

Executive Briefing #6

Early Access Programs – an Overview for the United States (FDA) and Europe (EMA)

David Schwicker, January 2017

The US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have recognised that paradigms of drug development, which are feasible for common diseases, may not be feasible for **rare diseases** and that **transformative orphan, specialty and advanced therapeutics** often **defy traditional regulatory routes**.

The **EMA's Support for Early Access** and the **FDA's Expedited Programs facilitate and accelerate** development and marketing authorisation with the aim to foster patients' **timely access** to new medicines that address **unmet medical needs**. The focus of early access, both in the United States and Europe, is on **life-threatening and debilitating diseases** with a **major impact on quality of life**, and on medicines with a **credible promise of significant improvements in clinical benefit and patient-relevant outcome(s)**.

While the FDA's programs are well established, certain of the EMA's early access tools have been launched more recently. These innovative initiatives emphasise **early dialogues**, the involvement of **multiple stakeholders, iterative development** in a **life-cycle** approach, and an **expanded toolbox** for evidence generation, with **pragmatic and real-world studies** complementing RCTs in areas where the collection of data via traditional routes is difficult.

The **key features** of early access are notably similar in both jurisdictions:

- **Enhanced early agency interaction** to identify potential for accelerated development.
- **Dedicated agency resources**, including access to senior management.
- **Reinforced scientific advice**, early and frequent dialogues on study design, protocol development, surrogate and intermediate clinical endpoints, post-authorisation, pragmatic and real-world studies, patient- and HTA- relevant endpoints, rolling and priority review, accelerated assessment and approval.
- **Earlier marketing authorisation**, allowing for a more rapid pace of drug development, involving fewer, smaller, shorter clinical trials and on the basis of less complete data. Comprehensive evidence generation post-authorisation within an agreed timeframe.
- **Earlier market access**, facilitated through a centralised compassionate use opinion by the EMA (CHMP), for unauthorised products, aimed at harmonising the conditions of use, distribution and the target population across the EU.
- **Accelerated review** of the marketing application, reduced assessment timelines.
- **Orphan drug designation**, providing access to a number of incentives.

There is substantial **crossover** in terms of objectives and features between the programs and they can be used in **combination**. For example, a product eligible for fast track in the US may be eligible for accelerated approval and priority review. In Europe, a medicine benefitting from

PRIME support may also qualify for conditional marketing authorisation. Additionally, drugs benefitting from early access are those eligible to the **EMA centralised procedure** and a **single marketing authorisation**.

Key Features	FDA Expedited Programs	EMA Support for Early Access
Enhanced Early Agency Interaction	Fast Track Designation <ul style="list-style-type: none"> frequent interactions assess potential for alternate trial design, endpoints, rolling review and accelerated approval 	PRIME (Priority Medicines) <ul style="list-style-type: none"> “early dialogues” to identify potential for accelerated development, AA and CMA Adaptive Pathways (AP) <ul style="list-style-type: none"> iterative, life-cycle development concept pragmatic trials and real-world evidence supplement RCTs early involvement of stakeholders (patients, HTAs)
Dedicated Agency Resources	Breakthrough Therapy Designation <ul style="list-style-type: none"> dedicated cross-disciplinary project lead senior management access shortened development program 	PRIME <ul style="list-style-type: none"> early rapporteur appointment dedicated EMA contact person
Earlier Marketing Authorisation / Market Access	Accelerated Approval <ul style="list-style-type: none"> based on surrogate/intermediate clinical endpoints rapid clinical development confirmatory trials post-marketing 	Conditional Marketing Authorisation (CMA) <ul style="list-style-type: none"> on the basis of less complete clinical data comprehensive evidence generation post-authorisation Compassionate Use Opinion (CHMP before MA/CMA)
Reinforced Scientific Advice	Fast Track Designation Breakthrough Therapy Designation Accelerated Approval Parallel EMA/FDA scientific advice (PSA)	PRIME and Adaptive Pathways Joint scientific and HTA advice Registries Initiative - “late dialogues” on real-world evidence Parallel EMA/FDA scientific advice
Accelerated Review of Marketing Application	Priority Review Designation <ul style="list-style-type: none"> assessment within 180 days (300 days standard) 	Accelerated Assessment (AA) <ul style="list-style-type: none"> maximum 150 days (210 days standard review)
Orphan Drug Designation	Medicine intended to treat a disease affecting fewer than 200.000 people in the US <ul style="list-style-type: none"> 7 years marketing exclusivity tax credits for clinical testing and grants common EMA/FDA application for orphan designation 	Drug addressing unmet medical need in a rare disease with a prevalence of not more than 5 in 10,000 <ul style="list-style-type: none"> 10 years marketing exclusivity centralised procedure orphan specific scientific advice reduced fees common EMA/FDA application for orphan designation

Early access is applicable to both **orphan and non-orphan medicines** in both jurisdictions, although the programs are more accepted for orphan drugs. Orphan drug designation is not an early access tool *per se*, and orphan medicines do not automatically qualify for accelerated procedures. Nevertheless, orphan drugs are highly likely to be eligible for early access. Therefore, the **feasibility of orphan designation** should be considered as part of any early access strategy, and equally, the potential benefits of early access should be considered as part of the decision to seek orphan designation.

Additionally, there are several **EMA/FDA collaborations** with the potential to speed up access:

- **Parallel scientific advice (PSA)**, due to limited resources, the scope of this program is limited to potential breakthrough products in diseases with little experience, including orphan drugs and fast track products in the US.
- **Common application for orphan designation** of the same medicinal product for the same use in both jurisdictions with a single form for the EMA and FDA.
- **Rare diseases cluster**, aimed at boosting medicine development for rare diseases. The agencies will exchange experiences and best practices on topics including trial design, endpoints, development support, risk management strategy, and post-marketing study design, in particular in the context of early access mechanisms.

It should be noted that early access **does not alter** the current FDA **standards of approval**, nor the EMA's data **quality standards** and **risk/benefit basis**. The agencies will review the full data submitted to determine whether drugs are safe and effective for their intended use before accelerated and conditional approval for marketing. Acceleration is justifiable only where the **benefit to public health** of the immediate availability on the market outweighs the **risk** inherent in the fact that additional data are still required.

The above table provides an overview of the **EMA's Support for Early Access** and the **FDA's Expedited Programs** and represents the **current regulatory context** – for Europe and the United States – within which an **early access strategy** for an innovative medicine is developed.

Further Information

Further information on current early access tools, programs, and initiatives is available at:

<https://www.orphastrategy.com/early-access/>

EMA Support for Early Access:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000856.jsp&mid=WC0b01ac0580b18c78

FDA Expedited Programs:

<http://www.fda.gov/forpatients/approvals/fast/ucm20041766.htm>

About ORPHA Strategy Consulting

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**.

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

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