Comparing and Contrasting Early Access Opportunities Across the EU4 and UK

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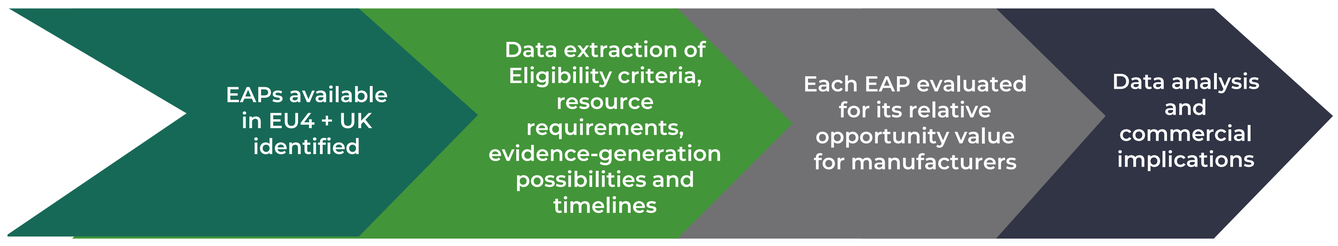
Introduction/Objective

- Early access programs (EAPs) help to give people with life-threatening or seriously debilitating conditions early access to new medicines that do not yet have marketing authorisation. They have clear benefits for patients, healthcare providers, payers and pharmaceutical companies. Manufacturers, for example, can benefit from generating real-world evidence which can facilitate their pricing and reimbursement (P&R) negotiations with payers, and patients can access critical medicines that are not yet commercially available.
- This study aimed to assess the opportunity for manufacturers to access EAPs across the EU4 and the United Kingdom (UK).

Methods

- EAPs available as of July 2022, in the EU4 and UK were identified through secondary research; extraordinary single patient requests were excluded as deemed not commercial opportunities.
- Eligibility criteria, resource requirements, evidence generation possibilities and timelines were extracted for each EAP. (Figure 1)
- The relative opportunity value of each EAP, for manufacturers, was evaluated.

Figure 1: Methods flow diagram



Results

- A total of seven early access programs were identified across EU4 and UK. Of these, France and Italy all had two program options and the UK, Germany and Spain had one.
- Fundamental to all schemes was the condition that the therapy is to treat a life-threatening, long-lasting or seriously debilitating illnesses, which cannot be treated satisfactorily with any currently authorised medicine1 although demonstration of innovation was not a criterion for all.
- Eligibility for the UK EAMs scheme was dependent on obtaining PIM designation and positive EAMS scientific opinion. PIM designation will be issued after MHRA scientific meeting and could be given several years before the product is licensed.
- Most countries did not have a requirement for the company to have marketing authorisation for the product. However, in Germany and Spain an application must have been submitted. In France, the manufacturer has the option to apply to the Early Access Authorisation either pre- or post-marketing authorisation.
- Given that a condition of EAPs is typically the rarity of the disease, expectations for clinical data packages were variable. The UK required evidence from phase III trial unlike Italy that accepted phase I (compassionate use) or II (Law 648) trial data
- In addition to clinical data requirements, France's AAP required inclusion of protocol therapeutic use (PTU) and Italy's law 648/1996 requires a scientific report outlining proposed therapeutic plan, estimated patients and cost for submission.
- Both France's Early access authorisation (AAP) and UK's Early Access Medicines Scheme (EAMS) provided data collection opportunities that could be utilised in their respective HTA bodies' assessment procedures. Other countries considered the data collection opportunities insufficient in the program compared to clinical trials.
- Only France's AAP and Italy's 648 program offered paid Early Access for manufacturers.

Table 1: Framework

Program	Demonstration of innovation	MA Requirements	Clinical data requirements	Eligibility criteria	Evidence generation	Funding opportunity
Early Access Authorisation (AAP)		Post and pre-MA options • Manufacturer must agree to apply for MA once EA granted and submit a request for reimbursement within one month of being granted MA	Protocol therapeutic use (PTU)	1. Presumed efficacy + safety 2. Serious, rare or disabling disorder 3. No appropriate therapy 4. Initiation cannot be delayed	Data can contribute to TC assessments	Free pricing but subject to a double system of rebates
Compassionate use access (CUA)				1. No commercialisation plan 2. No treatment alternative 3. Presumed efficacy + safety		If the product is not reimbursed in another indication, then free pricing
Arzneimittel-Härtefall-Verordnung (AMHV)		Application for marketing authorisation has been submitted or a clinical trial is being conducted on it.		Patients must have a disease that leads to severe disability or is life-threatening and unsatisfactorily treated with approved drugs	Cannot be used	Manufacturer provides free of charge
Law 648/1996			• Phase II trial • A scientific report;	1. No valid therapeutic alternative available 2. Acceptable risk profile 3. Efficacy demonstrated		• Price set by manufacturer if not yet reimbursed in other indications (reimbursement price if available) • Reimbursed by National Health Service
Compassionate Use		Medicines may not yet be authorised but must be involved in a clinical trial; medicines may have MA in other indications; or authorised but not available in national territory	Phase I sufficient for rare disease	1. For use outside the indication of the clinical trial, or where the patient cannot be included 2. Favourable opinion from the Ethics Committee which clinical centre submitting request belongs		Supplied free of charge by the manufacturer
Early Access to Medicines Scheme (EAMS)		PIM designation issued post-MHRA scientific meeting and could be given several years before the product is licensed	Phase III trial (phase II may be accepted in exceptional circumstances)	1. PIM designation: High unmet need; Serious or life-threatening condition; Therapeutic advantage; Positive risk: benefit ratio 2. EAM Scientific opinion	Use RWE generated during EAMS period in NICE appraisals	Company provides free of charge during the EAMS period and up until the point of a positive funding policy
The Royal Decree 1015/2009 (Authorisation for Temporary Use)		Company must have applied for MA, or be at a stage of clinical research designed to support an MA		1. No therapeutic alternatives 2. Serious disease 3. Patients not eligible for clinical trials 4. Intended to be used for significant group of patients		Reimbursed on case-by-base basis

Required Not specified Not required

Discussion and Conclusion

- Through undertaking this analysis, we have been able to populate a framework for early access opportunities, showing variation in qualifying criteria and evidence collection possibilities.
- There are multiple opportunities for EAPs for manufacturers across the EU4 and the UK, although only France and Italy provided paid access that allow manufacturers to set a price for their product.
- The limited number of EAPs that offer paid access could significantly limit the number of manufacturers able to provide early access to potentially life-saving medicines for patients. However, manufacturers need to weigh up the cost of providing their products against the valuable opportunity for engagement with stakeholders and collection of additional data that could be involved in future provision, reimbursement and funding.

AAP: Early Access Authorisation; EAMs: Early Access to Medicines; EAPs: Early Access Programs; HTA: Health Technology Assessment; MHRA: Medicines and Healthcare products Regulatory Agency; PIMS: Promising Innovative Medicine; PTU: Protocol for Therapeutic Use

References: 1. Early Access to Medicines. Development support and regulatory tools. Available at: https://www.ema.europa.eu/en/documents/leaflet/early-access-medicines-development-support-regulatory-tools_en.pdf [Accessed 28/09/22]

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