

Executive Briefing #1

Strategy Development for Early Marketing Authorisation and Rapid Market Access

David Schwicker, January 2017

Early access programs, legal tools and initiatives aim to foster patients' timely access to medicinal products that address unmet medical needs, i.e. that offer a major therapeutic advantage over existing treatments, or benefit patients with no treatment options, or are of a major interest to public health. The increased regulatory focus on adaptive and accelerated development pathways offers interesting opportunities for prospective early market authorisation and more rapid market access.

Developers and manufacturers with potentially transformative medicines in early development should consider explicitly formulating early access strategies to inform, complement and enhance strategic thinking on early benefit/risk and value demonstration, and the life-cycle planning of evidence generation.

The EMA's Support for Early Access and the FDA's Expedited Programs provide the regulatory framework for early access in Europe and the US. The programs are discussed in detail here: <https://www.orphastrategy.com/early-access/>

Within this regulatory context, early access strategy is created through innovative thinking, discussion and development of the following key elements:

Unmet Medical Need

An essential element for early access eligibility, unmet need is understood and comprehensively documented from a solid foundation of knowledge in epidemiology (rarity), natural disease history, diagnosis, management guidelines, standards of care, real-world effectiveness, pivotal research and, particularly, insights on patient preferences and patient-relevant outcomes.

Promise

A medicine's eligibility for early access is based on its intention to treat a serious condition and a credible promise of significant improvements in clinical benefit and patient-relevant outcome(s) over existing treatment.

Very early in development, evidence of the potential to address unmet medical need may be demonstrated in a nonclinical model, mechanistic rationale, or pharmacologic data. Later, preliminary clinical data should indicate the drug's potential.

Orphan Feasibility

Many products fulfilling the criteria for orphan designation will also qualify for early access. Therefore, the feasibility of orphan drug designation should be evaluated as part of any early access strategy, and vice versa.

Coordinated early access and orphan designation strategies are particularly crucial if a medicine has the potential for significant benefit in both rare and non-rare conditions or multiple orphan subsets.

Value

Given that it is not rational to commit resources to accelerated marketing authorisation if timely market access cannot be achieved, planning for early value demonstration is an essential component of early access and should include:

- Comprehensively documenting the burden of disease and unmet needs of patients
- Contextualising the potential benefits and value the new medicine will create as compared to existing treatments in an early value proposition strategy
- Conceptualizing study designs and endpoints that are relevant and actionable for HTA as well as regulatory decision-making

Real-World Evidence

Real-world evidence (RWE) has matured and its application in the regulatory setting offers unprecedented opportunities. Stakeholders are increasingly focussed on expanding the toolbox for evidence generation, with pragmatic and real-world studies complementing RCTs. Observational studies should ask the right questions, be underpinned by sound methodology, adhere to current guidelines, and provide a design and endpoint(s) that are relevant and actionable for regulatory and HTA decision-making.

Innovative adaptive, novel and non-conventional pathways utilizing RWE to shorten and accelerate development should be considered in early access strategy, particularly for orphan drugs and in rare diseases, where the collection of data by traditional routes is difficult.

This should include seeking early dialogues (before/during proof of concept) with either multiple HTA agencies or joint agency/HTA scientific advice to discuss potential adaptive pathways and study design options, with the objective of ideally agreeing on one set of studies that will address the requirements of both regulators and HTAs. A number of initiatives facilitate open and informal presubmission discussions in a “safe harbour” approach (i.e. without impacting the regulatory process). These include, for example, the EMA’s PRIME and Adaptive Pathways and EUnetHTA’s Joint Action 3 (Strand A – Early Dialogues). Further information: <https://www.orphastrategy.com/real-world-evidence/>

Patient Centricity

Patient-relevant outcome(s) are central to demonstrating unmet need and the significant benefit of transformative drugs in addressing this need.

The rising influence of patients and patient representatives and their active participation in decision-making emphasises patient preferences, which are increasingly relevant in both benefit/risk and value judgements. Patient-centered evidence is therefore a cornerstone of early access, and should be integrated and pre-planned early on in a life-cycle approach throughout the development process, including post authorisation.

Knowledge Gaps

Early in development there will be a number of caveats, uncertainties and unknowns that may impact strategy development and decision-making. It is recommendable to proactively identify and address the most crucial missing information in a gap analysis.

Benefit/Risk Appraisal

Under consideration of the intelligence and thinking assembled on the above key elements, early access strategy balances the potential benefits of several years of earlier marketing authorisation and market access against the risks inherent in demonstrating relevant improvements in patient-relevant outcome(s) and/or of a relevant effect size in surrogate endpoints for accelerated authorisation earlier in the development process (mostly in Phase II). Additionally, the feasibility of generating comprehensive and confirmatory evidence post-authorisation, and the demands of early value demonstration compared to existing treatments are considered. This results in a benefit/risk appraisal for each combination of targeted indication and product in early development.

Implementation and Rolling Reviews

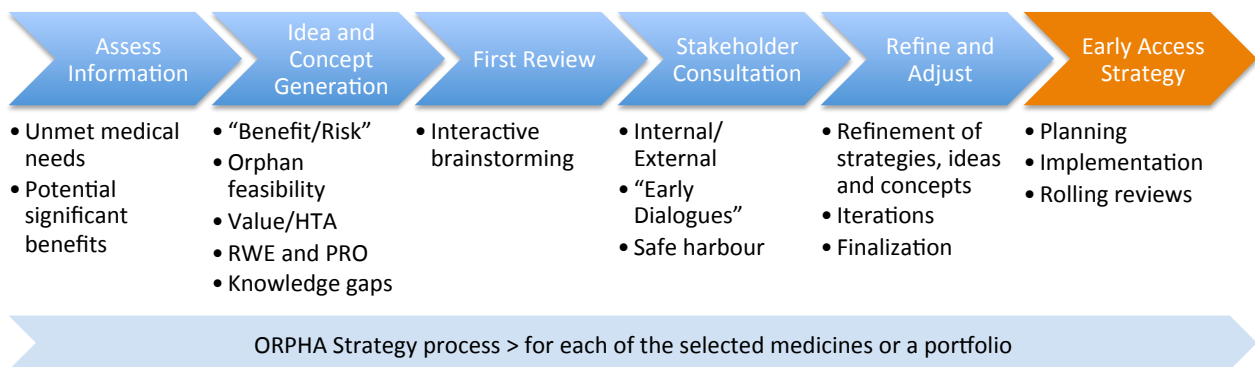
Initial early access strategies, often in the form of conceptual presentations or white papers, go through a number of iterations, involving tests, interactive reviews, brainstorming sessions, internal stakeholder consultations, selected external stakeholder meetings, and refinements, until the finalized early access strategy for each transformative medicine is ready for implementation, i.e. integration into the clinical development and evidence generation plans. Rolling reviews of the strategy are performed as new key information is learned and generated.

Collaborative Strategy Development

In rare diseases and for transformative medicines, early access strategies, benefit/risk and value demonstrations are often uncharted terrain, requiring highly specific expertise and experience. ORPHA Strategy's principal, David Schwicker (<https://www.orphastrategy.com/biography/>), has industry consulting expertise spanning more than 25 years, and has gained a unique understanding of how early access programs, initiatives, and rare disease and orphan drug incentives can benefit a client's transformative medicine to prospectively accelerate marketing authorization and market access. To this is added a focus on innovative development pathways that emphasise the use of real-world evidence.

ORPHA Strategy Consulting wishes to develop long-term partnerships with clients, for an individual compound or at the portfolio level. Every potential early access strategy is different. Success thus originates through collaboration, by merging our specific expertise with that of the client.

We pride ourselves on our responsiveness to clients' needs and our approach will flexibly adapt to individual requirements. This favours an iterative and highly interactive strategy development process:



Further Information

Thank you for your interest. To start a strategic discussion on early access, please contact:

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