Feedback on Uncertainties of Health Care Providers and Patients on MAPPS

April 2018

The work leading to these results was conducted as part of the ADAPT SMART consortium (Accelerated Development of Appropriate Patient Therapies: a Sustainable, Multi-stakeholder Approach from Research to Treatment-outcomes). For further information please refer to www.adaptsmart.eu. This paper is the result of the collective input from working group D3.04 and only reflects the views of the authors.

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LIST OF ABBREVIATIONS

Abbreviation	Explanation
AEs	Adverse Events
AP	Adaptive Pathways
CSA	Coordination and Support Action
EFPIA	European Federation of Pharmaceutical Industries and Associations
EMA	European medicines agency
HCPs	Health Care Professionals
IMI	Innovative Medicines Initiative
MAPPs	Medicines Adaptive Pathways to Patients
RWD	Real World Data
RWE	Real World Evidence
WP	Work Package
WS	Work Stream

Table of Contents

Executive Summary

ADAPT SMART was set up as a *Coordination and Support Action* under the European Innovative Medicines Initiative (IMI). The objective of ADAPT SMART was to establish a multi-stakeholder enabling platform to facilitate and accelerate the availability of MAPPs and engage a dialogue with relevant stakeholders for the coordination of MAPPs (Medicines Adaptive Pathways to Patients) related activities. Like the EMA Adaptive Pathway, MAPPs seeks to foster access to beneficial treatments for the right patient groups at the earliest appropriate time in the product life-span in a sustainable fashion. As part of the project which has looked at which product could be worth entering the MAPPs framework (deliverables D2.05 and D3.02) according to predefined engagement criteria (deliverable D2.03), Work Package 3 interviewed a few Health Care Providers and patients' organisations to understand better what could be their issues and uncertainties when confronted with MAPPS.

Given the small sample size of interviewees (10 HCPs and 5 patients' organisations), any conclusion must be interpreted with caution. However, considering the interviewees, and a review of the literature, these interactions provide a useful indication of what might be HCPs and patients' organisations main issues and uncertainties when confronted with a MAPPs product.

1 Introduction

The current drug development paradigms which seek to foster access to beneficial treatments for the right patient groups at the earliest appropriate time are challenged by transformative health ecosystem environmental developments. Advancing innovative therapies to patients with high unmet needs will require new ways of data generation and evaluation to register them, and new ways to manage their utilization in the clinical practice.

To address these environmental changes, major adaptations to current paradigms will be required, which would need to go far beyond the well-defined regulatory evidence standards. We posit that all decision makers and stakeholders in the healthcare ecosystem will need to explore a life-span approach for new pharmaceutical treatments where drug development, licensing, health technology assessment, pricing and reimbursement, use in clinical practice and monitoring will be viewed as a continuum.

Medicines Adaptive Pathways to Patients (MAPPs) is a concept that "seeks to foster access to [novel] beneficial treatments for the right patient groups at the earliest appropriate time in the product life-span, in a sustainable fashion." It is also commonly referred to as Adaptive Pathways (AP) by the European Medicines Agency (EMA).

The AP approach is part of the EMA efforts to improve timely access for patients to new transformative medicines. AP is a scientific concept for medicine development and data generation which allows for early and progressive patient access to a medicine. The approach builds on regulatory processes already in place within the existing EU legal framework, e.g. scientific advice; compassionate use; the conditional approval mechanism; patient registries and other pharmacovigilance tools that allow collection of real-life data and development of the risk-management plan for each medicine. The approach is based on three principles:

1. **Iterative development,** which either means:

    - Approval in stages, beginning with a restricted patient population then expanding to wider patient populations; or,

    - Confirming the benefit-risk balance of a product, following a conditional approval based on early data (e.g., using surrogate endpoints) considered predictive of important clinical outcomes;

2. **Gathering evidence through real-life use** to supplement clinical trial data;

3. **Early involvement of patients, regulators, health-technology-assessment bodies and payers** in discussions on a medicine's development.

This concept applies primarily to treatments in areas of high medical need where it is difficult to collect data via traditional routes or where large clinical trials would unnecessarily expose patients who are unlikely to benefit from the medicine (MAPPs engagement criteria). Finally, and quite importantly, there will not be any change in the standards for the evaluation of the benefits and risks or the requirement to demonstrate a positive benefit-risk balance to obtain marketing authorisation.

MAPPs seek to address the 'evidence versus access' conundrum faced by patients, physicians, healthcare decision makers and pharmaceutical innovators. The conundrum refers to the delicate trade-offs between ensuring rapid access to promising treatments for patients in urgent need on the one hand and ensuring that patients, healthcare professionals and other decision-makers possess adequate information on benefits and risks at the time of launch on the other hand. The MAPPs concept is not an official designation and is not intending to create new regulatory or legal frameworks. It instead aims to make better use of various existing development tools and methods, and regulatory procedures for medicines under development (1).

As part of ADAPT SMART Work Package 3, a specific workstream "**Inventory and analysis of increased uncertainties for patients and other stakeholders and the issues they raise"** was tasked to analyse the specific views and uncertainties of stakeholders facing MAPPs, and identify enablers to manage and reduce them. To this effect, the workstream members used tailored approaches to gather patients' and HCPs' views.

2 Methodology

In order to understand Health Care Providers' (HCPs) views on MAPPs, the ADAPT SMART (**A**ccelerated **D**evelopment of **A**ppropriate **P**atients **T**herapies, a **S**ustainable, **M**ulti-stakeholder **A**pproach from Research to **T**reatment-outcomes) consortium has decided to interview a group of European HCPs to determine their views as clinicians and prescribers, from a benefit/risk stand point, on using a MAPPs product for their patients with a severe disease with a high unmet medical need. This was also the opportunity to identify the potential impact on their clinical practice when helping to generate additional clinical evidence (Real World Data), or recommending their patients to agree to be included in a disease registry. Knowing the tight timelines, as this work was initiated while the project was closed to completion, it was decided to focus on prescribing physicians who were known of the workstream leaders. We also reached out to the Standing Committee of European Doctors, which was unable to participate within the given timeframe. A set of seven umbrella questions were identified and included in a questionnaire that the selected HCPs sent back once completed to the workstream leaders using a specific email address. In addition, information on MAPPs and a link to the ADAPT SMART website was included with the questionnaire (Annex 1). HCPs were asked to answer some of the questions (Questions A, B and C) using a 6-point scale where [0] means no concern/uncertainties and [5] the higher level of concern/uncertainty HCPs could have.

Similarly, to understand patients' views, a scientific and a grey literature review were conducted to verify the existence of evidence on patient uncertainties when entering the MAPPs pathways. Subsequently, since the first investigation only produced limited results, it was decided to perform semi-structured interviews with some patient representatives, to help gather some input from a patient perspective. To this effect, five EURORDIS and EPF member representatives with legal, ethical and patient advocacy expertise were interviewed, using a pre-determined set of open questions in combination with the opportunity for the interviewer to explore particular themes or responses further.

3 Results

3.1 HCPs interviews results

Within the given timeframe, we were only able to reach out to 10 HCPs who were all able to complete the questionnaire. Six were from Spain, 2 from France, one from the UK and one from Slovakia. They are all practicing at the hospital, and are all well recognised specialists either in paediatrics, respiratory or gastro-intestinal diseases.

Consolidated results are presented in a summary table (Annex 2).

➢ ***Question A: Would you prescribe this [MAPPs] medicine?***

To this question, one out of ten expressed the higher level of uncertainty if he had to prescribe a MAPPs product. The rest had a no (would not prescribe) (n=3) or low level (no concerns to prescribe) (n=4) score, and 2 HCPs scored their uncertainties with a score of 2.

➢ ***Question B: rate the level of uncertainty you might have in the following domains for this MAPPs medicine and its registered indication***

When asking to rate the level of uncertainty they might have with this MAPPs medicine and its registered indication, 3 out of 10 said they would have a moderate level of uncertainty related to its efficacy; 1 out of 10 would have the higher level of uncertainty related to short term safety; 2 out of 10 expressed a high level of uncertainty related its effectiveness (score= 4 or 5) and 5 out of 10 expressed the higher level of uncertainty related to long term safety (score was 4 or 5).

Related to cost of this MAPPs product, 5 out of 9 said they would have moderate to high level of concern, and one did not answer as considering the question was unclear; high ethical hesitation was an issue for 3 out of 10 HCPs meanwhile 4 out of 9 expressed moderate concerns in regard to legal issues (scored 3), and 5 out of 9 moderate to high liability consequences. One did not answer these last two questions considering that '*If the drug is approved through MAPPs by EMA there should not be [any] ethical issues!*'

➢ ***Question C: What are the issues that could be of concern if you were asked to generate this additional evidence?***

During the interviews and ulterior ones with HCPs we did explain that under the MAPPs concept, the iterative development, licensing and financial coverage decisions of a MAPPs medicine imply the generation of additional clinical evidence. Therefore, it requires additional data generation (e.g. real world data) in the clinical practice to potentially support an initial indication or expand the already registered indication to another patient population(s), hence the need to identify health care value and impact.

To the question what are the issues that could be of concern if they were asked to generate this additional evidence one out of 10 expressed the higher level of concern related to the impact of current care pattern; 5 out of 10 had moderate to high level concerns related to the need to monitor the patient. Resources in terms of the need for personnel was of moderate to high concern for 8 out of 10 HCPs; 6 out of 10 would have moderate to high concern related to the need for extra-time and extra-test meanwhile 5 out of 10 were highly concerned by the need to collect data in their practice. Five out of 10 were also highly interested in being part of the analysis of this additional evidence.

When asked whether they would be concerned on how to stop the treatment of their patients if the evidence does not confirm the expected benefits, 6 out of 10 said that this would not be a concern.

➢ ***Question D: Would you be ready to explain your patient benefiting of a MAPPs treatment, the advantages and reasons to join a disease registry to help gather additional clinical evidence?***

To this question all 10 HCPs responded positively. One even said: '*Yes, because if I do prescribe the drug, I am convinced this is the best option for the patient but I will explain him/her the need for further collecting information because not all is known yet, etc…*'

➢ ***Question E: Would you like to be part of the iterative decision making in early development, licensing and/or in financial coverage?***

Most of the HCPs, 8 out of 10, would like to be part of the iterative decision making.

➢ **Question F: What kind of information would you expect to receive in order to make an informed prescribing?**

With this question, 4 out of 10 mentioned the need to receive all available efficacy and safety data and product prescribing information, 2 would need preclinical information, 2 examples from other colleagues' experiences, and one information on next steps of development.

3.2 Patients' organisation interviews results

The semi-structured interviews with patients focused on the following questions:

- what is a MAPPs/adaptive pathway? what does it entail in terms of increased risks/uncertainties but possible benefits?
- what entering MAPPS would be: "entering" a clinical trial for the time of the product is taken?
- the patient has a key role in gathering evidence during the whole lifecycle of the product
- the risks of product exit from the market
- the potential risk of not qualifying for the target population
- the contact details of the Patient Organisation (when it exits)
- the how/what-to do if anything wrong happens during the product intake (should not be different from what is already in place, ie the treating physician who will also have an active contribution to generate additional evidence).

Key discussion points were the following:

➢ **Communication**

- The main take away message from both the brainstorming and the open source search was that communication is key to patients. The communication should be simple, understandable, coherent and short to address patient uncertainties.
- The outmost importance in the communication with patients will be the clear explanation of the MAPPs concept. Who does what; when and how; and who is responsible? The explanation of the legal basis is also important (i.e. within the current regulatory framework).
- With MAPPs there is an extra need for clarity and good and reliable communication.

➢ ***Trade-off benefits/risks***

- A closer consideration of the trade-off between benefits and risks is needed. Even terminally ill patients will not accept whatever risk to prolong their lives, if it implies painful side effects or adverse events (AEs) due to the treatment. However, published data haves indicated that the acceptable level of benefit-risk balance may differ depending on the natural course of the disease and the availability of treatment (2). For example, in the case of a life-threatening disease, a patient may be prepared to accept higher risks linked to a new treatment. However, when the medicine is not likely to give any essential benefits, the tolerated risks are expected to be much less.

- People should be aware of the level of trade-off between risks and benefits.

It was stressed that also in the context of MAPPs, the life cycle of a medicinal product should be presented as a development plan that looks at efficacy, safety and their re-assessment to allow an iterative decision-making process, which, in case of positive outcomes would lead to the availability of the product for a wider target population.

➢ ***Operational, legal and ethical aspects***

- Operational and legal aspect play an important role to reduce patient uncertainties about implications of MAPPs products
    - Time and rules of assessment should be defined beforehand and clearly explained to the patients involved in the process and being prescribed a MAPPs product.
    - Risk sharing of potential negative outcomes of a MAPPs product, with healthcare professionals, industry and other relevant stakeholders is key to insure an engagement and an appropriation of the concept.

➢ ***Exit strategy***

- MAPPs have to include an "exit strategy" and identify the one that will supervise and deliver a MAPPs product.
- The notion of exit of a product from the MAPPS pathways needs to be CLEARLY communicated and even more importantly the reason, the consequences, the process and the actions taken afterwards should be reported.

➢ ***Safety***

- Patients enrolled in Adaptive Pathways/MAPPs should be assured that the treatment has a positive benefit risk profile and both uncertainties and benefits should be explained
- Safety and efficacy have to be proven.

➢ **Informed consent to MAPPs treatment**

- Getting enrolled in Adaptive Pathways/MAPPs should happen through formal submission of informed consent, as it is usual practice based on data and patients' willingness to receive the medicinal product.

➢ ***Data***

- Patients have to be aware of how they can have access to information/data. Access to data e.g. through the EMA website, their HCP and/or patients' organisations, allows them to take over more responsibility in making a decision about enrolment in MAPPs.
- Arguments against Adaptive Pathways/MAPPs based on lack of data on side effects/adverse events are not so strong if we consider that it also happens that medicines can be dropped out after Phase III for safety reason.
- Uncertainty may come from the lack of information on long term implications.
- After Phase II information should be transparent and shared not only with the patient involved in the trial but also with patient advocates supporting the patient.
- A long-term approach to data collection in Adaptive Pathways/MAPPs is advisable because it helps gather a high quantity and quality information even when the product becomes accessible to the general population. This approach would help keep better track of the medicine development process and use.

➢ ***Role of patient advocates and patient organisations***

- The involvement of patient advocates and experts can help mitigate the shortcomings coming from the lack of available information in lay language.

- Patient Organisations should play an educational and informative role to increase the understanding of MAPPs among patients. To do so, sustainable funding should be granted to patient organisations, preferably not from companies that have a vested interest in MAPPs, to avoid misperceptions on potential conflict of interest.

➢ ***Promotion of the Adaptive Pathways/MAPPs concept***

- Early access to innovative treatments should be well promoted to the general public, and patients' organisations have a role to play.

➢ ***Patients access and reimbursement***

- Reimbursement should be available to patients and public promotion of the product should facilitated, while stakeholders obstructing the access to innovative products should be made public for the benefit of transparency.

➢ ***Patient involvement***

- In the context of MAPPs, patient involvement should be better promoted in the medicines development life-cycle, especially in the early stages where patients may provide guidance and after marketing authorisation, where patients may play an important role in generating additional evidence.
- Selection criteria should be well explained to the target population of patients.

➢ ***Patient education***

Educating patients and public on Adaptive Pathways/MAPPs is vital.

➢ ***National and cultural variables***

- National and cultural aspects should be considered. Education and information to patients should be provided in native language to ensure full understanding of the MAPPs concept.

4 Discussion

WS intention was to explore the views, main uncertainties and concerns clinicians or patients could have when prescribing or using a MAPPS product, respectively.

HCPs' interviews were performed using a small sample of clinicians, working mainly at high technology teaching hospitals, all specialists with international background and experience in chairing international medical societies. Most of the respondents expressed no concern if they would have to prescribe a MAPPs product for which a certain level of clinical uncertainties was to remain at the time of prescription, except for long term safety; but worth to mention that one third expressed concerns about efficacy. It is well known, that the level of uncertainty or, conversely, the interpretation of the robustness of the currently available data can vary among physicians within a country and across geographic regions (3-5). Impact on cost was an issue for almost two third of the respondents. In relation to the need to generate additional evidence, the main and higher concerns were associated also to the perception of the need to use additional resources, such as personnel, for patient monitoring and extra-testing. This result is consistent with other studies and deliberative papers (6;7) showing an increase of cost-consciousness in the medical community which is a consequence of the growing awareness of health care sustainability problems, and the need for planned solutions. However legal and liability issues were also a matter of moderate to high concern. Uncertainties related on how to disengage patients if the evidence does not confirm the expected benefits of a MAPPs product were an issue for more than one third of the respondents. It is however worth to mention that all HCPs expressed their willingness to be part of the iterative decision-making process in early development, licensing and financial coverage of MAPPs. Clinicians are increasingly expressing their willingness to be part of early

dialogue initiatives with regulators, HTAs, and P&R decision makers as they consider that their perspectives are key to align evidence requirements and discuss perceptions of unmet medical need and added therapeutic value. This would ideally improve the selection of drug candidates for expedited access, optimize evidence generation, and foster effective early drug adoption (8). All HCPs interviewed were willing to provide their patient benefiting of a MAPPs treatment with the appropriate information on the advantages and reasons to join a disease registry, which will help generate additional clinical evidence.

The outcomes from discussions with patient representatives were shared in the framework of the workshop "Patient uncertainties and exploring the ethical and legal considerations of MAPPs" organised by the ADAPT SMART Consortium in January 2017 (9). Results from the consultation were confirmed by a wider audience including patients, healthcare professionals, industry, European regulators, academics, HTA bodies representatives. The key messages both from the consultation with patients and workshop are that patients are not keen to take major risks, e.g. AEs due to treatment, whatever the status of their illness. Quite important to point out that other published data have indicated that a patient may be prepared to accept higher risks linked to a new treatment (treatment constraint or AEs) e.g. in the situation of a life-threatening disease (10-12). Communication to patients and transparent sharing of data will help - together with education and meaningful involvement - mitigate patient uncertainties. It is relevant to highlight also that this consultation on Adaptive Pathways/MAPPs allowed the interviewees to share their views on issues that are not specific to MAPPs but similarly applicable to standard pathways.

5 Recommendations and Conclusions

Given the small sample size of the HCPs and patients' organisations involved in these interviews, any conclusion must be interpreted with caution. However, given the characteristics of the clinicians and of the patients' representatives interviewed, the ulterior conversations we had with them and the literature reviewed in the field, we believe that this work provides a useful snapshot of what would be the issues of highest concerns for clinicians and patients in relation to a MAPPs product as well as their unanimous willingness to be part of the iterative decision-making process when developing, licensing, using and considering the financial coverage of a MAPPS medicine. It is however worth noting that patients' representatives have a more nuanced position than clinicians or the patients themselves with regards to the level of risk or uncertainties to be taken with a MAPPs product. Communication and appropriate information sharing is more than ever important to help progress the concept - together with education and meaningful involvement - and mitigate stakeholders' uncertainties.

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7 Annexes

7.1 Annex 1

IMI ADAPT SMART – 1st December 2017

Understanding Health Care Providers' views on MAPPs

Introduction

The current paradigms of bringing innovation to patients are challenged by transformative health ecosystem environmental developments. Advancing innovative therapies to patients with high unmet needs will require new ways of evaluation to register them, and new ways of managing their utilization in clinical practice.

To address these environmental changes while fully realizing the potential of scientific progress for patients in a timely and sustainable way will require major adaptations to current paradigms.

The changes required would need to go far beyond the well-defined remit of regulatory evidence standards. We posit that all decision makers and stakeholders in the healthcare ecosystem will need to explore **a life-span approach** for new pharmaceutical treatments where drug development, licensing, health technology assessment, pricing and reimbursement, use in clinical practice and monitoring will be viewed as a continuum**.**

What is MAPPS?

Medicines Adaptive Pathways to Patients (MAPPs) is a concept that "seeks to foster access to [novel] beneficial treatments for the right patient groups at the earliest appropriate time in the product life-span, in a sustainable fashion." It is also commonly referred to as Adaptive Pathways (AP) by the European Medicines Agency (EMA).

The AP approach is part of the EMA efforts to improve timely access for patients to new transformative medicines. AP is a scientific concept for medicine development and data generation which allows for early and progressive patient access to a medicine. The approach makes use of the existing EU regulatory framework for medicines, and is based on three principles:

- iterative development, which either means:
  - approval in stages, beginning with a restricted patient population then expanding to wider patient populations;
  - confirming the benefit-risk balance of a product, following a conditional approval based on early data (using surrogate endpoints) considered predictive of important clinical outcomes;
- gathering evidence through real-life use to supplement clinical trial data;

- early involvement of patients and health-technology-assessment bodies in discussions on a medicine's development.

The approach builds on **regulatory processes already in place** within the existing EU legal framework, e.g. scientific advice; compassionate use; the conditional approval mechanism; patient registries and other pharmacovigilance tools that allow collection of real-life data and development of the risk-management plan for each medicine. This concept applies primarily to treatments in areas of **high medical need** where it is difficult to collect data via traditional routes and where large clinical trials would unnecessarily expose patients who are unlikely to benefit from the medicine (MAPPs engagement criteria). Finally, and quite importantly, there will not be any change in the **standards for the evaluation** of benefits and risks or the requirement to demonstrate a positive benefit-risk balance to obtain marketing authorisation.

MAPPs seek to address the 'evidence versus access' conundrum faced by patients, physicians, healthcare decision makers and pharmaceutical innovators. The conundrum refers to the delicate trade-offs between ensuring rapid access to promising treatments for patients in urgent need on the one hand and ensuring that patients, healthcare professionals and other decision-makers possess adequate information on benefits and risks at the time of launch on the other hand. The MAPPs concept is not an official designation and is not intending to create new regulatory or legal frameworks. It instead aims to make better use of various existing development tools and methods, and regulatory procedures for medicines under development.

What is ADAPT SMART?

On September 4th, 2015, a coalition of 90 European healthcare stakeholders from 32 public and private organisations including patients, payers, regulators, Health Technology Assessment bodies, academic institutions, and industry took their first steps towards investigating the MAPPs pathway and its enablers, e.g. tools and methodologies, and engaging in a dialogue with all relevant stakeholders to prove and develop workable MAPPs products.

ADAPT SMART, (Accelerated Development of Appropriate Patients Therapies, a Sustainable, Multi-stakeholder Approach from Research to Treatment-outcomes) is a 30-month project funded through the EU Innovative Medicines Initiative (IMI) which has established a multi-stakeholder enabling platform for the coordination of MAPPs activities to facilitate and accelerate the availability of MAPPs products to all healthcare stakeholders.

For any additional information, visit the IMI ADAPT SMART website at
www.adaptsmart.eu

Objective of this survey to Health Care Providers

You are receiving this survey since the ADAPT SMART consortium would like to understand what would be your views as a clinician and prescriber, from a benefit/risk stand point, using a MAPPs product for your patients with a severe disease with a high unmet medical need. We would be thankful to also understand from you what could be the potential impact on your clinical practice when helping to generate additional clinical evidence (Real World Data), or recommending your patients to be included in a disease registry.

Questions to complete

What if a MAPPs registered medicine is at your disposal for prescription in a patient with a high unmet medical need, to treat a disease with an important degree of severity?

A. Would you prescribe this medicine? Please answer all questions using the 6 point scale where [0] means no concern/uncertainties and [5] the higher level of concern/uncertainty you could have, and add any comment you could have.

[0] [1] [2] [3] [4] [5]

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B. Please rate the level of uncertainty you might have in the following domains for this MAPPs medicine and its registered indication using the 6 point scale where [0] means no uncertainties and [5] the higher level of uncertainty you could have. For each one, please explain why.

- Efficacy: [0] [1] [2] [3] [4] [5]

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- Effectiveness: [0] [1] [2] [3] [4] [5]

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- Short-term Safety: [0] [1] [2] [3] [4] [5]

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- Long-term effectiveness: [0] [1] [2] [3] [4] [5]

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- Long-term safety: [0] [1] [2] [3] [4] [5]

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- Cost: [0] [1] [2] [3] [4] [5]

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- Ethical issues: [0] [1] [2] [3] [4] [5]

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- Legal issues: [0] [1] [2] [3] [4] [5]

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- Liability: [0] [1] [2] [3] [4] [5]

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- Other(s)? Please feel free to grade and describe in a short sentence

[0] [1] [2] [3] [4] [5]

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C. Under the MAPPS concept, the iterative development, licensing and financial coverage decisions of a MAPPs medicine implies the generation of additional clinical evidence. Therefore, it requires real world data generation in the clinical practice to potentially, 1. support an initial indication or expand the already registered indication to other patient population, and 2. identify health care value and impact. What are the issues that could be of concern if you were asked to generate this additional evidence? Feel free to add any comment.

- The impact on the way I provide care: [0] [1] [2] [3] [4] [5]

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- The need for monitoring the patient: [0] [1] [2] [3] [4] [5]

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- Resources (personnel): [0] [1] [2] [3] [4] [5]
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- Extra time: [0] [1] [2] [3] [4] [5]
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- Extra test: [0] [1] [2] [3] [4] [5]
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- The need to collect data: [0] [1] [2] [3] [4] [5]
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- Will I be part of the analysis of this additional evidence?
  [0] [1] [2] [3] [4] [5]
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- If evidence does not confirm the expected benefits, how to disengage my patient
  [0] [1] [2] [3] [4] [5]
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  ……

- Any other(s)? Please grade and feel free to describe in a short sentence
  [0] [1] [2] [3] [4] [5]
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D. Would you be ready to propose your patient benefiting of a treatment with a MAPPs product to explain him/her the advantages and reasons to join a disease registry to help gather additional clinical evidence?

Yes [ ] No [ ]
Please explain why?
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Any other concerns? Please feel free to describe in a short sentence
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…

E. Would you like to be part of the iterative decision making in early development, licensing and/or in financial coverage?

Yes [ ] No [ ]
Please explain why?
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F. What kind of information would you expect to receive in order to make an informed prescribing? Please comment

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G. Any other concerns? Please feel free to describe in a short sentence(s)

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THANK YOU!

Your name: ……

Affiliation/position: …….

Country: ……

Please note that it is recommended to look at our glossary where the terms used in this survey are defined. This will help the understanding of all involved and will make our analysis of the results more accurate.

Please send the completed survey by December 22 at the latest, and via email to:
survey@adaptsmart.eu

7.2 Annex 2

HCPs – Interview results

Questions	HCP1	HCP2	HCP3	HCP4	HCP5	HCP6	HCP7	HCP8	HCP9
A									
	1 (see comments)	2	0 (see comments)	1 (see comments)	2 (see comments)	1	1 (see comments)	0	5
B									
Efficacy	1 (see comments)	2	0	2 (see comments)	3 (see comments)	3	1 (see comments)	2	3
Effectiveness	2 (see comments)	2	0	3 (see comments)	4 (see comments)	5	3 (see comments)	2	3
Short-term S.	1 (see comments)	3	0	1	2 (see comments)	2	1 (see comments)	2	4
Long-term E.	2 (see comments)	3	0	4 (see comments)	3 (see comments)	5	2 (see comments)	3	2
Long-term S.	2 (see comments)	4	0	4	4 (see comments)	5	2 (see comments)	2	2
Cost	3 (see comments)	2	0	3 (see comments)	4 (see comments)	4	2	4	2
Ethical issues	1 (see comments)	4	0	1 (see comments)	4 (see comments)	1	1 (see comments)	1	4
Legal issues	3 (see comments)	3	0	1 (see comments)	3 (see comments)	0	0 (see comments)	1	3
Liability	3 (see comments)	4	0	4 (see comments)	3	2	0 (see comments)	2	3
Others	-	-	2 (see comments)	-	3 (see comments)	-	-	-	-
C									
Impact on care	2 (see comments)	0	0 (see comments)	2	3	1	2	1	4
Patient's monitoring	4 (see comments)	3	0 (see comments)	2	3	2	1 (see comments)	1	4
Ressources	4 (see comments)	4	0 (see comments)	4	4	3	2 (see comments)	3	3
Extra-time	4 (see comments)	4	0 (see comments)	5	4	3	2 (see comments)	2	3
Extra-test	4 (see comments)	4	0 (see comments)	3	4	4	2 (see comments)	2	4
Data collection	4 (see comments)	5	0 (see comments)	2 (see comments)	4	4	2 (see comments)	1	4

Questions	HCP1	HCP2	HCP3	HCP4	HCP5	HCP6	HCP7	HCP8	HCP9
Part of analysis	1 (see comments)	4	0 (see comments)	4	5	3	4	3	5
Patients' disengagement	1 (see comments)	3	0 (see comments)	4 (see comments)	1	4	3	1	3
Any other	-	-	None	-	None	-	-	-	
D									
Yes	x (see comments)	x (see comments)	x (see comments)	x In selected patients	x (see comments)	x (see comments)	x (see comments)	x (see comments)	x (see comments)
No	-	-	-	-	-	-	-	-	-
Other concerns	No	No	No	-	-	-	-	(see comments)	-
E									
Yes	x	x	x	-	-	x	x	x	x
No	-	-	-	x	x	-	-	-	-
Why	(see comments)	(see comments)	(see comments)	(see comments)	(see comments)	(see comments)	-	(see comments)	(see comments)
F									
	E/S, NC data	Detailed info on E&S	(see comments)	Examples & other colleagues' experiences	All available info	(see comments)	Effectiveness & Safety in target population	Data and experts' opinion	Tox. + Ph1 & 2
G – any other concerns?									
Yes	-	**-**	**-**	**-**	(see comments)	**-**	**-**		**-**
No	x	-	x	-	-	-	-		x

Questions	**HCP10**									
A										
	0 (see comments)									
B										
Efficacy	0									
Effectiveness	2									
Short-term S.	0									
Long-term E.	3									
Long-term S.	4									
Cost	- (see comments)									
Ethical issues	0 (see comments)									
Legal issues	- (see comments)									
Liability	0 (see comments)									
Others	-									
C										
Impact on care	1									
Patient's monitoring	2 (see comments)									
Ressources	3 (see comments)									
Extra-time	1 (see comments)									
Extra-test	- (see comments)									
Data collection	0									
Part of analysis	0									
Patients' disengagement	0 (see comments)									
Any other	-									
D										
Yes	x (see comments)									
No	-									
Other concerns	-									
E										
Yes	x									

Questions	**HCP10**								
No	-								
Why	-								
F									
	N; E/S; reco. for use & FU								
G – any other concerns?									
Yes	-								
No	-								