Early Access Programmes in Europe Versus Key Markets in Other Regions: An In-Depth Comparison

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Introduction

- Early access programmes allow patients to obtain novel medicinal products prior to local marketing authorisation and/or local pricing and reimbursement agreements, but the approach to access is highly variable among the countries in scope.
- The objectives of this study were to compare characteristics, regulations and usage of Early Access Programmes (EAPs) for medicines in Europe with those in Australia, Brazil, Canada, China, Japan, Saudi Arabia and US.

Methods

Information on EAPs and coverage decisions prior to market authorisation was obtained from national regulatory authorities' websites in 42 countries between June and October 2024.

Key search terms included "early access", "expanded access," "compassionate use," "unauthorised/non-authorised use," "unlicenced use," and "early access."

We analysed 10 criteria:
- Number and name of EAPs
- Transparency and maturity (time since EAP implementation)
- Monitoring requirements
- Funding options
- Eligibility and EAP stopping criteria
- Number of applications and success rates (past five years).

Results

- In Europe, 29 out of 35 countries had EAPs in place. Eleven countries offered funding options through EAPs, although sometimes only on a case-by-case basis and with variability as to when and how this reimbursement could occur. Ireland stands out as the most notable example that does not offer any opportunity for early access.
- Among the seven markets studied outside of Europe, all offer early access. Three have well-established EAPs in place (Australia, Canada, US), albeit without reimbursement. Australia and the US offer multiple pathways, each designed to match different levels of urgency, and these pathways have seen significant usage.
- Recently established EAPs in Brazil, China, Japan and Saudi Arabia are based on less detailed regulations, resulting in ambiguity and, in some cases (e.g. Japan) lower acceptance rates. EAP coverage in China is restricted to specific drugs and locations.

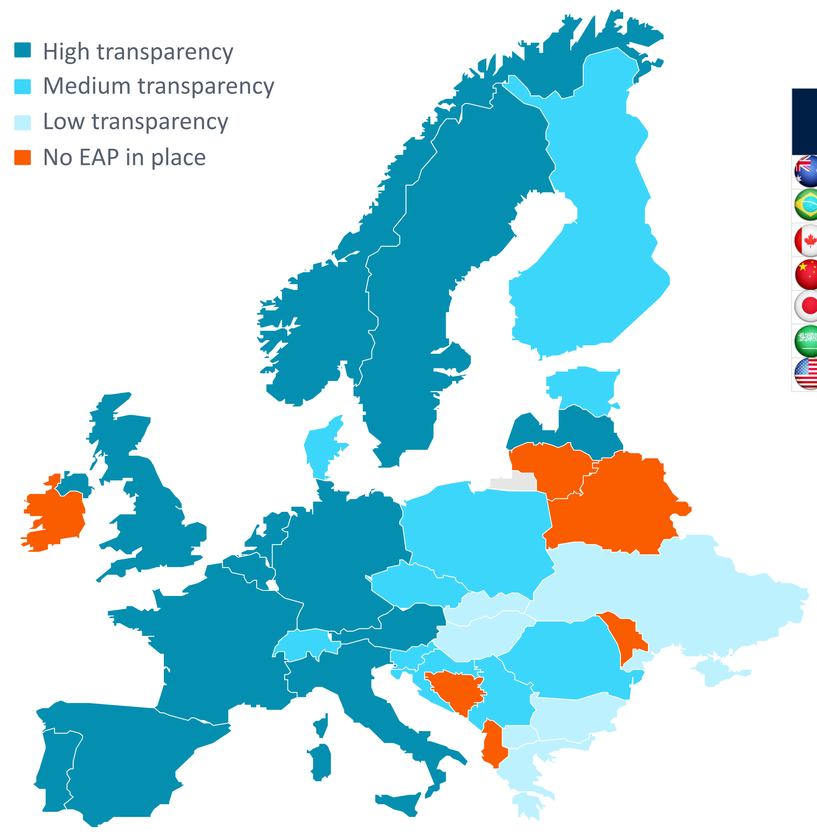
Table 1: EAPs identified for countries in Europe, Australia, Brazil, Canada, China, Japan, Saudi Arabia and US.

Country	Number of EAPs identified	EAPs available after MA?	Maturity of EAPs	Opportunities for reimbursement?
Australia	5	✓	●	✗
Brazil	3	✓	●	✗
Canada	1	✗	●	✗
China	3	✗	●	✗
Japan	1	✗	●	✗
Saudi Arabia	1	✗	●	✗
US	3	✗	●	✗
Austria	2	✗	●	✗
Belgium	3	✓	●	Direct reimbursement by health insurers
Bulgaria	2	✗	●	✗
Croatia	2	✗	●	✗
Czech Republic	2	✗	●	Under specific conditions, must be negotiated with insurers
Denmark	2	✗	●	✗
Estonia	2	✗	●	✗
Finland	2	✗	●	✗
France	2	✓	●	Reimbursed at first negotiated price
Germany	1	✗	●	✗
Greece	2	✓	Unclear	By insurers in urgent cases
Hungary	2	✗	●	✗
Italy	3	✗	●	Reimbursed following pricing approval
Latvia	1	✗	●	✗
Luxembourg	2	✗	Unclear	✗
Malta	2*	✗	●	✗
Netherlands	2	✗	●	Reimbursed by health insurance or hospital budget
Norway	1	✗	●	Reimbursed by government grant
Poland	1*	✓	●	Government reimbursement
Portugal	2	✓	●	✗
Romania	1	✗	●	✗
Serbia	2	✗	Unclear	✗
Slovakia	1*	✓	●	✗
Slovenia	2	✗	Unclear	✗
Spain	2	✗	●	Reimbursed from hospital budget (but rare)
Sweden	2	✓	●	Reimbursed via Individual patient licence
Switzerland	3	✗	Unclear	May be reimbursed if a pre-determined criterion is met
Ukraine	1	✓	●	✗
United Kingdom	2	✗	●	✗

*indicates programmes which reflect an EAP, but they are intended for a different use (i.e. emergency access) or are derived from European legislation. EAPs were not identified in the following countries: Albania, Belarus, Bosnia and Herzegovina, Ireland, Lithuania and Moldova.
Maturity of EAP systems was determined by year of program launch.

● High maturity (pre-2010) ● Medium maturity (2011-2020) ● Low maturity (2021 to present)

Figure 1: Transparency map for countries in scope



Non-European countries	EAP transparency
Australia	High
Brazil	Low
Canada	High
China	Low
Japan	Medium
Saudi Arabia	Medium
US	High

Criteria for transparency rating: High transparency = Government webpage identified, clear guidelines for manufacturers to follow, information primarily from these sources and confirmed by published sources; Medium transparency = Government webpage etc identified, but information largely supplemented from published sources; Low transparency = No government webpage etc identified, information from published sources

- Transparency of EAPs was found to be highest in more mature, developed markets in Western Europe, North America and Australia.
  - All countries provided clear inclusion criteria for EAPs – mostly based on the treatment being for life-threatening, long-lasting or seriously debilitating illnesses, which cannot be treated satisfactorily with any locally authorised medicines.
  - Most EAPs focus on use before market authorisation but across six countries (Japan, Canada, China, Portugal, Serbia, Spain) a product needs to be approved in another geography before inclusion in a local EAP; access after local MA but before P&R decision is available in ten countries.
  - Patient exclusion and EAP stopping criteria were less commonly provided and more present in Europe; overall they were identified for 34% and 47% of countries, respectively.
  - Common monitoring requirements included safety, efficacy, and patient monitoring (health and well-being). However, many countries stipulated that these data could not be used to support regulatory or P&R applications.
  - Information regarding the number of applications and acceptance rates for EAPs was generally limited, only being identified for nine countries (20%). Highest acceptance rates are found in France and the US, lowest in Japan and intermediate for other European markets such as Belgium, the Netherlands, Portugal, and the UK.
- In Europe, the most common types of EAP identified were compassionate use (access to experimental drugs) and named patient programmes (access to non-approved drugs), influenced by EU legislation 726/2004, through which EMA provides recommendations for compassionate use programmes across the EU.
  - So far, there is no evidence of EAP regulations adjusting to align with upcoming Joint Clinical Assessment (e.g. adjusting timelines or targeted data collection).
- Ex-European countries had a greater diversity in the EAP offerings, including expanded access (provides patients access to unapproved drugs outside clinical trials), special access (provides access to treatments under exceptional circumstances), regional access schemes (local programmes offering access to treatments not widely available) and several offer multiple (≥3) EAP routes (China, Brazil, Australia, US).

Conclusions

- Considerable variation exists in EAPs across 42 countries evaluated, with more mature programmes available in markets of greater commercial interest for manufacturers. These markets were generally associated with higher levels of transparency (Western Europe, Nordics, US, Canada and Australia). However, level of a country's economic development and existence of a well-established healthcare and regulatory system does not equate with existence of an EAP (Ireland).
- Less than half of countries with EAPs had highly transparent programmes (39%), clear patient exclusion criteria (34%), clear EAP stopping criteria (47%), or offered reimbursement opportunities (31%). Increased availability of these factors could provide greater incentives for manufacturers to consider early access when preparing to launch new products.
- In Eastern Europe, Brazil, China, Japan, and Saudi Arabia, insufficient detail on monitoring requirements, a lack of data collection infrastructure, and ambiguous regulations may pose challenges for manufacturers and could negatively impact the use of early access pathways.

Abbreviations: EAP, early access programme; EMA, European Medicines Agency; EU, Europe; MA, marketing authorisation; P&R, pricing and reimbursement; US, United States.
References: Information regarding early access programmes was primarily identified from public sources, such as freely available publications, government and agency websites.