



Andalusian Agency for Health Technology Assessment (AETSA)

Seville, 22nd of July, 2016

Comments on the concept paper “Facilitating the translation of advanced therapies to patients in Europe”

Introduction

AETSA welcomes the publication of this important and well-addressed concept paper on “Facilitating the translation of advanced therapies to patients in Europe”. Also we would like to thank the IMI for the opportunity to comment.

AETSA’s comments will reflect the perspective of a regional health technology assessment organisation with HTA activity on pharmaceutical and non-pharmaceutical products. We have also developed intensive collaborative joint work with the Spanish National HTA strategy on both lines (pharma and non-pharmaceuticals¹).

We understand the need to review and establish specific and adapted HTA processes for ATMPs as they represent a new and innovative health technology type. However, at the same time we would also like to stress the importance of establishing clearly stated and scientific rigorous methods for safety and effectiveness assessment that being known by ATMPs developers could be taken into account in designing clinical trials and also embraced by all HTA organizations. As it is mentioned in the concept paper, ATMPs’ development is an area of great interest for public health, patients and citizens. In this sense, all participants in defining access to ATMPs have the responsibility to minimize possible risks involved. Furthermore, but not less important, there is a necessity of new models for cost-effectiveness analysis in order to agree prices and reimbursement procedures that make the access to AMTPs sustainable for the public health systems.

Below we describe some issues and considerations that we would like to share alongside our experiences. We present them as answers to the proposed questions. AETSA would welcome the opportunity to participate as an

¹ The Andalusian Agency for Health Technology Assessment was established by the Government of Andalusia in 1996, as part of a new program to promote the use of cost-effectiveness analysis and evidence-based medicine in the regional health service. Since 2012, AETSA is a member of the Spanish HTA Network, a public HTA body that support decision to National Health Service Portfolio. Our main goal is to promote the appropriate use of health technologies (pharmaceuticals and non-pharmaceuticals), providing decision-makers with critically review information about their efficacy, safety, and effectiveness. We also consider the economic, social, ethic and legal impact. We work in coordination with the Spanish HTA Network (for assessment of medical devices and procedures) and the Therapeutic Positioning Report Group in the Spanish Medicine Agency, AEMPS (for pharmaceuticals). Our main products are systematic reviews and cost-analyses reports. We encourage the widespread participation of medical professionals in our assessment projects as part of our strategy to enhance quality of care and efficiency. AETSA also coordinates groups for developing evidence-based clinical guidelines and for developing recommendations about selection and use of new pharmaceuticals and new technologies that are likely to have a major cost or social impact in the Andalusian Public Health System. AETSA is a member of the following international networks: INAHTA, EuroScan, HTAi, and EUnetHTA (foundational member). More information at: <http://www.juntadeandalucia.es/salud/servicios/aetsa/>. We are also in Twitter: @AETSA_

interested party in some of the discussions that could take place alongside this paper.

Considerations and experiences

1. Have the key challenges that can be addressed through collaborative, public-private initiatives been properly identified?

We agree that IMI have identified the key challenges that are critical in facilitating the translation ATMPs to patients. Nevertheless, we consider that there is another important opportunity related to the ATMPs’ clinical development which has not been outlined i.e. collaboration between ATMPs developers and HTA organizations at the very early stage of Initial Evidence Generation (IEG), the step in the health technology life cycle in which the clinical trials are developed.

The collaborative process is considered to be essential in this early stage of IEG, and Early Dialogues (EDs) are the forum that has been designed to fulfil this need. EDs contribute to the development of high quality clinical trials protocols. The data and evidence generated by clinical trials resulting from these EDs process are expected to be adjusted to the requirement of the HTA process and consequently, HTA reports will be better to support the decision making process regarding early access to the ATMPs. EDs will lead to more timely and straightforward assessments, resulting in an appropriate access to, and coverage of, patients’ needs.

The methodology for these EDs have been already established at European level. AETSA has taken part in the project “Shaping European Early Dialogues (SEED)” funded by the European Commission and coordinated by HAS (France). Also we have participated in the Joint Action 2 on HTA (develop by EUnetHTA collaboration and funded as well by the European Commission) in the specific work package related to EDs. In both projects, process and methods for EDs among technologies developers and HTA organizations have been both specifically designed and piloted. Also we have taken part in designing and piloting experiences about parallel/joint scientific advice with EMA as a part of SEED project.

The EDs established process is going to be put in place and consolidated as a real-life exercise during the EUnetHTA Joint Action 3 (2015-2019), through the activities of a specific work package that is going to be dedicated to the life cycle approach to improving the process of Evidence Generation.

In general, collaboration among drug companies and all other participants that are involved in the development and access to new drugs is considered to be essential in order to avoid the duplication of work and uncoordinated study requests. As well as enabling the collection of consistent data that can be combined across organisations and countries to support assessments and decision making processes.

2. Which of the proposed potential initiatives should be prioritised?

Although we acknowledge that the development of reimbursement and payment mechanisms should have high priority, we consider that the review of HTA process for ATMPs, discussion among HTA organizations and those and stakeholders should be also prioritised.

Developing and/or adapting tools to assess ATMPs should happen along with the development of guidelines that establish the methods to assess the clinical studies (comparator, endpoints, duration of the trials) and with the design of specific ones to demonstrate the long-term efficacy and safety follow-up.

3. Are any areas missing?

AETSA would like the following missing issues in the topics indicated for future research investment to be taken into consideration.

- Regarding the HTA implications:

- The necessity and benefits of harmonization in methods for ATMPs HTA assessment among HTA organizations.
- The benefits of joint health technology assessments among HTA organizations in terms of efficiency in HTA (we would like to highlight again in this point the EUnetHTA Joint Action 3 that is going to continue with the joint work initiated in previous joint actions).
- It is necessary to take into account and further develop the methodology for indirect comparisons for ATMPs.
- It is also a requirement to develop and do research on statistical methods to extrapolate, when necessary, the data from the clinical trials to the long term and to elaborate guidance about them. Moreover, it would be necessary to define clear criteria and conditions in which these methods are going to be considered appropriate. We will need tools to evaluate the quality of evidence generated by these methods. In this regards, AETSA understands the need to avoid unnecessary studies at long term but would like to stress the importance of observational prospective studies in the practice of evidence-based medicine in this new field of ATMPs. Working with electronic health records and real-world data could help to answer clinical research questions about ATMPs effectiveness and safety.

- Regarding Hospital Exemption (HE):

- AETSA would remark the importance of observational prospective studies in this field, based on registries as possible, to generate new evidence about effectiveness and safety in cases of HE.

- Regarding reimbursement and payment mechanisms: there are other issues that could be taken under consideration such as patient access schemes used in special circumstances (i.e. oncology, cancer, etc.) and their adaptation for ATMPs. Based on the experience of orphan drug or end-of-life treatments, criteria for ATMPs reimbursement could be developed. In the same way, the use of risk sharing schemes that require the existence of registries, follow-up, and continuous assessment could be taken into account.

On the other hand, generating adequate data for pricing, reimbursement and market access during clinical development is one of the main challenges for manufactures. Therefore, the promotion and use of new models of public-private partnership to develop ATMPs and give access to them will bring potential benefits.

4. What are the key European or national initiatives that IMI shall synergise with?

- At European level and related with HTA activities: HTA Network and EUnetHTA collaboration. As we have mentioned before, the Joint Action 3 on HTA will have a work package (WP) that is going to be devoted to the life cycle approach to improve Evidence Generation. This WP will support developers of medical technologies (pharmaceuticals, medical devices and diagnostics) by providing a collaborative approach between a wide range of European HTA agencies on their product development plans. By integrating structures that facilitate the exchange of different perspectives, learning, efficiency, and consistency throughout EDs (or scientific advice), they will optimize the interaction with regulators for pharmaceuticals and medical devices. Alongside this, pilots regarding post-launch evidence generation will be conducted. A number of pilots will be using data from registries, others will be using data from sources other than registries. A wide range of stakeholders will be involved in the pilots in order to catch all the relevant aspects. This will lead to the development of a tool to support permanent collaboration on post-launch evidence generation. Thirty-nine organizations (among them AETSA) will participate in this WP.

- At national level: "Therapeutic position reports" initiative that is coordinated by the Spanish Medicine Agency (AEMPS). AETSA collaborates intensively in this initiative.

- At a regional level, we would like to remark the following initiative:

- Andalusian Initiative for Advanced Therapies, from Andalusia, Spain.
(<http://terapiasavanzadas.junta-andalucia.es/index.php/en/>)

The Andalusian Initiative for Advanced Therapies is promoted by the Andalusian Government to foster research in the field of advanced therapies to develop safe and efficient treatments to offer to the population.