Adaptive Pathways: Can we build better links between decision makers?

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Why adaptive pathways?
Adaptive pathways offers the opportunity to avoid a situation where a conditional MA is granted but a decision on value and reimbursement cannot be reached without collection of additional data. It is not for all medicines:

**Iteration – RWD – Downstream decision makers**

Real-world data used to **complement** RCTs in cases where conduct of trials is difficult

**Standards** for regulatory decision making remain the **same**: the amount of uncertainty acceptable in a marketing authorisation decision correlates to the degree of unmet medical need in the target population
An example of adaptive pathways development

Conditional approval scenarios:

- Early Proof of Concept
- Phase 3 RCT
  - In early symptomatic patients
- Interim analysis when x% reach end of treatment
- Primary analysis at end of treatment
- Full Approval symptomatic early disease
- Conditional Approval symptomatic early disease
- RCT in pre-symptomatic patients (Clinical Endpoint)
- OLE to Clinical EP
- RCT in pre-symptomatic patients (surrogate EP)
- Approval in pre-symptomatic patients

Validation Surrogate EP

No surrogate exists

OR

Possible surrogate Endpoint
Pilot Learnings (the glass half full)

• AP was a learning exercise with wide acceptance criteria

• The adaptive approach can take place within the existing regulatory tools and processes.

• A **prospective, life-span** discussion of product development with different stakeholders is **possible and desirable** in cases where decision making could be delayed by suboptimal planning.

• Choose clear-cut, methodologically reliable, **actionable** endpoints for decision making (for B/R, value, pricing)

• There is **added benefit in well-planned post authorisation activities**.

• Input in peri-approval advice should be explored

• **Trust** is important (in safe harbour and in capability to conduct the studies).
Pilot Learnings (the glass half empty)

- **Product selection** vs limited resources. Selection criteria and meaning of “need”: clinical, public health, cost reduction(?).

- Increase **patient participation** (product selection, risk management, feasibility, ethical aspects, support enrolment in trials and registries).

- Making the most use of available RWD data, feedback/access to other stakeholders for their decision making.

- Prescription controls, entry and exit schemes and data gathering for pricing commensurate to performance can only be answered with *payer’s* input on feasibility/desirability (NB no price discussion!!).

- **Resource** intensive procedure: felt particularly by HTAs. Challenge to bring right stakeholders with right expertise into the discussion.
Next steps (1): Integration in Scientific Advice

To make the process sustainable and utilise a well-tested and established framework, future submissions will be treated as parallel HTA/SA advice requests, granting an additional presubmission meeting to discuss the early draft:

- Established framework for patient participation
- More sustainable HTA input
- Publication of statistics and report annually as for other SA
- Two additional presubmissions for SMEs
- Other stakeholders (payers, FDA, WHO) may be invited where relevant
Next steps (2): Consult stakeholders at workshop

Workshop 8 December to discuss with stakeholders the areas for further discussion identified in report:

1. Patients and health care professionals involvement
2. RWD methodological challenges
3. Payers and HTA conditions of participation

Topics raised by civil society will also be discussed.

Briefing book available on EMA website and workshop will be broadcast