Innovative Access Models for Rare Disease's Medicines

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Orphan Drug Context

Orphan drugs target a very small patient population with high existing unmet medical needs and carry significant uncertainties, which requires payers and the healthcare system to accelerate their transition to alternative access and funding pathways

Payer mindset

- Robust evidence generation with high N, pivotal clinical trial, double-blinded, and with a comparator
- Hard endpoints with statistically significant results
- Robust epidemiology

CERTAINTY

Orphan drug reality

- Weaker evidence with small N, phase 1 or 2 single-arm and open-label trial
- Surrogate endpoints with no statistical analysis
- Unknown epidemiology or existing epidemiology with a wide range of uncertainty

UNCERTAINTY

Source: Alira Health analysis

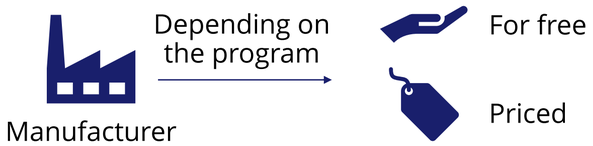
Access to Orphan Drugs

Patients with rare diseases can have access to orphan drugs through different pathways or funding schemes that can be complementary; early access programs, special access models, and special funds

EARLY ACCESS PROGRAMS

- EAPs allow for the provision of drugs **under clinical development or not yet commercialized** to patients with high unmet needs, with a serious disease with no approved alternatives, and who cannot be enrolled into a clinical trial

Funding



SPECIAL ACCESS MODELS

- **Financially-based agreements**: address concerns regarding the cost and budget impact
- **Outcome-based agreement (OBA)**: address data uncertainty

Funding

SPECIAL FUNDS

- **Government or external funds** allocated for financing of some treatments, which might include high-cost drugs, **orphan drugs**, or specific pathologies

Funding

Can be complementary

Special access models, particularly outcome-based agreements, and early access programs allow for the **collection of real-world data**

Source: Gammie T, et al., Access to Orphan Drugs: A Comprehensive Review of Legislations, Regulations and Policies in 35 Countries. PLoS One. 2015 Oct 9;10(10):e0140002; Patil S. Early access programs: Benefits, challenges, and key considerations for successful implementation. Perspect Clin Res. 2016 Jan-Mar;7(1):4-8; Alira Health analysis

Early Access Programs

Early Access Programs vary among countries and allow for the provision of medicines to patients with high unmet medical needs – which includes rare diseases with no approved therapies – prior to their commercialization

Although EAPs regulation vary among countries, developed countries usually have two different type of programs as defined by the common **EU legal framework**

	COMPASSIONATE USE	NAMED-PATIENT PROGRAM
Target population	Cohort/group of patients	Individual patients
Type of drugs	For medicines eligible for the EMA Centralized Procedure, undergoing clinical trials or in the marketing authorization application process	For medicines not specifically intended for clinical development or commercialization in the indication requested by the physician
Process	Initiated and run by the pharmaceutical company. The program is approved by the national health authority	Initiated by a physician's request. Regulatory approval by the national competent authority on a case-by-case basis
Funding	Usually, provided for free (except in France and Italy)	Usually, priced

EAP: early access program; EMA: European Medicines Agency
Source: European Commission; Alira Health analysis

Special Access Models (1/2): Mature Systems

Both financial and outcome-based agreements are being implemented in high-income countries for orphan high-cost drug with a special focus on registries and real-world data collection

GERMANY

German payers have historically been resistant to OBAs but have shown **willingness in the past years**

KYMRIAH® (tisagenlecleucel) Dispersion for IV infusion
zolgensma

ITALY

Greater experience with OBAs than in other countries

KYMRIAH® (tisagenlecleucel) Dispersion for IV infusion
Strimvelis® (autologous CD34+ cells transduced to express ADA)

UK

The majority of special access models in the UK are **discounts while the manufacturer collects RWD**

SPINRAZA® (nusinersen) injection 12 mg/5 mL
zolgensma

SPAIN

The use of special access models is increasing, especially through the creation of the national platform **VALTERMED**

POLIVY® polatuzumab vedotin-piiq INJECTION FOR INTRAVENOUS USE 30MG | 140MG
zolgensma

US

Generally, outcome-based payments or rebates offered to **providers or payers** based on **individual patient data**, and **payments in installments**

KYMRIAH® (tisagenlecleucel) Dispersion for IV infusion
LUXTURNA™ voretigene neparvovec-rzyl for subretinal injection

CANADA

Working group

The Canadian **RWE and OBA working group** brings together RWE generation organizations to **support the implementation of OBAs**

Work in progress

Key learnings from special access models with RWD collection:

- Agree a **statistical analysis plan in advance**, and ensure extra time provided by the access agreement to ensure **robust analyses of RWD**
- Be mindful of the **burden that RWD collection** puts on healthcare staff, patients and relatives
- Make the most of **data from patient organizations** on outcomes that really matter, particularly in economic modelling

OBA: outcome-based agreement; RWD: real-world data
Source: Jørgensen J, Kefalas P. The use of innovative payment mechanisms for gene therapies in Europe and the USA. Regen Med. 2021 Apr;16(4):405-422; NICE; Alira Health analysis

Predominant type of special access model:
Financially-based agreement
Outcome-based agreement

Special Access Models (2/2): Emergent Systems

Middle and low-income countries are also adopting policies towards the implementation of special access models to ensure that patients have affordable access to innovative therapies

UKRAINE

The MoH approved measures to introduce HTA and determine whether a **new drug is suitable for special access models in February 2021**

Work in progress

BULGARIA

Special access models were **introduced in 2015**

SPINRAZA® (nusinersen) injection 12 mg/5 mL

BRAZIL

Agreement for the treatment of SMA consisting of a **patient cap**, a **negotiated price discount**, and **payment based on performance**

SPINRAZA® (nusinersen) injection 12 mg/5 mL

CHINA

Utilization-price cap for the treatment for patients with **metastatic HCC** (rare disease) with the overall cost to patients capped at 3 months

Nexavar® (sorafenib) tablets

THAILAND

Risk-agreement for Gaucher Disease

Cerezyme imiglucerase for injection

HCC: hepatocellular carcinoma; HTA: Health Technology Assessment; SMA: spinal muscular atrophy
Source: Facey KM, et al., Implementing Outcomes-Based Managed Entry Agreements for Rare Disease Treatments: Nusinersen and Tisagenlecleucel. Pharmacoeconomics. 2021 Sep;39(9):1021-1044; Castro HE, et al., Sharing knowledge for policy action in low- and middle-income countries: A literature review of managed entry agreements. Medicine Access @ Point of Care. January 2019; Health Intervention and Technology Assessment Program (HITAP), Thailand; Alira Health analysis

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Special National Funds for innovative products

The funding challenges associated with rare diseases has led to the creation of national health budget programs to facilitate access to treatments

	Fund	Key Insights	Examples
ITALY	**AIFA fund for innovative oncological and non-oncological medicines**	• Drugs with innovative status (can include orphan drugs)[1] are funded by **specific allocated funds by AIFA** (1,000M EUR/year, 50% for oncological and 50% for non-oncological drugs)	LUXTURNA™ voretigene neparvovec-rzyl for subretinal injection
UNITED KINGDOM	**Innovative Medicines Fund/ Cancer Drugs Fund[2]**	• Provide early access to orphan drugs or cancer drugs that have **efficacy and cost-effectiveness uncertainties** while manufacturers generate additional evidence (680M GBP in total, 340M GBP for each fund)	TECARTUS® (brexucabtagene autoleucel) Suspension for IV infusion
CHILE	**Ley Ricarte Soto**	• Provides **full coverage for the diagnosis and treatment of high-cost drugs**, including oncologic, immunologic and **rare diseases** previously defined by a MoH decree	HAE, PAH, Fabry Disease, Gaucher Disease
PHILIPPINES	**Rare Disease Medicines Access Program**	• **Initial target beneficiaries** are children with type 1 and 3 **Gaucher Disease**	Gaucher Disease
ROMANIA	**National Rare Disease Program**	• Covers **25 rare diseases** with a budget of ~100M USD • 22% of the budget is for treating SMA patients	SPINRAZA® (nusinersen) injection 12 mg/5 mL

Note: [1]Innovative status is determined by the therapeutic need, added therapeutic value and robustness of the scientific evidence; [2]Drugs funded by the Cancer Drugs Fund can be provided under a special access model | HAE: hereditary angioedema; PAH: pulmonary arterial hypertension
Source: AIFA; NHS; Superintendencia de Salud, Chile; Department of Health, Philippines; Alira Health analysis

Future Trends

There are different initiatives aimed at facilitating patient access to innovative drugs and at reducing drugs' prices

- The development of high-cost innovative therapies has started raising in the past years
- **More products**, such as gene and cell therapies, targeting niche populations at very high price **will make it to market in the future**, which raises different concerns:
  - *How can the price of these therapies be optimized?*
  - *Can the funding gap for rare diseases be addressed?*

Examples

Global Buyers Club

- **EQRx**, founded in 2020, is a biotechnology company focused on re-engineering the drug development process through partnerships in order to offer its therapies at **substantially lower prices** compared to today's innovative medicines **(50%-70% below)**

The company is building a "**global buyers club**" of insurers and healthcare systems

Orphan drugs in pipeline:

EQ176 — Primary liver cancer (phase III)

Crowdfunding

National Rare Disease Policy 2021

- The government set a **voluntary crowdfunding platform** for the financing of one-time curative treatments and lifelong treatments

Crowdfunding in the US and Canada

- There are also platforms for the **voluntary donation of funds** to finance high-cost treatments in the US and Canada; however, these are not regulated

Source: EQRx; Ministry of Health and Family Welfare, India; Alira Health analysis