Workshop report: Patient uncertainties and exploring the ethical and legal considerations of MAPPs

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1. Introduction

In order to continue the instructive discussions of the ADAPTSMART programme of work, on January 17th 2017, the ADAPT SMART consortium hosted a multi-stakeholder workshop on '**Patient uncertainties and exploring the ethical and legal considerations of MAPPs***',* bringing together two work streams - D3.04 and D3.08. This workshop comprised of 40 representatives including; European regulators, Health Technology Assessment (HTA) bodies, the pharmaceutical industry, patient organizations, health care professionals, and academics.

2. Objectives

- To share an understanding of the ethical and legal aspects of MAPPs between all major stakeholders, with a special focus on patients, healthcare professionals and medicines developers (industry), under the proposed MAPPs pathway.
- To jointly explore potential recommendations to address the legal and ethical concerns for major stakeholders, and uncertainties of patients and healthcare professionals, under MAPPs, and any impact those solutions may have.

3. Workshop Summary

The workshop was opened by Alicia Granados (Sanofi Genzyme) who provided a background to the MAPPs concept and a status report. Paul Robinson (MSD) provided an industry perspective on the reality of early access schemes, and Anne-Sophie Lapointe (EURORDIS) provided a patients' perspective.

Participants then joined one of three parallel breakout groups for the day. Participants considered one for three hypothetical scenarios – one oncology, one paediatric rare disease, and one gene therapy. They were asked to explore uncertainties that may impact on an individual patient and any ethical and legal barriers to implementation of MAPPs. As a follow up, participants were presented with additional possible scenarios to consider, such as a negative shift in benefit: risk balance following further data collection, or a negative shift in cost effectiveness such that continued access to the medicine is placed in jeopardy.

4. Outputs

<u>Legal Concerns</u>

- In general, no new legal barriers were identified with respects to MAPPs - primarily because products under MAPPs will have achieved a marketing authorisation (MA) - having met the regulatory standards of quality, safety, efficacy, and positive benefit: risk, as seen today.

- In terms of legal risks, whilst it is theoretically possible that there may be a higher risk of litigation in the event of a change in benefit: risk or efficacy, the generally accepted principles of standard legal defence would apply, as is the case today.

- Provision of adequate information to patients, that includes the known risks and uncertainties, followed by consent, was considered essential and a key element to defending any legal claim (see below).

Ethical Concerns

Consent to treatment

- This was seen as a critical element to the successful implementation of MAPPs and mitigation of legal and ethical risks. Whilst there was no consensus that consent should be in the form usually associated with clinical trial, it was considered critical that a written record was made of the issues discussed between patients and HCP, which should include the known and anticipated benefits, risks, and associated uncertainties. The possibility of product withdrawal should be expressly discussed, in the event of a shift in the benefit: risk balance, or for commercial reasons.

- Whilst surgeons are used to providing information and documenting consent to a surgical procedure, physicians are less so; training and tools may be needed to enable this. Similarly, prescribers are rarely aware of the MA status of a medicine (i.e. conditional MA) - as such this area needs better, and more structured education for physicians and prescribers regarding the emerging evidence base.

Use of registries as post authorisation tools

- In general, there was support for the proportionate use of post-authorisation safety and efficacy assessments, which may include registries. However, there was no support for making entry into a registry a condition of receiving the medicine. Whilst it is highly desirable for medicine usage to be supervised and data collected - and this may be particularly important in a MAPPs context where patient numbers are small - the tension between a patients' right to consent (or otherwise) and the need for society to collect additional data did not justify making it an absolute requirement for access.

- The distinction was noted between registries which collect routine clinical data but in a standardised form, from a structured follow-up program which mandates investigations such as scans, blood tests which are not clinically indicated, and should form a post authorisation clinical study. Questions remained as to how much extra data collection could be expected from patients, beyond routine clinical care, before it becomes an interventional clinical trial (requiring written consent).

- There was limited discussion on questions of data ownership and access. There was a preference for longitudinal disease-based registries, rather than product-based registries. Making use of existing European networks and registries to support MAPPs rather than creating bespoke registries per product, was strongly supported.

Equity of Access

- Variation in the availability of a medicine from country-to-country was seen as a substantial ethical problem, although the legality of country or regionally specific decision making is established and was acknowledged. Likewise, whilst current

cross-border legislation allowed patients to travel, it did not facilitate access to treatments that were not available in one's home country.

- Early dialogue with HTA bodies and national payers was seen as critical to understand how cost effectiveness could be assessed under MAPPs - flexible pricing models were seen as one way forward.

- Early dialogues with patient organisations are also critical for all stakeholders to understand the impact of the new medicine. Patient organisations in particular urged flexibility on the part of industry, HTA bodies and payers, to ensure equitable access across disease status and across MS could be maintained under MAPPs.

- There was an acknowledgment that there would be occasions where a product was no longer commercially viable, or did not demonstrate clinical outcomes that supported its cost effectiveness, so that continued access would cease. To address and prepare for such situations, a strategy should ideally be prepared at launch to address all stakeholders' concerns, particularly those of patients and healthcare professionals, regarding continuity of treatment. In cases of withdrawal due to negative cost-effectiveness assessment, a multi-stakeholder agreement could be envisaged to explore continued access for those patients already being treated.

Information and Patient Education

- Patient access to reliable information was considered key to mitigate patient uncertainties on ethical and legal matters. Information and communication about adaptive pathways and MAPPs, amongst patients and civil society, represents a starting point for many of the above-mentioned themes – it requires a continued dialogue with other stakeholders to ensure ongoing and accurate mechanisms to disseminate information effectively.

- Ongoing patient education in the medicine development pathway was also considered important. There was agreement that informed and educated patients would be more empowered and able to participate as equal partners in shared decision-making regarding the choice of therapy, and this in turn would increase their willingness and ability to comply with ongoing data collection to support MAPPs.