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SCIENCE MEDICINES HEALTH

The Adaptive Pathways pilot: complementing the EMA early access tools

Adaptive pathways workshop- EMA 8 December 2018

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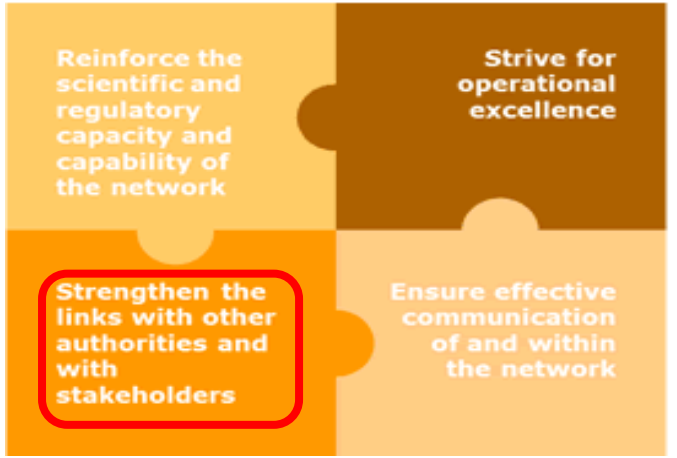
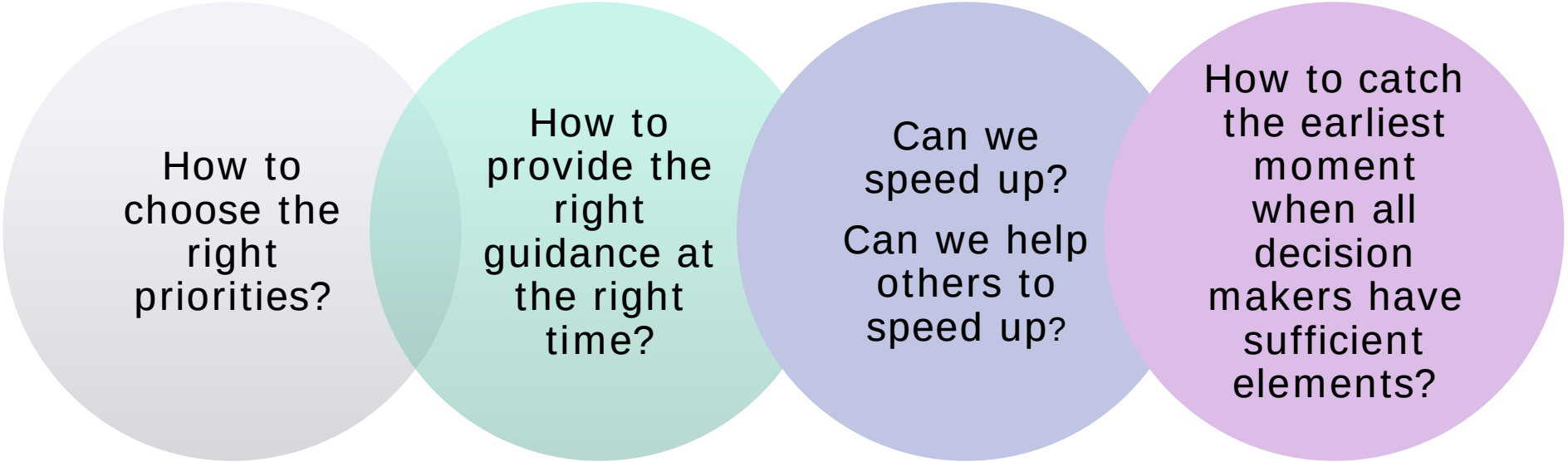


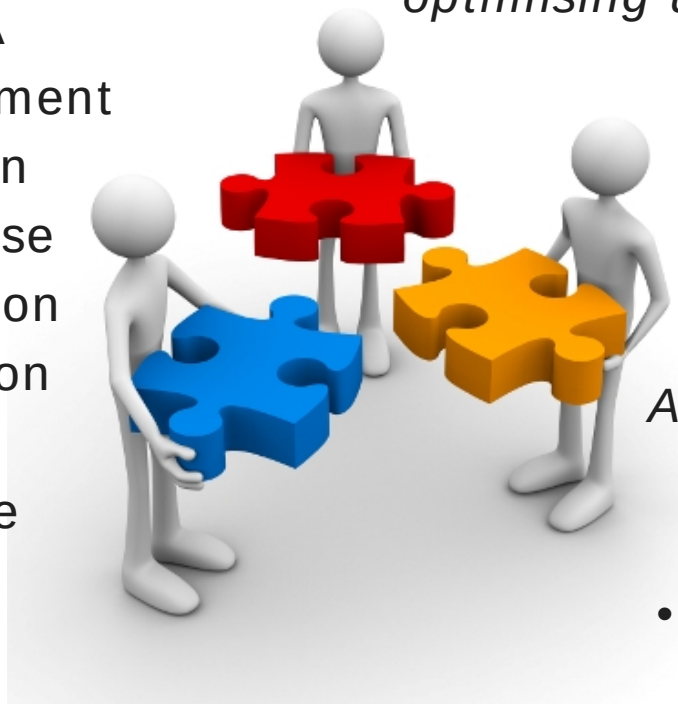
Role of regulators to foster early access



Development support and early access at EMA

Legal tools

- Conditional MA
- Accelerated assessment
- CHMP opinion on compassionate use
- Orphan designation
- ATMP classification
- SME office
- Scientific advice



Development support initiatives

optimising use of existing legal tools

- PRIME
- ITF

Content concept

Adaptive pathways defines the product development route

- Expansion/confirmation
- Involvement of stakeholders
- Use of Real World Data

PRIME - Goal & Scope

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Foster the development of *medicines with major public health interest.*

Reinforce scientific and regulatory advice

- Foster and facilitate early interaction
- Raise awareness of requirements earlier in development

Optimise development for robust data generation

- via frequent SA/regulatory interaction

Enable accelerated assessment

- Facilitated by knowledge gained throughout development
- Feedback of relevant SA aspects to CHMP

Adaptive pathways - Goal & Scope

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Unmet medical need that cannot be met in a **timely way with conventional development approaches**

Expansion /confirmation: acquisition of further data

- Finding the earliest time point where sufficient data have been collected for all decision makers, in a given population

Multistakeholder discussion

- Input on development plan: suitability, feasibility, plausibility
- Trust

Use of observational data for decision making

- Added value of well-planned pharmacovigilance
- Knowledge of B/R and value in clinical practice
- Maximise use of all available data sources

Timely access balances:

- Optimisation of the data package
- Efficient R&D process
- Robust data collection to inform on actual use and effects

Not all medicines are suitable for adaptive pathways

The experience in the pilot and the format of this workshop

3 topics from the AP pilot report:

- Patients/HCP;
- RWD challenges;
- stakeholders involvement

10 civil society issues to be discussed within topics and the floor discussion

The briefing book presents the experience via anonymised product examples.

Presentations from the speakers will introduce the topics

Commenters from stakeholders groups will open the floor discussion

1 hr floor discussion to hear your views!

Topic 1: Patient and HCP involvement

Patients:

- product prioritisation
- risk acceptability and management,
- endpoints relevance, quantifiable clinically meaningful response
- registry feasibility, recruitment in trials and registries

HCP:

Limited experience in the pilot. Input should be sought e.g. on SOC, trial/registry feasibility, quality of existing data sources

Topic 2: RWE/observational evidence

RWD is an **opportunity to reduce uncertainty**

- Capture real clinical practice, adherence, compliance
- Capture rare, long-term events (safety and/or efficacy)
- *All* subjects could be followed for long term outcomes
- Less costly way to monitor long-term outcomes – important for degenerative and chronic diseases
- Useful for geriatrics and paediatrics
- Useful to validate biomarkers
- Personalised medicine: capture more strata than RCT

Not all endpoints are suitable
Consider effort *vs.* need

Registries to supplement RCTs: an oncology scenario

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Benefit/Risk balance in RCT interim analysis (IA)	MA route at IA	Uncertainties at MAA	Vehicle to address	Timeline of in-market RWD
Compelling	**Full MAA at IA**	In-market safety surveillance (per any marketed product)	RMP (+registry?)	PhV reporting
Efficacy demonstrated, additional safety required	**CMA at IA**	Safety database not adequate or additional safety concerns	Global registry: Early Access Program with protocol and database	X months of data collection to convert to full MAA
Promising efficacy, safety data acceptable	**CMA at IA**	Additional OS data	Global registry: In-market collection of RWD within registry	Y months of data collection to convert to full MAA
Inconclusive	**Await final analysis**	Unknown	Global registry (?)	TBD

Topic 3: Downstream stakeholders involvement

Illustrative questions for stakeholders

- Discussion/selection of potential development routes in presubmission.
- Define minimum dataset. Checkpoints where to reevaluate if more conservative path should be taken depending on results
- Is the surrogate EP acceptable for decision making on B/R, value, price?
- Will the B/R reevaluation impact value, price? Exit strategies?
- Is “adaptive pricing” feasible? What data would be needed?
- Do registries already exist which are acceptable to draw conclusions?

Stakeholders answer according to their remit

Topics raised by civil society

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1. Definition of “unmet need”
2. Methodological challenges of real world data for decision making
3. How to ensure that post marketing obligations will be honoured
4. How to ensure appropriate utilisation/prescription
5. What if expectations not met/Are there exit strategies?
6. Involve patients in the discussion
7. Will patients be exposed to increased risk?
8. Is there a risk of lowering the regulatory requirements?
9. Is affordability a criterion to be taken into account?
10. Will AP apply to all MA applications at a later stage?

Adaptive pathways offers the opportunity to
fill gaps in the decision chain
and, ultimately,
patient access.

Thank you for your attention

A special thanks to all who have worked to explore this concept and its feasibility