WHO webinar series on country pharmaceutical pricing policies

Pricing of medicines for rare diseases

Housekeeping

Use Q&A window to post questions (not “Chat”)
- “Q&A” to send your questions to the panellists
- “Chat” ONLY when sharing comments or documents with all participants

Please keep all comments respectful and constructive

The session is recorded for viewing on demand
- Slides and recording will be shared after the session
Today’s session

1. Presentations on global/regional and patient perspectives
2. Presentations on specific country policies
3. Full panel discussion
4. Q&A with audience
5. Closing
Panellists

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Global Access and Unmet Needs of Orphan Drugs

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Access and Unmet Needs of Orphan Drugs in 194 Countries and 6 Areas: A Global Policy Review With Content Analysis

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Objectives: Three hundred million people living with rare diseases worldwide are disproportionately deprived of in-time diagnosis and treatment compared with other patients. This review provides an overview of global policies that optimize development, licensing, pricing, and reimbursement of orphan drugs.

Methods: Pharmaceutical legislation and policies related to access and regulation of orphan drugs were examined from 194 World Health Organization member countries and 6 areas. Orphan drug policies (ODPs) were identified through internet search, emails to national pharmacovigilance centers, and systematic academic literature search. Texts from selected publications were extracted for content analysis.

Results: One hundred seventy-two drug regulation documents and 77 academic publications from 162 countries/areas were included. Ninety-two of 200 countries/areas (46.0%) had documentation on ODPs. Thirty-four subthemes from content analysis were categorized into 6 policy themes, namely, orphan drug designation, marketing authorization, safety and efficacy requirements, price regulation, incentives that encourage market availability, and incentives that encourage research and development. Countries/areas with ODPs were statistically wealthier (gross national income per capita = $10,875 vs $3,950, P < .001). Country/area income was also positively correlated with the scope of the respective ODP (correlation coefficient = 0.37, P < .001).

Conclusions: Globally, the number of countries with an ODP has grown rapidly since 2013. Nevertheless, disparities in geographical distribution and income levels affect the establishment of ODPs. Furthermore, identified policy gaps in price regulation, incentives that encourage market availability, and incentives that encourage research and development should be addressed to improve access to affordable orphan drugs.

Keywords: drug regulatory, health equity, orphan drug policy, rare diseases, treatment access.

VALUE HEALTH. 2020; 23(12):1580-1591.
Geographical distribution

Total number of countries/regions with orphan drug policy: 92 (46%, out of 200 studied countries/regions)
Trajectory of orphan drug policy establishment

HIC: high-income countries
UMIC: upper middle-income countries
LMIC: lower middle-income countries
LIC: low income countries

Countries/areas with orphan drug policy are statistically wealthier (GNI per capita = $10875 vs $3950, p < 0.001)

Orphan Drug Act in the US
Orphan Drug Act in the EU
# Orphan drug policy scope

<table>
<thead>
<tr>
<th>1. Orphan drug designation</th>
<th>Definition of rare diseases</th>
<th>Designation or official list of orphan drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Designation or official list of rare diseases</td>
<td>Criteria and procedures for orphan drug designation</td>
<td></td>
</tr>
<tr>
<td>Definition of orphan drugs</td>
<td>Designation committee</td>
<td></td>
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<tr>
<td>Criteria for obtaining marketing authorization</td>
<td>Reference to overseas orphan drug approval</td>
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<tr>
<td>Validity duration of marketing authorization</td>
<td>Premarket authorization access</td>
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<tr>
<td>3. Safety and efficacy requirements</td>
<td>Proof of efficacy/safety/cost-effectiveness</td>
<td>Definition/requirements of sponsor or applicant</td>
</tr>
<tr>
<td>Clinical trial authorization/exemption</td>
<td>Pharmacovigilance requirement/adverse event monitoring</td>
<td></td>
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<tr>
<td>Health technology assessment criteria</td>
<td>Recall of products</td>
<td></td>
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<tr>
<td>4. Price regulation</td>
<td>Provisions and guidelines for price regulation</td>
<td>Exemption from price regulation</td>
</tr>
<tr>
<td>Mode of price regulation</td>
<td>Maximum retail price</td>
<td></td>
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<tr>
<td>Managed entry agreements</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Incentives that encourage market availability</td>
<td>Payer subsidies/reimbursement/funding/co-payment</td>
<td>Tax credits or exemptions</td>
</tr>
<tr>
<td>Financial assistance for cross-border health access</td>
<td>Fee refund/reduction/waiver</td>
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<tr>
<td>Compassionate use</td>
<td>Sponsor/applicant reimbursement</td>
<td></td>
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<tr>
<td>6. Incentives that encourage research and development</td>
<td>Patent protection/market exclusivity/monopolization</td>
<td>Scientific advice/consultation</td>
</tr>
<tr>
<td>Funding for research/development/clinical trials</td>
<td>National plan or strategy</td>
<td></td>
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<tr>
<td>Protocol assistance</td>
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</tbody>
</table>
Orphan drug policy scope by income level

1. Orphan drug designation
2. Marketing authorization
3. Safety and efficacy requirements
4. Price regulation
5. Incentives that encourage market availability
6. Incentives that encourage research and development

34 subthemes under 6 major themes
Summary

- **92 (46%)** countries/areas established ODP, with a notable increase in non-high-income countries/areas since Late 2000s.
- **Disparities** exist in ODP establishment and scope, high-income countries covers more ODP scopes.
- Be prepared to develop or refine current policies:
  - In the thematic areas of price regulation;
  - Incentives that encourage market availability and encourage research;
  - Balance between payer’s affordability and sufficient returns for manufacturers;
- **Rare disease registry and orphan drug designation** are the essentials steps to collect reliable longitudinal real-world evidence for orphan drugs, for evidence-based decision making.
- **Innovative solutions are warranted**, such as mining big data for reposing drug development, risk-sharing agreement for early treatment access and dynamic value-for-money assessment.
- **Case practices** from countries with ODP provide good references for other countries to develop their own ODP.
- **More** policy, clinical, epidemiological, health economics research should be encouraged.
THANK YOU

Regulatory agency, industry, academia and patient groups should work closely to achieve a win-win situation.
PRICING OF MEDICINES FOR RARE DISEASES

WHO Webinar

25 January 2022

Yann Le Cam, Chief Executive Officer
Our mission

EURORDIS works across borders and diseases to improve the lives of people living with a rare disease

984
Member patient organisations

74
countries (28 EU countries)

44
National Alliances of rare disease patient organisations

72
European Federations for specific rare diseases

1997
Founded in

2,500
Outreach to over patient groups

440
volunteers

40+
Staff members with offices in Paris, Brussels and Barcelona
About rare diseases

- Over 6000 distinct rare diseases
- Each one affects fewer than 1 in 2000 people
- Affects between 3.5% - 5.9% of their lives
- No cure for the vast majority of diseases and few treatments available
- All together, an estimated 30 million people are living with a rare disease in Europe and 300 million worldwide
- 72% of rare diseases are genetic
- Onset of 70% of rare diseases is in childhood
Painting a picture of rare diseases

Most (89.1%) of rare diseases are very rare (prevalence less than 1 per 100,000)

Almost all of the people with rare disease (>98%) have one of the 390 most prevalent diseases (more common than 1 per 100,000)

45% of all MAs, 40% of all ODs (up until 2020)

55% of all MAs, 40% of all ODs (up until 2020)

SOURCE: Wakap et al. (2019) ; EMA (2021)
High prices are part of a systemic failure that is hampering access to treatments to those who need it the most.
Important time to availability differences between EU countries

<table>
<thead>
<tr>
<th>Measure</th>
<th>EU average for all products</th>
<th>Oncology</th>
<th>Orphan</th>
<th>Non-oncology orphan</th>
<th>Combination therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rate of availability</td>
<td>49%</td>
<td>58%</td>
<td>41%</td>
<td>34%</td>
<td>64%</td>
</tr>
<tr>
<td>Average time to availability</td>
<td>504 days</td>
<td>561 days</td>
<td>653 days</td>
<td>667 days</td>
<td>411 days</td>
</tr>
</tbody>
</table>

SOURCE: IQVIA (2021)
What happens if we don’t act now

Between 675 and 807 orphan designated products, and between 2485 and 3088 non-orphan products, can be expected to be launched between 2020 and 2030.

We will actually fall 200 to 400 therapies short of the IRDiRC goal of 1000 therapies by 2027 without policy changes (or other changes).

(Rare2030 Work Package 5)
EURORDIS propositions for improvement of access to medicines

- Well established safe treatment at reduced cost not yet available to patients in low and middle income countries
- Pooling procurement across regions facilitated by WHO
- Innovative treatments with life transforming potential but with high price tags
- Innovative pilot projects pulling together all international actors (WHO, World Bank, etc.) through global networks for rare diseases
A reminder of our ambition

Breaking the Access Deadlock to Leave No One Behind

A Position Paper by EURORDIS and its Members

“The ambition of EURORDIS is to have 3 to 5 times more new rare disease therapies approved per year, 3 to 5 times cheaper than today by 2025.”
The ambition of EURORDIS is to have 3 to 5 times more new rare disease therapies approved per year, 3 to 5 times cheaper than today by 2025.
Shining a global light on person living with a rare disease

1. Inclusion and participation in society of persons living with a rare disease & their families
2. Ensure universal and equitable access to quality health services without financial hardship
3. Promote national strategies and actions
4. Integrate rare diseases into UN agencies, programmes and priorities
THANK YOU

EURORDIS.ORG
Global/regional and patient perspectives

1. In your view, to what extent are the *pricing/prices* of medicines for rare diseases a *barrier to access* in different country contexts?

2. To what extent and in what way do you think countries should seek to *harmonize policies* regarding evidence generation, registration of medicines, pricing, access, and clinical care relating to the use of medicines for rare disease?

3. Based on your review/involvement, are *cross-country initiatives* (e.g. Rare 2030, APEC Rare Disease Network, BeNeLuxA) the *future* policy direction for rare disease medicines?
English Rare Disease Landscape

Sheela Upadhyaya
Rare Disease & RAPID C-19 Strategic Adviser

NICE National Institute for Health and Care Excellence
Rare Disease Framework 2021 – priorities

Helping patients get a final diagnosis faster

- Rare disease patients across the UK to get a final diagnosis faster and for research into previously unrecognised conditions to identify new rare diseases and provide new diagnoses.

Increasing awareness of rare diseases among healthcare professionals

- Healthcare professionals to have an increased awareness of rare diseases, use of genomic testing and digital tools to support quicker diagnosis and better patient care.

Better coordination of care

- Rare disease patients to experience better coordination of care throughout the patient journey.

Improving access to specialist care, treatments and drugs

- Rare disease patients to have improved access to specialist care, treatments and drugs.
Rare Disease Framework 2021 – Underpinning themes

Five underpinning themes have been identified in which work will continue to be progressed to support the priorities of the framework and improve the lives of those living with rare diseases.

- **Patient voice**
  - Collaboration with patients and patient organisations.

- **Pioneering research**
  - Harnessing the potential of cutting-edge science and further utilising genomics capabilities and research.
  - Continued investment in research for rare diseases, outcomes are translated into frontline clinical care.
  - Utilise technology to benefit rare disease patients
  - Consider how digital tools could be appropriately used to improve efficiency and patient experience and support research.

- **Digital, data and technology**
  - Collaborate with the rare diseases community across the UK and the world.

- **Collaboration**
  - Ensure the needs of rare disease patients are recognised in wider government policy development, Align with related government strategies on wider work.
NICE programmes involved in developing HTA guidance

- Technology Appraisals *
- Diagnostics Assessment
- Medical Technologies Evaluation
- Highly Specialised Technologies *

*Funding requirement for technologies recommended through the TA and HST programmes.
Innovative Licensing and Access Pathway (ILAP)

• The Innovative Licensing and Access Pathway (ILAP) aims to accelerate patient access to safe and innovative medicines in the UK.

• These medicines include new chemical entities, biological medicines, new indications and repurposed medicines

• The ILAP is delivered in partnership by the All Wales Therapeutics and Toxicology Centre, Medicines and Healthcare products Regulatory Agency, National Institute for Health and Care Excellence and the Scottish Medicines Consortium, part of Health Improvement Scotland

www.gov.uk/guidance/innovative-licensing-and-access-pathway
Innovative Medicines Fund

- The Innovative Medicines Fund, which will operate alongside, and on similar terms to, the Cancer Drugs Fund (CDF), will have a fixed funding envelope of £340 million per annum, creating a total of £680 million of ringfenced NHS England funding for early access to potentially life-saving new medicines.

- The creation of the Innovative Medicines Fund as a dedicated managed access fund for non-cancer drugs, will ensure that there is an established route to access the latest treatments for both cancer and non-cancer patients.

- The IMF presents an opportunity to accelerate the introduction of proven treatments where NICE is able to recommend a medicine for routine use in the NHS.

- These proposals will amplify the impact of the increased commercial flexibilities that NHSEI, working in partnership with NICE, can offer to those companies that are willing to price their products realistically and responsibly.

South Africa’s experience in managing access to medicines through compassionate regulatory pathway and industry programmes

Fatima Suleman
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Introduction: South African Health Care System

When premiums are expired, private sector will move to public sector
Proportion of public might also access private sector
Medicines and Related Substances Act of 1965 (as amended)

Registration of Medicines

South African Health Products Regulatory Authority – registration of medicines, and medical devices includes in vitro diagnostics (IVD)

Quality

Efficacy

Safety

Pricing of Medicines

Pricing Committee

Private Sector Price Regulation

Legislative Framework
Section 21: Authority may authorize sale of unregistered medicines, medical devices or IVDs for certain purposes.

(1) The Authority may in writing authorize any person to sell during a specified period to any specified person or institution a specified quantity of any particular medicine, medical device or IVD which is not registered.

(2) Any medicine, medical device or IVD sold in pursuance of any authority granted under subsection (1) may be used for such purposes and in such manner and during such period as the Authority may in writing determine.

(3) The Authority may at any time by notice in writing withdraw any authority granted in terms of subsection (1) if effect is not given to any determination made in terms of subsection (2).
• **Clinical Trials**
  
• **Individual Named Patients** - physician and applicant holder – unregistered medicine required for clinical care

• **Bulk stock held by a health establishment** - bulk stock of the unregistered medicine may need to be maintained at a health establishment for use in, for example, an intensive care unit or theatre

• **Bulk stock held by the holder of a licence issued in terms of section 22C(1)(b)** - certain unregistered medicines may need to be maintained at a single point of storage for distribution on an urgent basis to one or more health care providers or health establishments.

• **State Procurement** - The State may designate a health care provider as a representative in order to apply for authorization for the supply or sale of an unregistered medicine by health establishments.

• In all instances, the applicant should be the individual who accepts responsibility for the submission of the application and clinical care of the patient, while co-applicants will be all institutions involved in the supply or sale of the unregistered medicine.
Section 21: Deals with special access like clinical trials, industry access programmes and access to medicines not yet registered in the country

- Clinical trial access
- S21 – defined period and for defined patients – can be free or sold – individual physician
- If free in terms of industry access programmes - issues about who advocates strongest, and generally medical schemes with strong negotiators or physicians are able to get these for their patients, but those in State and OOP are left without voices – also sustainability if product is registered
  - What happens to patient that is part of the programme but can no longer afford the medication?
- If sold - poses with post registration pricing and access
  - What price is it sold at under S21 and what price when registered? Sometimes 3 times more than initial price? Patients on previous historic price?

Lack of transparency of pricing and registration issues.
Section 36: Exclusion of any medicine, Scheduled substance, medical device or IVD from operation of Act.

(1) The Minister may, on the recommendation of the Authority, by notice in the Gazette exclude, subject to such conditions as he or she may determine, any medicine, Schedule substance, medical device or IVD from the operation of any or all of the provisions of this Act, and may in like manner amend or withdraw any such notice.

(2) Notwithstanding subsection (1), the exclusion of any medicine or Scheduled substance from the operation of sections 18A and 22G shall be effected by the Minister on the recommendation of the Pricing Committee.
Proposed interventions

- ARM schemes
  - Proposed but who monitors? Who benefits? How financial aspect is going to be dealt with? No legislative space

  - The application of the IBM methodology lowered the SA private sector ex-manufacturer price in 68%, 85% and 85% of products in 2016, 2017 and 2018, respectively.
  - Australia consistently had the highest frequency of the lowest price
  - Looking at the BRICS countries, ex-manufacturer pricing data were obtained for Brazil and Russia.
  - By comparison against these two countries, the SA private sector ex-manufacturer price was lowered in 81%, 90% and 81% of products where a comparator price was available in 2016, 2017 and 2018, respectively.
    - In the majority of products in 2016, 2017 and 2018, Russia had the highest frequency of the lowest price.
Thank You!
Applying competition law to address excessive pricing of medicines for rare diseases
The Leadiant case

Ilan Akker
Senior Inspector
Authority for Consumers and Markets, The Netherlands
Leadiant price hike

Markets that work well for people and businesses

January 25, 2022
Contribution of competition law on fair pricing

I. Traditional hesitance among scholars and practitioners
   • Risk of undermining innovation
   • Competitive response preferred
   • Role of (price) regulators

II. Special characteristics of pharma
    • Basic need / Public / Collective good
    • Extremely low elasticity of demand
    • Role of prescribers and 3rd party payers
Contribution of competition law on fair pricing 2

III. A cure for unfair prices?
   • Resource intensive
   • Case by case
   • Conceptual difficulties (increasingly so when innovation is involved)

IV. Complementary rather than alternatives
   • Dialogue between competition rules and regulation
   • Sign of regulatory inbalance
   • Agenda setting
Some thoughts on the orphan regime (EU)

1. Orphan designation > very strong bargaining position

2. Include obligations (pricing, accessibility) mirroring the concept of special responsibility in competition law

3. Focus the incentives on unmet medical needs, use lighter instruments if possible
The way forward

Excessive pricing
• Profit versus risk & innovation (approaches EU Aspen and NL Leadiant)
• Greater role for prima facie analysis (shifting the burden of proof)
• Contribute to structural solutions

Reading
• Excessive pricing of pharmaceuticals in EU law: balancing competition, innovation and regulation by Wolf Sauter, Ilan Akker SSRN
Country policies

4 In your view, how should country policies balance early access with good evidence and judicious use of public resources?

5 Industry-led access programmes are often the only access option for patients in lower income countries, but these programmes are implemented on a case-by-case and country-by-country basis which are known to have worsen inequitable access. What are the alternatives?

6 What are the long-term policy implications of the Leadiant case? Should there be broader policy reforms in competition laws to better protect the public from exploitative/excessive pricing, particularly in the context of medicines for rare disease medicines where market dominance is prevalent?
Panel discussion

With the increasing number of rare disease medicines with hundred-thousand price tags, how could government policies be better connected with **community expectations on access**? What needs to happen?

How much would universal access to medicines for rare diseases cost?

- **5%** of 300 million people living with rare diseases
- **US$1.5 trillion** per year

**US$100,000** per patient-year

Current levels of per capita health expenditure

- **US$5,000** HIC
- **US$433** UMIC
- **US$80** LMIC
- **US$46** LIC

VS
Panel discussion

Pricing issues for rare disease medicines are understandably emotive as society has the proclivity to save lives of people who are most vulnerable. In what way could we prevent *undue influences* from industry on policy making process?

“Price”/”Pricing” seem to be a forbidden word in these commissioned publications.
Panel discussion

Should the pricing debate for rare disease medicines be better ‘integrated’ with the general debate about unaffordable prices of medicines? Why or why not?

• Many government agencies already have separate ‘rules’ for rare disease medicines, including R&D incentives, regulatory flexibilities, and less restrictive requirements for QALY/ICER etc.
  • Why should these ‘rules’ be different?
  • Have the good intention of these rules been misused? e.g. company pursuing an indication for rare disease in the first instance and then expand the indication to other more common diseases.
Q&A with the audience
February webinar
What went on before, during and after pharmaceutical pricing negotiations: Stories behind closed doors

Where to ask your burning questions?

Comments and suggestions
fairpricing@who.int