Orphan Drug Development Guidebook

Building Block I405

This document defines the content of the Building Block created for each identified tool, incentives, initiative or practice introduced by public bodies or used by developers to expedite drug development in Rare Diseases (RDs).

ITEM	DESCRIPTION
Building Block (BB) Title	National programs for early access
References	USA: https://www.fda.gov/news-events/public-health-focus/expanded-access https://www.fda.gov/media/85675/download Europe: http://www.hma.eu/fileadmin/dateien/Human_Medicines/01-About_HMA/Working_Groups/Timely_Access/2018_09_CUP_27-6-18.pdf
Description	Sometimes called "compassionate use", expanded access is a potential pathway for a patient with an **immediately life-threatening condition** or **serious disease or condition** to gain access to an **investigational medical product** (drug, biologic, or medical device) for treatment outside of clinical trials when no comparable or satisfactory alternative therapy options are available. Patient access to medicines during their development may be seen as a necessity for those who have a disease with no satisfactory authorised therapies and who cannot wait until their eventual approval. Clinical trials (CT) offer access to medicines for patients while high quality knowledge on the effects and safety of medicines is produced. However, CT are not always available everywhere and/or the trial may not be intended to include all patients. In the **USA**, expanded access refers to the use of an investigational drug when the primary purpose is to diagnose, monitor, or treat a patient's disease or condition rather than to obtain the kind of information about the drug that is generally derived from clinical trials. FDA has a long history of facilitating expanded access to investigational drugs for treatment use for patients with serious or immediately life-threatening diseases or conditions who lack therapeutic alternatives.

	Under FDA's current regulations, there are three categories of expanded access: • Expanded access for individual patients, including for emergency use (21 CFR 312.310) • Expanded access for intermediate-size patient populations (generally smaller than those typical of a treatment IND or treatment protocol — a treatment protocol is submitted as a protocol to an existing IND by the sponsor of the existing IND) (21 CFR 312.315) • Expanded access for widespread treatment use through a treatment IND or treatment protocol (designed for use in larger patient populations) (21 CFR 312.320) In the **European Union** and the EEA, early access programmes are an option for accessing medicines before approval. There are roughly two different ways for using an unauthorised medicine outside a CT: - cohort access (compassionate use programmes, CUPs) under the provisions of the Article 83 of the Regulation (EC) No 726/2004, and - individual access (named patient programmes) under the Article 5(1) of Directive 2001/83/EC. Both CUPs and named patient use are governed by national legislation and rules. The individual NCA decide whether or not they include a regulatory framework for CUPs and named patient use in their legislation. Moreover, the conditions for application and approval of such programs are defined at national level. In addition to national regulations there is a procedure to request the opinion of the CHMP in place under Article 83 of Regulation (EC) No 726/2004 (https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/guideline-compassionate-use-medicinal-products-pursuant-article-83-regulation-ec-no-726/2004_en.pdf). Early access programs have a focus on patient access. However, there may be opportunities to collect real world data to supplement the knowledge base of the product still under investigation.
Category	Regulatory Building Block
Geographical scope	International (European Union and Unites States of America)
Availability	Applicants developing medicines (any modalities) in areas of unmet medical need for rare and non-rare diseases.

Scope of use	Consideration of requirements and need for early access should be prospectively planned in the development program. Engage with individual EU member states or FDA on the requirements – for an EU overview see tables in the link below: http://www.hma.eu/fileadmin/dateien/Human_Medicines/01-About_HMA/Working_Groups/Timely_Access/2018_09_CUP_27-6-18.pdf
Stakeholders	USA: even if the **patient** meet the criteria under the law and **FDA** regulations, the **licensed physician**, the Institutional Review Board (**IRB**), and the **company** all need to agree that expanded access is appropriate for this patient in order to receive the investigational medical product. In addition, there may be costs not covered by third-party payers such as private insurance or Medicare. EU: • Sponsors, • National competent authorities, • Healthcare professionals and health systems, • Patients
Enablers/ Requirements	Individual national competent authorities/FDA may have a specific regulatory framework for early access in their legislation. Often the conditions for application and approval of such programs are defined at a national level.
Output	Patient access in advance of a marketing authorization with the potential to collect real world evidence, as appropriate. In few cases, a reimbursement of the investigation drug is envisaged (i.e., ATU in France, 648/96 law in Italy)
Best time to apply and time window	The tool has its best use later in development when data on the benefits and risks of using the medicines are available and before the product is placed on the market.
Expert tips	Can be a useful way to provide patient access and simultaneously collect real world data to support regulatory decision making e.g. future commissioning decisions. PROs:

	– Fulfilling patient need – Engagement with KOL in the health systems, health systems also gain experience of using the medicine – Potential to collect real world evidence – Reimbursement of the drug costs in few cases CONs: – Different member states have different rules and procedures, may be burdensome application processes – There are financial costs and resources needed (e.g. pharmacovigilance systems) in order to run a scheme and for supplying the medicines to patients