payers: Martin van der Graaff EMA: Kristina Dunder
7.	Indication and Labelling, specific aspects a) Cross-references within the SmPC b) Information on the use of medicines in the elderly	Payers: Michael Ermisch EMA: Kristina Dunder EMA: Francesca Cerreta
8.	Create clarity on the several definitions of unmet medical need	Payers: Menno Aarnout EMA: Jordi Llinares-Garcia
9.	AOB and Closing remarks	Payers: Menno Aarnout EMA: Hans-Georg Eichler

This was the first meeting between the European Medicines Agency (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). 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.

In the introductory notes it was highlighted that regulators, HTA bodies and payers perform an important task as gatekeepers for medicines to the healthcare systems in the EU but also as enablers of medicine development. Collaboration across these decision makers is expected to support access to innovative, beneficial medicines and to address some of the inefficiencies of the current system of clinical research. The common goal is to bring the right medicine to the patient and to ensure that each decision maker has the evidence they need for their evaluation within their respective remits.

Multi stakeholder Late & Early dialogue

The MOCA collaboration (Mechanisms of Coordinated Access to Orphan Medicinal Products) aims at enabling a comprehensive discussion of all aspects of patient access. In this space, interaction between payers and companies can occur at various stages, during development (mostly when moving from phase II and III) but also in view of post-approval data collection. So far 11 companies are working with MoCA; the collaboration ranges from small molecules to ATMPs. The benefits for companies include increased predictability and better understanding of expectations; from payers' side such dialogue allows for better appreciations why certain requirements may not be met. MOCA recently reflected how to move this work forward and make it even more useful through alignment with others decision makers.

EMA provided a review on the evolution of the regulatory scientific advice concept on European level starting in 1996 and the recent development of the parallel regulatory-HTA platform, which started with general discussions in 2008 and formal procedures in 2010. More efficient and targeted engagement

involving various decision makers should be ensured through the recently launched Parallel Consultation platform; relevant aspects include: single gateway for requests, establishment of the Early Dialogue Working Party by HTA bodies, selection criteria for the Consolidated (with involvement of the entire EDWP) and the Individualised pathway (with the involvement of single HTA bodies), HTA coordination through the EUnetHTA Early Dialogue Secretariat, single consolidated response from all HTA bodies in the consolidated procedures, and individual responses from participating HTA bodies in the individual procedures. It was highlighted that the development of this new procedure is a joint achievement by both EMA and EUnetHTA, who are equal partners in the new Parallel consultations platform. There will be a possibility of involving other stakeholders in the future (e.g. MOCA, payers) when relevant and agreed with the company.

In view of specific interest expressed by payers to engage on orphan medicines, it was noted that only 13% of the requests of parallel regulatory-HTA scientific advice were for orphan drugs (compared to 25% of the regular SA being for orphan drugs) and only 4 of them had questions about significant benefit. Furthermore, post-licensing evidence generation is a particular area of interest also for payers. It was mentioned that the number of questions on registries/ non randomised studies has been increasing in recent years and that this trend is expected to continue. Overall, there are opportunities for more intensified engagement in the space of advice for the evidence needs for orphan medicines.

During the discussion, it was voiced that registries can sometimes provide a biased view e.g. in case of unequal geographic distribution of patients. Ideally there is real time access to patients' data, and a clear plan about usage of data and data collection. The possibility of having a registry pilot involving regulators and payers (e.g. ultra-orphan drug) was discussed. Another suggestion was that instead of focusing on products/pilots, an agreement about concrete topics related to what requirements registries need to address (from the different stakeholders point of view) could be reached. This includes the need for registries for ATMPs to observe long-term effects. The importance of having a clear understanding about what do stakeholders need/want from a registry was consensual among the audience.

Another focus was on the need to have an early discussion on evidence requirements to support the evaluation of significant benefit and added value, respectively. In this regard it would be paramount to jointly discuss the review regarding the expected benefits and what type of evidence is needed to support this. It was noted that maintenance of orphan designation only occurs at the point of marketing authorisation. Therefore sufficient data needs to be generated in the pre-authorisation setting to support claims of significant benefit, otherwise the designation may not be maintained.

Parallel Consultation with involvement of payers was agreed as the most efficient way forward. As a starting point it was suggested that MOCA payers engage with EMA and EUnetHTA partners to participate in an upcoming Parallel Consultation for an orphan medicine as observers.

Horizon Scanning for pharmaceuticals

The background for this session was that payers would like to explore opportunities for exchanging information on (upcoming) dossiers and assessments, for the purpose of horizon scanning. As a starting point the proposal from KCE for the BeNeLuxA initiative was presented ([Synopsis of KCE report](#), [Full KCE report](#)). This proposal includes the establishment of a horizon scanning database with different datasets (Baseline data [pipeline, gaps in research, CT register]; Filtered products; High impact / opportunities to collaborate; Withdrawn / failed products; Registered products; Patent data; Generics and biosimilars). The intention is to set up a multi-country initiative with involvement of payers on a voluntary basis. An invitation to express interest by payers is open until 1st November.

EMA noted that "Horizon scanning" means different things to different people. Elements that drive the approach to horizon scanning include the objectives / desired impact, scope of technologies / interventions,

observation period, data sources and detection methodology, triage as well as reporting mechanisms. Based on the KCE report it appears that the focus was on pharmaceuticals mostly later in development and during the regulatory approval process plus some specific early development (e.g. orphan designations); further considerations included the impact on health care systems. EMA therefore provided a review of information that is publicly available and can be used as source data to address the needs by payers. This includes information during the review of marketing authorisation applications as well as data during the development phase. Also experience with the establishment and conduct of business pipeline meetings was shared. Finally it was highlighted that "Horizon scanning" has also been identified as area for collaboration between regulators and HTA bodies and that there are opportunities to link up activities on European level, capitalising from data needs whilst recognising differences in objectives.

In conclusion, part of the data needs identified by payers can be addressed already through publicly available information; emphasis would be on exploring ways to optimise the reporting. Furthermore, there are potential benefits by leveraging learning from performing business pipeline monitoring; also there might be opportunities to explore how data held by different actors may become mutually beneficial. It would be important to avoid duplication of efforts hence there is a need to link up with other initiatives on European level. The next step will therefore be to broaden this discussion to also include EUnetHTA and to jointly address the actions listed above.

Indication and Labelling

General aspects including cross-references within the SmPC

An introductory review was provided on regulatory perspectives concerning the wording of the Summary of Product Characteristics (SmPC). The SmPC is the basis of information for healthcare professionals on how to use the medicinal product safely and effectively. It is not a treatment guideline. It defines the conditions in which the product could be used, not when it should be used. From a regulatory point of view, a therapeutic indication (minus contraindications) reflects the disease and population in which the benefit risk balance of the product has been assessed as positive. The wording of the therapeutic indication results from a multidimensional analysis of the data submitted, the applicant's claimed indication, the therapeutic context and the benefit risk assessment. Population studied in clinical trials may never be fully representative of the target population or provide full evidence in all subgroups. Therefore, the benefit risk assessment is performed not only among the studied population but also within its subgroups and possibly beyond, taking the totality of the data into account. As a result, the population of the indication may be wider or more restricted compared to the studied population. Appropriate qualitative or quantitative data will however have to support extrapolation. Other sections of the SmPC provide additional information on how to use the product or summarises evidence supporting its use in the approved indication(s), but they should aim neither at extending nor at restricting the indication(s). The benefit risk section of European Public Assessment Report informs on Regulators' reasoning when assessing the benefit risk and defining the therapeutic indication. Its template has been recently revised to optimise communication of the decision making process.

An important clarification was provided concerning the cross references to other sections in the SmPC. Sometimes, the therapeutic indications cross-refer to other section(s) of the SmPC, e.g. 5.1, to attract healthcare professionals' attention on the information provided. It was confirmed however that what constitutes the approved patient population is what is stated in section 4.1 (minus 4.3); any cross-references (e.g. to section 5.1) do neither restrict nor expand the approved labelling.

Payers observed that there seems to be a trend towards less specified populations covered by the approved labelling, which leads to problems for reimbursement decisions, like in the area of diabetes. Whilst acknowledging that there are expected to be scientifically sound considerations behind such labelling claims

it was highlighted that it would be important for regulators to be explicit about their reasoning; in this context it was raised that in some reports the clinical assessment is more descriptive and not always leading to firm conclusions. As an example, it would be important in the published assessment report (EPAR) not only to report about patient stratification but – of relevance – to also provide a judgement which sub-group is expected to be performing well and where there are more uncertainties. In case of apparent subgroup differences a clear reasoning should be provided why the apparent difference was - or was not – considered meaningful and has – or has not – been the basis for a modification of the population defined in the indication. It was highlighted that this does not challenge the actual decision by regulators but should facilitate a better understanding of this outcome by payers.

It was agreed that payers provide consolidate comments and suggestions for improvement on EPAR and SmPC. This activity will be taken up by MEDEV. The discussion will then also occur in the context of the activities with EUnetHTA; it was noted that the upcoming work plan by EMA and EUnetHTA has identified this as an area for action.

Information on the use of medicines in the elderly

The current status of application of the SmPC guideline to the information relevant to the older population was presented. In advance of the meeting a questionnaire was sent to the payers to explore their views on the relevance of information provided in sections 4.1, 4.2, 4.3 and 4.4. The principal findings were:

- Description of population and dose adjustment is important for economic modelling
- The studied population should be described accurately. Discrepancies with the expected use population should be discussed to shed light on the weight of evidence supporting extrapolation of benefit/risk to non-studied patient subgroups. The example of a generally worse ECOG status was made. Frail and older- old patients are an increasingly large group and information should also be presented and discussed for those.
- It would be important to understand whether a population was not studied because excluded from the trial protocol, because not enrolled, or because safety risks prevented enrolment. A consistent approach should be taken in expressing the information in the SmPC (e.g. if not studied it should be clear in 4.4)
- The survey conducted prior to the meeting on SmPC wording highlighted that expressions like “use caution” or “should not be used” are interpreted differently from different stakeholders. An accurate and transparent definition of their meaning by regulators and consistency in the use of each wording was considered important.

The leanings from this specific discussion will be taken up in the above-mentioned comments by payers on EPAR and SmPCs.

Create clarity on the several definitions of unmet medical need

The discussion started with an introduction from the payer community on the concept of unmet medical need in their framework; reference was made to the comparison of the different definitions found in procedures from the EMA, including Conditional Marketing authorisation, accelerated assessment and others.

From the regulators' perspective it was pointed out that the definition of unmet medical need (UMN) comes from Regulation 507/2006 and it was acknowledged that the definition includes terms that are subject to interpretation such as "satisfactory" or "major therapeutic advantage". In terms of use of the UMN concept it was noted that fulfilling an UMN is a requirement to apply certain procedures (like accelerated

assessment) or decision-making frameworks (like conditional marketing authorisation); specific for the PRIME scheme it was highlighted that the UNM concept also allows for priority setting in terms of the use of resources from regulatory network. A point of discussion was that unmet medical need can be approached from different perspectives, for instance from a patient or a population focus. It is agreed that this constitutes one of the key elements that may lead to divergent outcomes and therefore needs further discussion.

The concept of having a single definition of unmet medical needs was challenged and the overall view was that instead of a common definition of unmet medical need it is necessary to improve the communication on how unmet medical need can be quantified and to understand how to address UMN and put it in context with the severity of disease.

As actions it was agreed to continue with the relevant work initiated as part of the EMA/EUnetHTA work plan. In this context there will be a collection of concrete examples to further clarify definitions. As a first step EMA and EUnetHTA will analyse UMN in PRIME products and Parallel Consultation (aka parallel scientific advice involving HTAs and regulators) to collect cases for discussion. Other stakeholders like payer organisation should join the discussion on this topic.

Closing remarks

This was the first engagement between different communities; hence the objective was to facilitate mutual understanding for different perspectives. The reflections did span across the medicines life-cycle, from benefit/risk evaluation through to value and affordability.

Experience over the last decades has shown that delays in pricing and reimbursement negotiations at national and regional level can sometimes occur, because drug developers are primarily focused on demonstrating the quality, safety and efficacy of a medicine for regulatory assessment but often do not generate sufficient comparative evidence for cost-effectiveness assessments and pricing and reimbursement decisions. As a consequence, more research is required post-authorisation. Timely, adequate information could streamline decision-making and facilitate faster access to appropriate care.

Collaboration between regulators and healthcare payers is an important approach to tackle these challenges because it creates synergies that help to improve and speed up patients' access to new treatments across the EU. The discussion might foster future cooperation and will complement the already existing collaboration with HTA bodies, represented by EUnetHTA, with a focus on synergies in activities of mutual interest.

The discussion throughout the day demonstrated a genuine willingness to engage. It was recognised that there will always be cases where decision makers have different views. It is considered important to develop a better understanding why this might be the case and make the reasons for different views transparent. At the same time it is also expected that through such collaboration over time synergies and common perspectives will emerge. EMA and EU payers will consider organising follow-up meetings to explore the above and other areas of collaboration, and discuss how to create a more effective partnership in order to improve the exchange of knowledge and information between regulators and payers.