Early access for innovative medicines in Australia, EU4 and UK: a comparison between different pathways

HTA290

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Background and Objectives.

Regulatory agencies worldwide face the challenge of balancing the need for rapid access to new therapies with the thorough assessment of benefit/risk. To expedite market access for drugs with high unmet needs, Early Access Programs (EAPs) have been implemented in many countries over the years. EAPs generally allow patient access to drugs or indications before marketing authorization is granted.

In Europe, access to medicines is centrally regulated by **the European Medicines Agency (EMA).** After EMA approval, each medicine undergoes a local **Health Technology Assessment (HTA),** which can delay patient access to treatments. To address these delays, various programs have emerged over the years to accelerate access to medicines. The EU has introduced several initiatives, such as the PRIME scheme, **early access programs (EAPs)**, and Compassionate Use programs [1]. EAPs enable early access to unlicensed drugs under development (pre-marketing authorization) or for off-label use. These programs generally allow patient access to drugs/indications before marketing authorization and can extend to the period between approval and the national HTA decision. EMA also recommends that EU countries include patients from clinical trials in EAPs if they wish to continue treatment.

In Australia, before companies can sell therapeutic goods, they must apply to the **Therapeutic Goods Administration (TGA)** for market authorization. The TGA, part of the Department of Health, evaluates, assesses, and monitors therapeutic goods [2]. Health practitioners are encouraged to use medicines listed on the **Australian Register of Therapeutic Goods (ARTG),** as these have been evaluated for quality, safety, and effectiveness. However, in some cases, unapproved drugs that are not on the ARTG may be necessary. To access such medicines, pathways like the **Special Access Scheme (SAS)** and Authorised Prescriber (AP) Scheme are available.

The objective of this analysis is to examine the similarities and differences of **EAPs** in Australia, the EU-4 countries (France, Germany, Italy, Spain), and the UK.

Methods.

The analysis was conducted through a national and international literature review for each Country. Regulatory agency websites were reviewed, including the Therapeutic Good Administration (TGA) for Australia, Haute Autorité de santé (HAS) for France, Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (IQWiG) and Gemeinsamer Bundesausschuss (G-BA) for Germany, Agenzia Italiana del farmaco (AIFA) for Italy, Agencia Española de Medicamentos y Productos Sanitarios (AEMPS) for Spain, National Institute for Health and Care Excellence (NICE) for UK.

The research was centrally coordinated by Productlife Group global, with local research conducted by PLG's Market Access teams in each country.

Results.

In **Australia**, unapproved drugs can be supplied through the Therapeutic Goods Administration (TGA) Special Access Scheme (SAS). There are three pathways within the SAS:

- Category A: For patients who are seriously ill and for whom death is likely to occur within months.
- Category B: For patients who do not fit Category A criteria. This is an application pathway where TGA approval must be granted before supply.
- Category C: For patients using drugs with an established history of use that are listed on the TGA Authorized Supply list for the specific indication.

Categories A and C are notification pathways and do not require prior TGA approval, but notification must be sent to the TGA within 28 days of supply. Category B requires TGA approval prior to drug supply. Importantly, the Commonwealth does not subsidize the cost of these treatments.

Authorised Prescribers (AP) are medical practitioners with specific expertise who have applied for and been granted authority to prescribe an unapproved product to patients requiring access to unapproved therapies.

Additionally, early access to regulatory-approved but unfunded therapies can be provided through Product Familiarisation Programs (PFPs) or Compassionate Use Programs (CAPs):

- Product Familiarisation Programs (PFPs): Sponsored by pharmaceutical companies, these programs allow prescribers to evaluate and become familiar with a product before it is listed on the Australian Register of Therapeutic Goods (ARTG).
- Compassionate Access Programs (CAPs): Initiated by pharmaceutical companies, CAPs provide medicines that are not reimbursed or included in other funding schemes. CAPs typically support off-label use or treatment for an indication that is not reimbursed, often as a rescue treatment for patients with serious or life-threatening conditions. Enrolment in CAPs is carefully managed on a case-by-case basis.

■ Since 2020, **FRANCE** has implemented a new Early Access Program (EAP), which replaced the former ATU and PEC-T programs. The EAP can be applied for by either pharmaceutical companies or physicians (hospitals), and it remains open until the commercial availability of the drug. The EAP cannot exceed one year but can be renewed with updated product information.

There is no dedicated fund for this program; hospitals cover the costs (after receiving an internal permit), although companies can choose to provide the medicine for free. The price is freely set by the company, but once the drug is commercially launched and a price is negotiated, any difference between the initial price and the final negotiated price must be reimbursed. If this difference is significant, fines may apply.

In cases where the Haute Autorité de Santé (HAS) gives a negative opinion at the time of negotiation, the company is required to continue providing the drug to patients for one year before discontinuing supply.

■ **GERMAN** pharmaceutical legislation allows compassionate use programs, enabling treatment for groups of patients on a cohort basis. The program requires notification of the competent federal authority. For small molecules, the Federal Institute for Drugs and Medical Devices (BfArM) is responsible, while for biologics, it is the Paul-Ehrlich-Institut (PEI).

The authority typically provides feedback on the application within two weeks, though more complex cases may take up to 60 days. The official approval timeline ranges from one to three months. Once approved, compassionate use is valid for one year and may be renewed as needed.

There is no dedicated fund for compassionate use programs in Germany, so the cost of treatment is covered by pharmaceutical companies.

■ The **ITALIAN** Medicines Agency (AIFA) has implemented several tools to provide early access to important drugs, including Law 326, Law 648/96, and Compassionate Use Programs (CUPs) for named patients or cohorts.

Law 648/96 allows early access to drugs at the expense of the National Health Service (NHS). Initially, this law applied only when no valid therapeutic alternatives were available. However, with the amendment introduced by Law 79/2014 (Art. 4-bis), AIFA can now include a drug in the official list even when therapeutic alternatives exist, based on an economic evaluation. Health operators or patient associations can request early access, with the application reviewed by the Scientific and Economic Committee (CSE). The price is then negotiated with the pharmaceutical company, and the drug is made available to patients under inclusion and exclusion criteria set by AIFA. These drugs are subject to a surveillance program and are listed in a registry that is periodically updated.

Compassionate Use Programs (CUPs) are applied in cases where no valid therapeutic alternatives exist or for patient's ineligible for clinical trials. Pharmaceutical companies must notify AIFA before initiating a CUP, at least 30 days before its completion. The CUP can be for a named patient or a cohort of patients, and the drug is provided free of charge by the manufacturer.

The AIFA 5% Fund (Law 326/2003) supports early access for orphan drugs used to treat rare diseases or drugs offering hope of a cure for severe diseases before commercialization. The fund is financed by pharmaceutical companies and AIFA, and AIFA provides an online service for submitting applications and reimbursement requests under the 5% Fund.

■ In **SPAIN**, there is a program that allows access to drugs under special circumstances on a named-patient basis. Applications are made by physicians, typically from hospitals, and the costs are covered by hospitals through regional funding (in most compassionate use cases). There is no dedicated national fund for this program.

The program remains active until the drug becomes commercially available. For approved but not yet reimbursed products (where pricing and reimbursement negotiations are still ongoing), the price is freely set by the company. Once the national reimbursement price is finalized, any difference between the initially charged price and the final negotiated price must be repaid.

The Early Access to Medicines Scheme (EAMS) was launched in the **UK** in 2014 to provide patients with access to promising medicines before full marketing authorization. The application process for manufacturers involves submitting a dossier with the most recent data, meeting both regulatory requirements and those needed for NICE (National Institute for Health and Care Excellence) appraisal. This data can contribute to the marketing authorization (MA) application and subsequent appraisal. Applications can be made by both companies and physicians (hospitals). There is no dedicated fund for EAMS, so the cost of the medicines is borne by the pharmaceutical companies [10].

Conclusion.

Our research highlighted significant differences in the implementation of Early Access Programs (EAPs) across the EU4, the UK, and Australia. These disparities contribute to inequalities in patient access to medicines. This comparative analysis of existing early access schemes serves as a starting point for discussions on harmonizing these programs, with the aim of optimizing patient access and reducing inequalities.

Country	Regulatory body	HTA body	Early access economic coverage	Evaluation criteria	Reference law
Australia	Therapeutic Goods Administration (TGA)	Therapeutic Goods Administration (TGA) Pharmaceutical Benefits Advisory Committee (PBAC)	NO	Unmet need, no access to similar approved therapeutics, patient illness severity, established history of use list	Therapeutic Goods Act 1989 (Cth) [3]
France	Agence Nationale de Sécurité du Médicament et des Produits de Santé (ANSM)	Haute Autorité de Santé (HTA)	YES	Unmet need, no access to similar approved therapeutics, efficacy and safety for patients	LOI n° 2020-1576 du 14 décembre 2020 de financement de la sécurité sociale pour 2021 [4]
Germany	German Federal Institute for Drugs and Medical Devices (BfArM) and The Paul-Ehrlich Institute (PEI)	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (IQWiG) and Gemeinsamer Bundesausschuss (G-BA)	YES	Show product's safety and suspected efficacy, medical need and urgency, as well as provide justification as to why patients cannot be included in clinical trials	Arzneimittel-Härtefall-Verordnung (AMHV), or Ordinance on Medicinal Products for Compassionate Use [5]
Italy	AIFA- Agenzia Italiana del Farmaco	AIFA- Agenzia Italiana del Farmaco	YES	Unmet need, added therapeutic value, quality of evidence	Legge 648/96 (published on the Italian Official Journal (GURI) n.300 – Dec 23rd, 1996) [6], Compassionate use (9th of September 2017, published on the Official Gazette no. 256 of November 2nd, 2017, and entered into force on December 3, 2017) [7], Legge 326/2003 [8]
Spain	AEMPS- Agencia Española de Medicamentos y Productos Sanitarios	AEMPS- Agencia Española de Medicamentos y Productos Sanitarios	YES	Severe or debilitating disease, Unmet medical need, Hospital setting only, Not taking part in a clinical trial	Royal Decree 1015/2009 [9]
UK	Medicine and Healthcare products Regulatory Agency (MHRA)	National Institute for Health and Care Excellence (NICE)	YES	Severe and disabling disease, high unmet need, the product is likely to offer benefit or significant advantage over and above existing options	No regulatory references

REFERENCES

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