EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

STAMP questionnaire on Adaptive Pathways Summary of Results (with a post Dutch presidency meeting flavour)

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Background

Following the STAMP meeting on Oct 2015, a Questionnaire was sent to STAMP, EUNetHTA and CAPR members

It investigated feasibility aspects of the Adaptive Pathways approach at Member State and stakeholder level

Results were received up to 25 February 2016

On March 1-2 2016 the Dutch presidency meeting on Innovation to patients brought togehether many of the respondents for further discussions on the issues.

Adaptive pathways is a scientific concept that makes better use of the existing regulatory framework. Goal is to address unmet need.

EU regulation permits:

- Initial Marketing Authorisation and subsequent variations
- Conditional Marketing Authorisation
- Post-authorisation studies, including observational research

- Scientific Advice (including patient representatives)
- Parallel Scientific Advice with Health Technology Appraisal

Interaction between the three "worlds" (regulators, payers, HTA) and enabling strategies

To realise the benefit and smooth the road to access, other stakeholders need to be involved, for planning and implementation. **No benefit to a 'regulator-only' advancement.**

- product prioritisation in a world of limited resources– Who should select the products?
- Selection criteria and meaning of "need" (clinical, public health)
- Entry and exit schemes
- Prescription controls
- Feasibility/desirability of post-authorisation data acquisition vs other risk sharing schemes. Making the most use of available data

Adaptive Pathways

Support the definition of pathway of product development and (potential) earlier access to medicines through early dialogue involving all stakeholders (regulators, HTAs, payers, patients…).

Criteria

1. An **iterative** development plan: start in a well-defined subpopulation with unmet medical need and **expand**, or have a Conditional Marketing Authorisation, maybe on surrogate endpoints and **confirm**.

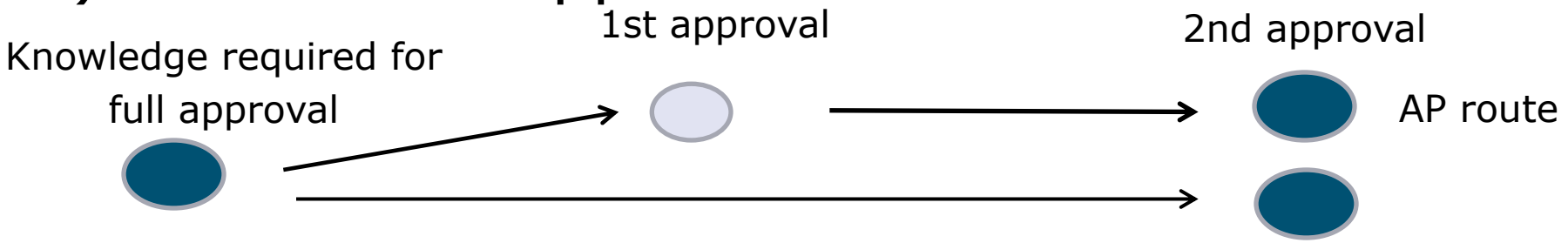
2. **Real World Data** (safety and efficacy) can be acquired to supplement Clinical Trials, e.g. through well planned registries

3. Input of all **stakeholders**, particularly HTAs, is fundamental

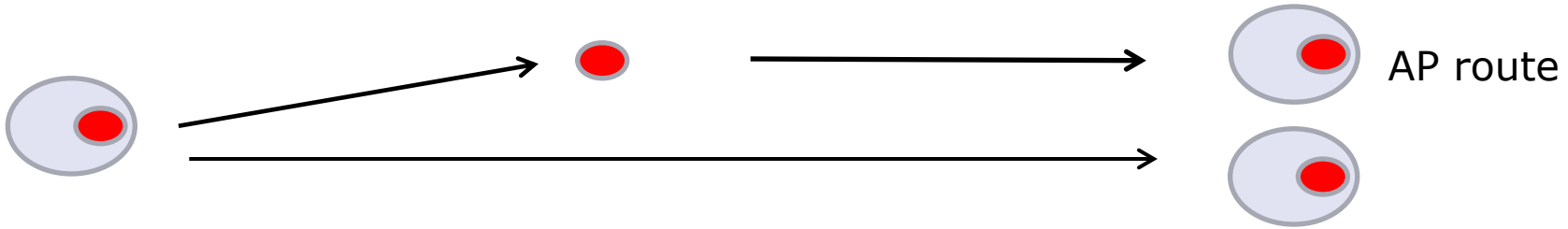
Is the available regulatory toolset fit for purpose? Does the potential of real world data change the licensing paradigm?

The Adaptive Pathways concept

1) Conditional approval scenario



2) Expansion of indication scenario



Prescription control to initially licensed population

Influenced by: frequency of disease, precision of diagnosis, availability of therapeutic alternatives, price and reimbursement, point of dispensing (hospital, specialised doctor), societal pressure and expectations.

Achievable?

- Not for private prescription,
- facilitated by single IT prescription system which includes diagnosis
- balance resources required to achieve the control and cost of the drugs

How?

- all treated patients in registries (cost, plausibility, feasibility of registry).
- model on the traceability schedules in place for medicinal blood products?

Clear communication in SmPC

improve sections 4.2 and 5.1 of the SmPC so that the indicated population is unequivocal:

- kind of pre-treatment,
- combination with other medicines,
- treatment duration or number of cycles,
- the investigated population
- transferability to other populations.

ELECTRONIC PRESCRIPTION AND RW DATA CAPTURE

resource intensive activities.

monitoring the effectiveness of the prescription control measures.

The investment in infrastructure and administration should be considered.

For products with multiple indications, these should be distinguishable.

A clear methodology and harmonisation/interoperability of systems is important. These systems should also be interlinkable to registries so that the data for the prescription can be utilised for effectiveness analyses

Data ownership and accessibility by third parties should be considered, particularly with public funding

Some RWE examples in AP applications

- Registries: natural history of the disease, SoC, resource utilisation, adherence to treatment, effectiveness, long-term outcomes, drug utilisation, PROs, time to treatment failure..
- Single arm studies for rare diseases compared with outcomes inferred from disease registries;
- Open label salvage studies to obtain expansion of the indication;
- Efficacy and safety data from early access/compassionate use to supplement RCTs in small populations;
- Linking drug registries to risk-sharing schemes for reimbursement (pay per performance, annuity payments…)
- Investigation of non-serological outcomes for vaccines

RWE acquisition should be designed to address justified uncertainties emerging during the evaluation process

Post MA data: PAY PER PERFORMANCE- RISK SHARING

A managed entry approach is essential to the AP paradigm

resource investment – minimum impact on clinical practice

Must be designed to be useful to patient and prescriber, correctly communicated

clear-cut ACTIONABLE performance measures should be chosen (eg Sustained Virologic Response, survival rates) for re-assessment of B/R value and P&R

Risk-sharing price reductions are simpler to implement and easier to negotiate solution for drugs with marginal benefit :not affect practice of treatment and low burden of additional data collection, but miss the opportunity of RWD collection and B/R refinement.

Little experience on data collection from compassionate use programs. Opportunity to use better?

A new way of working

cross ministerial work and liaison with other national/international bodies some of which have never yet been involved. A revised system of the process of the decision making may be required.

International collaboration is a key for smaller countries

request the views of patients/patient organisations on unmet need (prioritisation) and potential for higher uncertainties

Sustainability, greater challenges for smaller NCAs

Create a platform to exchange documents and information to maximise opportunity to align the requirements (confidentiality arrangements between authorities) and the processes

Results of AP survey to companies

Adaptive Pathways concept fits well within the EU regulatory landscape

No strong concerns in terms of **data protection** were expressed

global acceptability of the supplementation of clinical trials with Real World Data?

difficulties in **engaging HTAs** in a sustainable way were recognised: further support to their engagement was advocated.

Payers did not participate: unpredictable acceptability of the development plan/risk

establishment of **confidentiality arrangements** between authorities to exchange documents.

If it’s worth it- we can support it

What? unmet need, public health need

Most instruments are in place

Identify areas with quick wins (exchange of documents) and longer term objectives (efficient reliable RWD capture systems)

In summary

Adaptive Pathways offer an opportunity to prospectively shape and optimize post-authorization data acquisition, with actionable outcomes that fulfil the need of several stakeholders. This also avoids exposing patients to redundant or duplicated trials.

The areas of need may be defined by a public stakeholder consultation, including patients and Health care professionals (potential proposal from Dutch presidency)

A call for expression of interest to participate to the discussions (actively- as observer) is renewed

Further efforts to support participation and refine processes are ongoing within the wider framework of regulatory/HTA interaction