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Multi-stakeholder approach to rare disease care in Latin America: focus on Pompe and Fabry diseases

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Introduction and objectives

- A varied landscape exists in terms of legislative and regulatory frameworks for rare diseases (RDs) across Latin America. Despite global efforts to improve RD care,[1] patients in the region face challenges in accessing specialized medicines.
- This study aimed to understand the RD care landscape in Argentina, Brazil, Chile, Colombia, Mexico, Peru, and Uruguay. Specifically, to determine patient access to diagnosis and treatments from a multi-stakeholder perspective, identifying cross-regional best practices translatable to RD care strategies among countries, and provide recommendations on addressing challenges.

Conclusions/recommendations

Challenges	Recommendations
The absence of official patient registries leads to underestimated patient counts, impacting accurate resource allocation.	**Establish regional or national patient registries** that are accurately populated to guide policy, resource allocation, and research.
Health technology assessment (HTA) methodologies are not tailored to RD medicines, affecting accuracy, viability, and efficiency of evaluations.	**Implement differentiated HTA Mechanisms** tailored to RD treatments to promote accurate treatment evaluation, ensure meaningful representation, and facilitate efficient evaluation processes, prioritizing the patient perspective.
Significant delays in RD diagnosis result in treatment initiation delays, affect quality of life, and negatively impact patient outcomes.	**Improve education on RDs for stakeholders**, including healthcare providers (especially at the primary care level), payors, regulatory agencies, and the general public. **Improve access to newborn screening and genetic counseling** to reduce diagnostic delays.
High costs of RD medicines challenge healthcare system budgets and sustainability.	Leverage negotiation approaches that have proven successful in other countries to secure optimal terms and conditions for treatment procurement, such as Uruguay's portfolio scheme and Argentina's risk-sharing for gene therapy. **Establish a specific budget allocation** for RDs, with innovative funding mechanisms, to ensure sustained access to RD treatments. **Prioritize system sustainability** as financial viability is critical to ensuring long-term access to treatments. **Digitalize medical records** to facilitate information sharing and avoid redundancy in care and resources.
As RDs are generally not a national priority, changes in government administration affect the continuity of implemented initiatives.	**Prioritize RDs to ensure continuity** and sustained implementation of RD initiatives across government transitions. **Recognize the importance of PAOs** as a stakeholder with valuable knowledge, insights, and inputs to guide policy.
Absent or outdated clinical practice guidelines (CPGs) for RDs lead to unstandardized care and often limit access.	**Develop local guidelines for RD** through collaboration with local healthcare authorities and medical societies. **Establish physician training programs** to foster adherence to guidelines.

[1]This research is aligned with advancing the objectives of the UN resolution on RDs, which underscores the importance of meeting the needs of those living with RDs as crucial to the 2030 Sustainable Development Goals and the UN declaration, which includes RDs in universal health coverage.

Methods

- Five experts from each country were invited to participate in a virtual task force. Participants included patient organization leaders, physicians, payors, regulators, and policymakers. They were recruited through a stakeholder mapping process and compensated for their time, in line with fair market value.
- Experts were provided with a literature search, agenda, and questions as preparation material for the task force. Seven virtual meetings were conducted (one per country) with the experts to discuss and compile data.
- The literature search was conducted using the terms "rare diseases", "access", "Fabry disease", and "Pompe disease" plus each "Latin America", "Argentina", "Brazil", "Chile", "Colombia", "Mexico", "Peru", and "Uruguay". The search included scientific publications, conference proceedings, local websites, and other gray literature.
- Each task force was moderated to ensure all participants were able to provide input, and comprehensive notes were taken. Each meeting lasted approximately 5 hours.
- Following the meetings, country-level reports were developed incorporating the literature search findings and task force insights.

Results

- A scorecard was developed to rate each country based on ease of access, availability of treatments, and impact of medical societies and patient advocacy organizations (PAOs) on access.

Figure 1. Regional scorecard

Countries	Ease of access to RD medicines	Contribution of medical societies to access	Contribution of PAO to access	Access to Fabry disease treatment in PHS	Access to Pompe disease treatment in PHS
Argentina	Medium, High	Medium	High	High	High
Brazil	Medium, High	Low	High	High	High
Chile	Medium	Low	Medium	High	High
Colombia	Medium, High	Medium	High	High	High
Mexico	Low	Medium	Medium	High	High
Peru	Low	Medium	High	High	Low
Uruguay	Medium	High	High	High	Medium

High
Medium
Low

Ratings are assigned considering each country's RD legislation and practices. For treatments, rating is based on disease recognition, available treatments in the PHS, and sanitary approval for in-country commercialization.
PHS, public healthcare system.

Argentina

Key challenges

1. The extent of RD medicine and healthcare coverage is unclear. Sistema Unico de Reintegro por Gestion de Enfermedades (SURGE) is the reimbursement system for disease management. Insurers obtain partial to no reimbursement with long wait terms. Some treatments for Fabry disease and Pompe disease qualify for reimbursement through SURGE.
2. Treatment interruptions happen primarily because of lack of reimbursement by the health system to the insurers. Considering Argentina's annual inflation to be around 130%, insurers are reluctant to purchase or maintain treatment.
3. While the Administración Nacional de Medicamentos, Alimentos y Tecnología Médica (regulatory agency) has issued regulations that compel those with marketing authorization certificates to report their product's suggested retail price, there is no pricing regulation in Argentina.
4. 58% of the total legal recourses for medicines in the first semester of 2022 were for RD treatments.

Key opportunities

1. Leverage direct negotiation with Obras Sociales (social security) and Private Insurance and strengthen collaboration between the private and public sectors.
2. Engage in regional price negotiations with neighboring countries Uruguay and Chile.
3. Develop additional support services, such as patient support programs, therapeutic adherence monitoring, and complementary added-value services to improve patient access to care.

Case examples

- Argentina guaranteed access to onasemnogene abeparvovec, a gene therapy for spinal muscular atrophy (SMA), regardless of patient health insurance, negotiated under an innovative risk-sharing strategy.
- The Cystic Fibrosis Law 27.552 was approved in 2020, stating that medications in CPGs will be added to the Bank of Special Drugs plan, ensuring access.

Brazil

Key challenges

1. Marketing authorization does not guarantee swift incorporation into the Sistema Único de Saúde (SUS; PHS). Elaprase's case, approved in 2008 but not incorporated by the Comissão Nacional de Incorporação de Tecnologias no Sistema Único de Saúde (CONITEC; regulatory agency) until 2018, exemplifies the time gap.
2. International reference pricing is often used for suggested Câmara de Regulação do Mercado de Medicamentos (CMED; chamber that approves treatment price) prices. This referencing was considered inadequate owing to diverse country budgets and price variations considered in dossier evaluation.
3. In 2019, the Ministry of Health spent R$1.3 billion (~263 million USD) in providing treatments through judicialization, of which R$1.2 billion were for RD treatments.

Key opportunities

1. Streamline treatment incorporation pathway through collaboration with CONITEC for quicker RD treatment inclusion after approval from the Agência Nacional de Vigilância Sanitária (HTA agency) by using the oral presentation space offered to the industry and participating in public consultations. Engage stakeholders to emphasize patient urgency for life-transforming treatments during incorporation processes.
2. The government should engage industry stakeholders to align on more comprehensive contributions to patient access and diagnostic/patient support programs. Consider regulatory mechanisms to encourage industry commitment to access and support initiatives.
3. CMED could use pricing benchmarks from countries that are more economically similar to Brazil for more accurate assessments (including other Latin American countries).
4. The Ministry of Health should ensure continuity of medicine procurement to address treatment delays and interruptions that affect patient outcomes.

Case examples

- Price tends to be the main point of reference when there is not enough evidence to justify the expense during the CONITEC review. Price reductions of treatments for Fabry disease, infantile hemangioma, and an SGLT2 inhibitor for type 2 diabetes mellitus also led to SUS incorporation.
- High-cost Gaucher treatments provided by RD reference center: with adequate vial dosage and storage conditions, patients no longer have to travel to main hospitals to receive treatment, reducing the peripheral access cost to patients and expediting time to access.

Chile

Key challenges

1. Ricarte Soto law was implemented in 2015 to manage the provision of high-cost medications. As of 2023, the law covers 27 diseases, and the decree through which new diseases and technologies will be incorporated has been delayed since 2021.
2. There is no suitable alternative in place for RD treatment reimbursement by the health system. RD treatments not in the Ricarte Soto law are often denied unless indicated by judicialization.
3. Despite no negotiation limitations or restrictions, these do not often take place. Industry has presented many strategies (over 80) to both sectors, public and private, without success.
4. Strengthen HTA framework to improve the assessment process.

Key opportunities

1. Work with PAOs to demonstrate to the Ministry of Health the need to reopen the Ricarte Soto law to provide broader access to treatment.
2. Instituciones de Salud Previsional (private insurers) could purchase drugs from a distributor or directly from manufacturer and engage in negotiations to secure better pricing and payment conditions.

Case examples

- Significant price reductions were achieved owing to the implementation of a new law that allows negotiations between distributors and local pharmacies. The price of fingolimod for multiple sclerosis was reduced by almost 80%.

Colombia

Key challenges

1. The current government proposed a health reform aimed at restructuring the system to eliminate the private Entidad Promotora de Salud (EPS; health insurers of the public system) and centralizing healthcare provision and financing. Although it was revoked by the Senate, there is uncertainty and a lack of confidence in the healthcare system and its payors.
2. Despite having one of the region's most robust legislative frameworks for RDs, implementation issues leave a large gap between what the law states and the reality.
3. Institución Prestadora de Salud (IPS; care-providing institutions) have limited ability to finance high-cost treatments because reimbursement terms with the EPS average >200 days and are often even more delayed.

Key opportunities

1. Collaborate with governmental bodies, medical societies, and PAOs to bridge the gap between legislation and implementation, establish working groups to address challenges, streamline processes, and ensure effective execution of RD-focused policies.
2. Collaborate with IPS and relevant stakeholders to develop financial mechanisms that mitigate reimbursement delays. Explore options such as advance payment systems or financial partnerships to ensure timely access to treatments.
3. Implement procurement strategies that foster supplier diversity, promoting healthy competition and a range of options for RD treatments.

Case examples

- Nusinersen for SMA is one of the most expensive drugs available in Colombia. Owing to its cost, the Ministry of Health asked the Instituto de Evaluación de Tecnologías en Salud (HTA agency) to develop guidelines for its use. These guidelines became a tool for care providers. Funds are transferred directly from the Administrador de Recursos del SGSSS (social security resource administrator) to the health provider, facilitating reimbursement; while this example may serve as a potential model for introducing other high-cost drugs, there are no official channels for this mechanism, and it came after legal demands of treatment and action from PAOs.

Mexico

Key challenges:

1. Mexico lacks specific legislation for RD. The General Health Law outlines the approval process for treatments, without distinct RD differentiation.
2. As of 2015, genetic diseases are not covered through private insurance, impeding patient access to treatments. Patients bear a significant financial burden.
3. Varying clinical practice guidelines by each institution result in unstandardized care.
4. The closure of the Negotiating Commission in 2019 left a void in the price negotiation process. Under the current administration, a "base price" is now established, and institutions must individually negotiate prices.

Key opportunities:

1. Collaborate with local healthcare authorities to develop standardized clinical practice guidelines that promote consistent patient care and equitable drug access.
2. Develop new (or re-establish previous) negotiation mechanisms that ensure transparent drug pricing and improve affordability.
3. The Acquisitions law restricts performance-based risk-sharing agreements. Mechanisms have emerged to overcome limitations, such as maximum price per beneficiary, volume discounts, shared cost arrangements, and additional units (no publicly available examples).

Peru

Key challenges

1. The absence of standardized processes to access high-cost treatments raises challenges in availability and affordability.
2. High importation taxes, particularly the 36% rate imposed after 2001, create significant commercial barriers.
3. The RD law requires the establishment of Advisory Committees by the Instituciones Administradoras de Fondos de Aseguramiento en Salud (health insurers) and by each department to evaluate RD diagnosis and treatment requests. However, only 19 out of 24 committees have been created, with only two active in Lima.
4. Medicine prices significantly impact treatment continuity. While Advisory Committees may grant approval, institutions may deny medicines because of budget constraints, even within Seguro Social de Salud (ESSALUD; social security).
5. As of July 2023, approximately 30 treatments have not been procured despite patients receiving approvals, which is likely due to a lack of assigned responsibility for follow-up, undefined timelines, and unclear agency responsibilities.
6. While a law enabling innovative purchasing mechanisms exists, its implementation is hindered by conflicts with the Law of Acquisitions, which prohibits these.

Key opportunities

1. Most patients living with RD fall under ESSALUD for access to treatment; therefore, this is a key stakeholder for negotiation and procurement of RD treatments.
2. Harmonize regulations to allow price negotiations and innovative financing mechanisms.
3. Complete and implement the RD Multicriteria HTA Manual.
4. Create the outstanding Advisory Committees.

Uruguay

Key challenges

1. There are no specific laws for RD coverage in Uruguay. The decision-making process for treatment reimbursement by the Fondo Nacional de Recursos (FNR; national resource fund) lacks clarity.
2. The FNR requires patients to complete testing to guarantee continuous access to treatment. If these tests are not submitted, treatment is interrupted.

Key opportunities

1. FNR is open to negotiations with industry and is the only purchaser of high-priced medications in the country, and several$innovative purchasing mechanisms have been implemented, including volume-based, portfolio-based, and risk-sharing agreements.
2. Highlight the benefit of continuous treatment access while supporting patient programs that facilitate patient compliance with FNR required testing.

Case examples

- Uruguay has one of the most complete mandatory newborn screening programs in the region, with 19 included diseases, facilitating RD diagnosis.
- A tax exemption was granted in 2020 to encourage supply of agalsidase alfa for patients living with Fabry disease during the pandemic.
- Nusinersen was first introduced to Uruguay by a protective appeal process: "recurso de amparo". In 2022, the "Modifying treatment for SMA program" eliminated the need for a legal recourse.
- In addition, there is evidence of models whereby the FNR pays a fixed monthly fee for a group of drugs for the same disease, with a wide range of patient needs (e.g., breast cancer).

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