Medicines Adaptive Pathways to Patients (MAPPs): Guiding Principles for IMI2 Projects

1. What are MAPPs?

Please refer to the attached document.

2. Call for action

Medicines Adaptive Pathways to Patients (MAPPs) have the potential to accelerate access to crucial therapies for patients in need and simultaneously generate other benefits for healthcare systems.

The Innovative Medicines Initiative (IMI) is one of the key platforms to develop and test new methodologies and tools that can optimise medicines development, licencing and access pathways. Development of the tools and methodologies that will support MAPPs implementation by IMI projects was prioritised by the EFPIA Research Directors Group.

EFPIA therefore invites SGGs covering therapeutic areas, data & knowledge management and translational safety, and other IMI project teams to consider the following:

- **For new IMI2 projects**: to address the MAPPs enablers described in this document when designing and implementing the project;
- **For ongoing IMI projects**: to identify potential MAPPs enablers and engage in dialogue with EFPIA to allow their inclusion in regulatory science work or policy dialogue.

3. MAPPs deliverables sought in IMI programmes

Through IMI projects EFPIA aims to determine:

- How can efficacy and safety be determined at an earlier stage in medicines development through more efficient data collection of a pre-identified sub-population of responding patients;
- How can data capture and processing using e- and m- technologies be enhanced and used in both pre- and post- launch phases (e.g. patient reported outcomes) and how can standards be secured for access to extensive population databases without compromising security and privacy;
- How can industry, regulators and payers manage post-launch obligations and potential consequences for the real-world use of medicines in adaptive pathways and the continued reassessment of the medicine throughout its lifecycle;
- How can innovation for certain patient groups be supported in future by systematic off-label data collection through tracking methodologies (including patient adherence) and point of care diagnostics;
- How to define business models that secure business and healthcare budget viability and sustainability.

4. Examples of key MAPPs enablers

4.1. Enablers for adaptive development

- Tools for stratifying patient populations e.g. biomarkers, genetic screening, clinical markers;
- Convincing pre-clinical evidence of impact on primary or secondary endpoints (clinical/surrogate);
- Innovative trial design (e.g. adaptive, Bayesian) and modelling & simulation methodologies;

- Iterative benefit/risk methodologies for which assumptions have been aligned with key stakeholder groups (e.g. HTAs, patients, regulators, payers, and industry);
- Processes and technology to ensure collection of Real World Evidence (RWE) quality and reliability;
- Statistical and other methodologies to evaluate multiple sources of targeted datasets (e.g. RCTs, observational studies, RWE) and predictive preclinical tools which demonstrate a positive benefit/risk conclusion at iterative time-points (including meta-analysis of health data bases);
- Sustainable databases, health registries and monitoring systems required for the MAPPs evidence base and new combinations of those.

4.2. Enablers for adaptive licensing

- All above and in addition:
- Safety and risk minimization programmes adequate to balance uncertainty at time of initial registration based on smaller data sets
- Feasibility of collecting more data - follow-on RCTs or any other confirmatory data collection to expand the initial license;
- Processes/procedures for collecting, analysing and presenting further evidence from mixed sources;
- Tools for regulatory reassessment:
    a. Definition of reassessment criteria and the evidence base acceptable to regulators (e.g. periodic benefit risk evaluation report (PBRER)[1], Post-authorisation Safety Studies (PASS)[2] and Post-authorisation Efficacy Studies (PAES)[3]);
    b. Processes to remove medicines from the market that do not confirm a positive benefit/risk balance.

4.3. Enablers for adaptive access (HTA, Pricing & Reimbursement)

- Methodologies that best allow for the incorporation of new data allowing pricing and volume adjustments, both up and down, based on the evolution of the MAPPs' evidence (e.g. adaptive or outcomes based pricing);
- Models of health economic impact assessment of MAPPs in contrast to a traditional pathway, to inter alia test if the assumptions made on pricing/reimbursement are reasonable, and can lead to a favourable value proposition;
- Modelling changes to the HTA/pricing/reimbursement/regulatory protection frameworks to deal with uncertainties at launch;
- Tools for HTA reassessment:
    - Develop or test infrastructure for companies, payers, and regulators to meet the required post-launch obligations of a MAPP;
    - Development and testing of tools/methodologies to evaluate the risk of the potential for broader off-label prescriptions.

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[1] http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2012/12/WC500136402.pdf
[2] http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2012/06/WC500129137.pdf
[3] http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=OJ:JOL_2014_107_R_0001&from=EN