

The regulation and adoption of health technologies under Brazil's Unified Health System: barriers to access to medicines for diseases of poverty?

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Abstract *The study aimed to examine the regulation and adoption of health technologies for the diseases of poverty in the Brazil's Unified Health System (SUS). An exploratory, descriptive study was conducted between January and May 2016 consisting of the search and analysis of relevant documents on the websites of Brazil's National Health Surveillance Agency, the U.S. Food and Drug Administration (FDA), the European Medicines Agency (EMA), the National Commission for the Adoption of Technologies by the SUS, and Saúde Legis (the Ministry of Health's Legislation System). The 2014 version of the Brazilian National List of Essential Medicines (RENAME, acronym in Portuguese) contained 132 medicines for diseases of poverty. Over one-third of these (49) had only one national producer, while 24 were not registered in the country. The number of medicines contained in the RENAME dedicated to this group of diseases increased by 46% between 2006 and 2014. Despite advances in the regulation and incorporation of technologies by the SUS, given the lack of market interest and neglect of diseases of poverty, the government has a vital role to play in ensuring access to the best available therapies in order to reduce health inequalities. It therefore follows that Brazil needs to improve the regulation of medicines that do not attract market interest.*

Key words *Pharmaceutical care, Neglected diseases, Product registration, Pharmaceutical preparations, Unified Health System*

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Introduction

The Brazilian constitution provides for universal and equal access to health actions and services. Besides being addressed by complementary legislation, the Brazilian government has adopted the following specific policies to ensure access to pharmaceutical care: the National Medicines Policy (*Política Nacional de Medicamentos*) and the National Pharmaceutical Care Policy (*Política Nacional de Assistência Farmacêutica*).

The Unified Health System (*Sistema Único de Saúde* – SUS) plays a critical role in the “formulation and execution of economic and social policies” aimed at ensuring access to medicines¹, given that this area is deeply influenced by commercial practices and interests that are often in conflict with the public interest.

Government intervention in the market through the SUS to guarantee the quality and safety of medicines produced in the country has been materialized through the creation of the National Health Surveillance Agency (*Agência Nacional de Vigilância Sanitária* - Anvisa) in 1999 and improvements in the legal and regulatory framework².

It is important to stress that Anvisa plays a wide role encompassing the registration and authorization of medicines on the national market, including products that are not necessarily used under the SUS. Currently, the evaluation of health technologies falls within the scope of the National Commission for the Adoption of Technologies by the SUS (*Comissão Nacional de Incorporação de Tecnologias no SUS* - CONITEC), which advises the Ministry of Health on the adoption, exclusion or alteration of health technologies under the SUS.

Established by Law N° 12.401/2011, it could be said that CONITEC is a strategic body within Brazil's public health system when it comes to the evaluation and adoption of technology. Regulated by Decree N° 7.646/2011, the main functions of the commission are to: (i) issue reports on the adoption, exclusion or alteration of health technologies by the SUS and establish or alter clinical protocols and treatment guidelines; (ii) update the National Essential Medicines List (*Relação Nacional de Medicamentos Essenciais* – Rename).

However, divergent opinions exist as to the selection of essential medicines and scope of the Rename. Some authors argue that these and other regulatory measures adopted by the government have helped to promote harmonization between “lists of recommendations” and “funding lists”

by institutionalizing the assessment of efficacy, safety and cost-effectiveness and defining funding responsibilities³, while others claim that the loose application of the essential medicines concept in the definition proposed by the Rename is a step backward and recommend that priorities should be set with due regard to Brazil's disease burden and health concerns⁴.

Another challenge in relation to the regulation and adoption of health technologies is guaranteeing the analysis, registration and availability of products that are of little interest to the pharmaceutical industry or those used for diseases that have few treatment options, such as medicines for rare diseases or illnesses that typically affect vulnerable groups⁵⁻⁷.

The target of numerous studies warning about the lack of investment in drug research, the so-called neglected diseases, or tropical diseases, reflect health inequalities and are today referred to as poverty-related diseases, or simply diseases of poverty, in order to draw attention to the vulnerability dimension of these illnesses⁵⁻⁷.

A review conducted by Pedrique et al.⁸ concerning the period 2000 to 2011 showed that only 37 (4%) of the 850 new therapeutic products approved by the main regulatory agencies around the world were for diseases of poverty, of which 29 were medicines and eight vaccines. Astonishingly, only four of these products were classified as a new chemical entity.

Given that the pharmaceutical industry is primarily oriented towards specific chronic diseases treated with highly profitable drugs, there is an urgent need to increase the availability of incentives to promote the research and development of medicines for diseases of poverty. The government therefore has a vital role to play in reducing health inequalities and ensuring access to the best available therapies, an issue that is rarely addressed in the existing literature^{7,9}.

In light of the above, this article examines the potential barriers to access to medicines for diseases of poverty associated with regulatory processes and the adoption of health technologies and innovations by the SUS and offers suggestions for advancing the health agenda.

Methods

An exploratory descriptive study was conducted consisting of the search and analysis of documents addressing the registration of medicines for treating poverty-related diseases and their

adoption by the SUS. The study comprised five stages undertaken between January and May 2016 as set out below:

Stage 1 consisted of a direct search for normative instruments and national regulations specifically regarding the registration of medicines for diseases of poverty using Anvisa's website and *Saúde Legis* (the Ministry of Health's Health Legislation System), employing the following terms: *doenças da pobreza* (diseases of poverty), *doenças negligenciadas*, (neglected diseases), *medicamentos órfãos* (orphan drugs), and *medicamentos estratégicos* (strategic medicines).

In stage 2, with a view to comparing Brazilian and international regulations, a similar search was conducted using the websites of the U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA).

Stage 3 comprised a search for active records of medicines for diseases of poverty using Anvisa's database and the database of the Pharmaceutical Market Regulatory Chamber (*Câmara de Regulação do Mercado de Medicines* - CMED). The search encompassed all medicines used for the prevention and treatment of diseases and conditions related to poverty included in the Rename 2014.

Stage 4 consisted of a review of medicines used for poverty-related diseases included in the different editions of the Rename (2006, 2008, 2010, 2012, and 2014) in order to gauge the level of inclusion and adoption of these products by the SUS.

In stage 5, we determined the percentage of medicines and technologies for poverty-related diseases adopted by the SUS after the creation of the National Commission for the Adoption of Technologies into the SUS (*Comissão Nacional de Incorporação de Tecnologias no SUS* - CONITEC) by Law N° 12.401/2011. For this purpose, all reports issued by the CONITEC between 2012 and 2015 were analyzed with regard to the technology, requesting party, and final recommendation. In addition, we accessed the commission's website to check for regulations regarding adoption that may affect the submission of applications for inclusion of medicines for diseases of poverty into the SUS.

Since there is a lack of consensus in the literature as to what may be considered a disease of poverty, for the purposes of the present study we used criteria adopted by a previous study based on an adaptation of the classification of diseases of the World Health Organization (WHO) and Doctors Without Borders (*Médecins Sans Fron-*

tières - MSF), which categorized diseases as follows: (i) global noncommunicable diseases, (ii) global communicable diseases, and (iii) poverty-related diseases^{5,10,11}.

Category (iii) was subdivided according to the characteristics of poverty-related diseases: (i) vaccine-preventable infectious diseases; (ii) nonvaccine-preventable infectious diseases; (iii) other conditions and diseases of poverty.

Finally, the data was tabulated and organized into spreadsheets using Microsoft Office Excel 2010.

Results and Discussion

The authorization and commercialization of medicines and their distribution throughout the public health system is, without doubt, a major component of social responsibility. A number of historic cases have shown the risks associated with the use of potentially unsafe medicines, dating back to preregulatory periods and phocomelia caused by thalidomide in the 1950s and 1960s and, more recently, the abortifacient property of misoprostol, discovered after its commercialization was authorized in the 1990s, and the recent withdrawal of rofecoxib due to its association with an increased risk of coronary heart disease, which was not detected prior to its registration, despite modern regulatory criteria¹².

In light of this, the Brazilian government is making efforts to modernize regulatory mechanisms in order to ensure the efficacy and safety of medicines authorized by Anvisa and those adopted by the SUS based on the recommendations of Conitec.

However, it is important to consider that, in the case of technologies that attract little investment and commercial interest, certain regulatory parameters may act as an impediment to ensuring access to essential medicines and thus aggravate the scarcity of treatments for diseases that are to a greater or lesser extent neglected. The following sections outline some of the barriers to access to medicines for diseases of poverty and offer some suggestions for advancing the health agenda.

Regulations and incentives for medicines that do not attract commercial interest: measures adopted outside Brazil

Conditions neglected by the pharmaceutical industry must not be equally neglected by regula-

tory bodies. For this reason, agencies such as the FDA and EMA have developed specific regulations to encourage research and development in this area with specific emphasis on the so-called “orphan drugs”, developed specifically to treat rare diseases, and medicines and formulations for pediatric use^{13,14}.

It therefore follows that Brazil needs to improve the regulatory framework for conditions that are not attractive to the pharmaceutical industry, be they poverty-related diseases, rare diseases or childhood diseases. Chart 1 shows the differences between the regulations of the three agencies and reveals a number of gaps in Brazil’s regulatory framework.

Specific legislation to stimulate the development of orphan drugs that would otherwise not attract commercial interest was first adopted by the United States in 1983, through the Orphan Drug Act, and later by Japan (1993), Australia (1997), and the European Parliament (1999). In 2007, the FDA and EMA adopted common forms and procedures for orphan medicinal product designation, thus facilitating the application and review process, while maintaining separate decision making procedures¹³.

According to international regulatory authorities, for a drug to be orphan: (i) it must be intended for the diagnosis, prevention or treatment of a life-threatening or disabling disease; (ii) no satisfactory alternative therapy exists for the disease in question or it represents a meaningful therapeutic benefit over existing treat-

ments; (iii) the prevalence of the disease in question should be relatively low, affecting no more than 5/10,000 population in the European Union and 6.3/10,000 in the USA^{15,16}.

Although orphan drugs do not specifically address poverty-related diseases, it is evident that their designation has the potential to contribute to the development of medicines for a large part of these illnesses. A prime example is Chagas disease, an extremely debilitating illness typical to Latin America. The only drug available for the treatment of Chagas disease is not very effective in patients who present the severe form of the disease and ineffective for the chronic form of the disease. Currently, the prevalence of Chagas in its severe form is in line with the criteria for rare diseases (0.061 cases/100,000 population), although the prevalence of the chronic form is high due to previous epidemiological scenarios¹⁷.

The existence of specific FDA regulations has also led to the designation of medicines specifically designed for diseases that affect vulnerable groups in the United States. The same cannot be said for Brazil, despite the higher prevalence of such diseases and therefore potentially larger consumer market. The following paragraphs describe two such examples.

Miltefosine, the only orally administered medication for treating leishmaniasis, was granted orphan drug designation by the FDA in 2013, even though cases in the US are normally related to migration flows and restricted to the States of Texas and Oklahoma. In Brazil the drug remains

Chart 1. A comparison between the regulations and incentives of ANVISA, the FDA, and the EMA.

Regulatory incentives	ANVISA	FDA	EMA
Specific regulations for registering orphan drugs and pediatric medicines	No	Yes	Yes
Regulatory agency provides assistance in the elaboration of research protocols	No	Yes	Yes
Reduced fees and tax credits	No	Yes	Yes
Regulatory agencies have common assessment processes	No	Yes	Yes
Mechanisms for expanding market exclusivity	No	Yes	Yes
Government commissions define priority medicines, regulations, and incentives	No	Yes	Yes
Possibility of “conditional authorization” for medicines that require further research to elucidate evidence	No*	Yes	Yes
Regulations for importing nonregistered medicines into the country under special conditions	Yes	Yes	Yes
Regulations for accelerating the assessment of medicines that are of interest to the public health service (fast track)	Yes	Yes	Yes

* It is important to note that specific regulations apply to the expanded access program, compassionate use and post-study provision of medicines, in accordance with Resolution RDC N° 38 of 12 August, 2013.

Source: fda.gov; ema.europa.eu; anvisa.gov.br; Parra¹³; Seoane-Vazquez *et al.*¹⁴.

unregistered and the medication is not imported for use in the National Leishmaniasis Control Program (*Programa Nacional de Controle das Leishmanioses*), despite the fact that 20,000 cases of the cutaneous form and around 4,000 cases of the disease in its visceral form are reported annually. It is important to highlight that miltefosine is included on the WHO's essential medicines list and in the Pan American Health Organization's guidelines, *Leishmaniasis in the Americas: Recommendations for Treatment (Leishmaniasis en las Américas: recomendaciones para el tratamiento)*^{16,18}.

Another example is hydroxyurea, used in the treatment of sickle cell disease, a congenital disorder that affects between 25,000 and 50,000 Brazilians, particularly black people and socially vulnerable groups. Hydroxyurea (formulation: 200 mg, 300 mg, and 400 mg capsules) was granted designation as an orphan drug by the FDA and EMA almost a decade ago, despite only an estimated 22,000 patients in the whole of Europe. In Brazil, only the 500 mg capsule is registered and its indication is restricted to certain types of cancer. The funding of this medication and its use on the SUS in the treatment of sickle cell disease is regulated on an off-label basis^{19,20}.

Seoane-Vazquez et al.¹⁴ show that the incentives provided by the FDA to stimulate the development of drugs that attract little industry interest resulted in 322 new approvals between 1983 and 2007. The study cited the following successful support mechanisms: (i) grants awarded to academic-based researchers; (ii) 50% tax credit for costs incurred during the clinical testing phase; and (iii) a seven-year period of marketing exclusivity granted upon approval of a drug.

Similar support mechanisms were also adopted by the EMA, notably the provision of an additional two years of market exclusivity for conducting pediatric studies, regardless of whether or not they result in an additional indication for this group²⁰.

Some of the approved products received a so-called "conditional authorization", where the applicant is given a short period of time to complete ongoing studies or conduct new studies with a view to granting final approval. Certain scholars suggest that these mechanisms may result in authorizations based on low quality clinical evidence and spur manufacturers to attempt to introduce medicines into the market through these fast track mechanisms, despite questionable justifications. Currently, almost 25% of the products approved by the EMA are classified

as orphans. However, the approval success rate (62.9%) for products that take this route is lower than that of nonorphan drugs (70%)^{13,21}.

Registration and the sustainability of the production of medicines for more vulnerable groups – an overview

Some authors have discussed the difficulties experienced by regulatory agencies in ensuring that medicines that do not strictly provide meaningful therapeutic benefit to patients over existing treatments are not approved. This is also a concern in Brazil, as Botelho et al.²² have demonstrated. The authors found that of 159 new medicines approved between 2003 and 2013 only 28 (17.6%) were considered to be important therapeutic innovations.

Furthermore, it is important to note that regulatory mechanisms have limited capacity to strike a balance between the numbers of different classes of medicinal products that are approved. Certain medicines whose use is authorized under the SUS have a limited number of manufacturers despite having secured funding.

An analysis of the products included on the Rename 2014 shows that there are 120 medicines that can be used for the prevention and treatment of diseases and conditions associated with poverty. Despite the existence of established funding mechanisms for all of these products, there are on average only three registered manufacturers for each medicine. Over one-third (41) are produced by only one national manufacturer, generating the risk of potential drug shortages if there are any setbacks in regulatory or manufacturing processes. An even greater concern is the fact that 23 of these medicines are not registered in the country, a large part of which have to be acquired by the Ministry of Health through international health organizations. These two situations account for 53.3% (64) of the medicines used for these diseases (Graph 1).

The compounding of medications that are not registered in the country does not seem to be an alternative facilitated by the agency, since, strictly speaking, according to the provisions of the resolution RDC N° 204/2006, "the importation and commercialization of pharmaceutical inputs destined for the manufacturing of medicines whose therapeutic efficacy has not been assessed by Anvisa is prohibited". It is not clear, however, whether prior assessment refers to discontinued products, a specific assessment of the input or an active registration²³.

An example of the above situation is Anvisa's response to an inquiry about the use of chloral hydrate, widely used for sedation in children. The agency interpreted that, despite being on the list of medicines subject to special controls, the absence of a registered medicine containing this active ingredient in the country means that "the importation of the input is not authorized" for preparation in pharmacies^{23,24}.

The number of registered medicines for global noncommunicable diseases included under Brazil's Popular Pharmacy Program (*Programa Farmácia Popular*), together with the presence of 31 manufacturers of antihypertensive drugs and 29 manufacturers of antidiabetic drugs, represents a stark contrast and gives rise to uncertainty regarding the sustainability of medicines for diseases of poverty.

When it comes to research, the pharmaceutical industry's preference for certain diseases over others is notorious^{25,26}, and the lack of incentives provided by the regulations and bureaucratic hurdles are likely to make this imbalance even more acute.

Incorporation of medicines for diseases of poverty into the SUS list

Brazil's essential medicines policies have led to significant advances in the provision of multiple treatment options over recent years, as can be seen in Table 1. The number of medicines included on the Rename dedicated to this group of dis-

eases and conditions increased by 53% between 2006 and 2014.

In line with international trends, the ongoing inclusion of medicines for diseases of poverty into the national list is without doubt a decisive strategy in improving access to treatment of diseases that have few adequate treatment alternatives. Cohen et al.²⁷ identified 46 new medicines for neglected diseases launched between 1975 and 1999, 85% of which are on the WHO Model List of Essential Medicines. Between 2000 and 2009, 26 new medicines and vaccines for this group of diseases were commercialized, half of which are included on the WHO list.

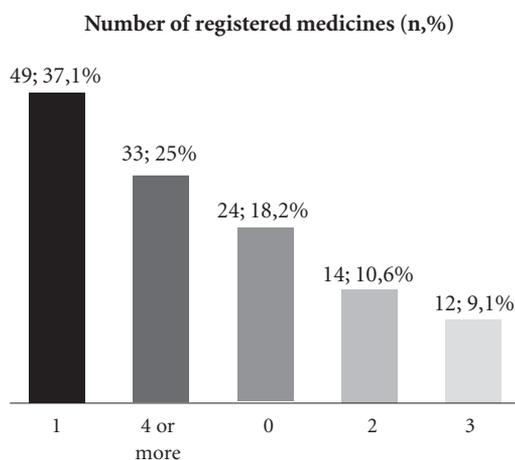
Brazil has a tradition of enabling access to these technologies. Perhaps the best example is its long-running vaccine program. Over the last 40 years, the program has provided 100% of the vaccines recommended by the WHO for diseases found in Brazil, accounting for 20 of the items on the latest edition of the essential medicine list (Rename 2014).

The wide vaccination coverage achieved over the last decade – over 90% coverage for the majority of child vaccines administered throughout a network of over 35,000 vaccination centers – is the result of a health policy that is recognized as a reference for many countries that have yet to achieve the same level of access. Despite progress in terms of access to essential medicines, one in every five African children does not have access to vaccines and only nine countries register coverage rates^{28,29}.

The technology assessment agenda and diseases of poverty

The analysis of the recommendation reports produced by CONITEC shows that 131 of the 162 recommendations issued between 2012 and 2015 were related to global noncommunicable diseases, accounting for 81% of the demands assessed by the commission during this period (Graph 2).

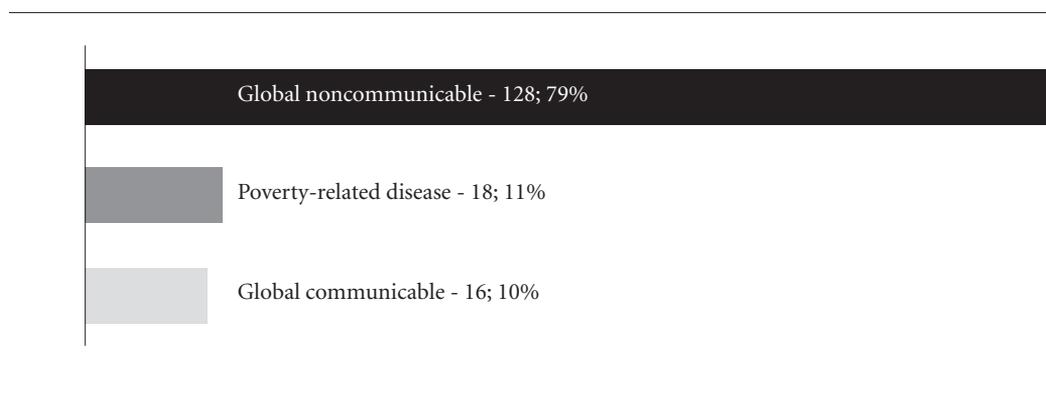
The predominance of recommendations related to global noncommunicable diseases can be explained by the methods and tendencies of the health technology assessment process, which are oriented towards high technology and innovations and are not very open to soft and low-cost technologies. In Brazil, market pressure for innovations together with a phenomenon known as the "judicialization" of health continually impinge upon government budgets and deepen the dilemma between the principles of comprehen-



Graphic 1. Number of medicines for diseases of poverty registered by ANVISA (n = 132).

Table 1. Number of medicines and other technologies for diseases of poverty contained in the different editions of the RENAME.

Group	RENAME 2006	RENAME 2008	RENAME 2010	RENAME 2012	RENAME 2014	Main diseases and conditions
Immunopreventable Infectious Diseases	15	16	16	25	28	Mumps, Diphtheria, Yellow Fever, Meningitis, Poliomyelitis, Measles, Rabies, Rubella, Chickenpox.
Nonimmunopreventable Infectious Diseases	57	57	66	77	79	Accidents with Venomous Animals, Chagas Disease, Dengue, Acute Diarrhea, Blue Disease, Geo-helminth Infection, Hansen's disease, Leishmaniasis, Malaria, Tuberculosis
Other Diseases of poverty	6	9	9	11	13	Sickle cell disease, Nutrient Deficiencies, Problems Caused by Sexual Violence
Total	78	82	91	113	120	--

**Graphic 2.** Number of recommendations issued by CONITEC during the period 2012 to 2015, classified by type of disease.

siveness and equity within the public health service³⁰.

The large proportion of applications from the pharmaceutical industry, accounting for 40.7% (66) of the reports, exemplifies the market pressure suffered by the SUS. The judiciary and health associations accounted for only 4.3% (7) of the requesting parties during the period studied. Efforts are being made to increase the number of requests from entities linked to the SUS (Ministry of Health programs, state and municipal health departments) without affecting the application process, criteria and transparency of the reviews carried out by CONITEC and maintaining working standards that are comparable to international standards³¹.

The assessment of technologies for global communicable diseases accounted for 10% of applications and were basically centered around two specific themes: hepatitis and HIV, which accounted for 13 of the 16 requests reviewed by the commission. The characteristically high degree of innovation and strong history of specific programs and exclusive care networks associated with these diseases heighten market pressure for the rapid ongoing adoption of new medicines by the SUS and inclusion on international essential medicine lists^{32,33}.

Although in smaller numbers, 11% of the reports issued during the study period contained decisions on medicines and other technologies for poverty-related diseases. Of the 18 recom-

mendations, 15 were related to medicines, two to diagnostic tests, and one to health procedures. Chart 2 shows these recommendations in greater detail.

Given the lack of interest on the part of the pharmaceutical industry, these requests are essentially made by the Ministry of Health, the requesting party in 86% (13) of the above cases. Requests for incorporating or expanding the use of the above medications were approved in 80% (12) of the cases.

It is evident therefore that few approved products are effectively new, since the majority of applications are requests to widen the use of medicines already used for other diseases or to make small modifications in the treatment regimen. However, certain products deserve to be highlighted for their role in enhancing care provision.

Two vaccines were adopted by the SUS during the study period, one of which was a tetraviral vaccine included in immunization schedules for children that replaced a triple vaccine by adding protection against chickenpox. Another notable inclusion was a micronutrient supplement used to combat anemia in school-age children and help promote growth and development. The incorporation of oral penicillin to help prevent infections in children with sickle cell disease is another advance, thus contributing to improving quality of life among these patients³⁴⁻³⁶.

Although not strictly speaking an innovation or significant improvement, widening the coverage of prophylaxis by approving its use in the treatment of Hansen's disease, leishmaniasis, whooping cough and spotted fever also has the potential to ensure access to treatment. Three

Table 2. Recommendation reports issued by CONTEC related to medicines and technologies for diseases of poverty (2012-2015).

Group	Recommendations (n=15)	Report and main diseases and conditions
Immunopreventable Infectious Diseases	03	Report 46 - Acellular Pertussis and Tetanus Vaccine Adsorbed - dTpa – for the vaccination of pregnant women Report 21 - Tetraviral vaccine (chickenpox, measles, mumps and rubella) Report 131 - Azithromycin 250mg for treatment and chemoprophylaxis of pertussis
Nonimmunopreventable Infectious Diseases	07	Report 96 - Doxycycline for injection and o chloramphenicol suspension for Brazilian spotted fever and other types of rickettsiosis Report 150 - Benzathine penicillin for preventing congenital syphilis Report 165 - Chemoprophylaxis of contacts of patients with Hansen's disease with rifampicin in single dose Report 157 - Doxycycline 100mg tablets for treating syphilis Report 153 - Ceftriaxone 500mg for injection for treating syphilis Report 154 - Ceftriaxone 500mg for injection for treating ciprofloxacin resistant gonorrhea Report 199 - Pentoxifylline 400mg combined with antimony for treating cutaneous mucous Leishmaniasis
Other Diseases of Poverty	05	Report 130 - Powdered food supplement – NutriSUS with multiple micronutrients Report 57 - Hydroxyurea for children with sickle cell disease Report 56 - Oral penicillin for prophylaxis in children aged under 5 years with sickle cell disease Report 137 - Risperidone for treating cocaine / crack dependence Report 147 - Erythropoietin for treating sickle cell disease

recommendations dealt with alternatives for the treatment of syphilis, given the penicillin shortage that occurred in the country, a worrying situation that was the subject of a public hearing in the National Congress in 2015 and led the Ministry of Health to pass access prioritization measures and purchase penicillin on the international market^{37,38}.

The requirements for the submission of evidence may pose an obstacle to applications related to diseases of poverty in view of the dearth of investment in research and development and the frequent lack of quality of scientific evidence in comparison to high-cost innovative technologies given that focus of global scientific evidence production are chronic diseases such as cancer, with limited regard to developing countries and tackling common diseases in this part of the world³⁹.

Despite CONITEC guidance on admissible documents and mechanisms to reduce applications for products that are noncompliant with the legislation, formally, there is no specific application process or regulations governing the review of products with little commercial interest, which means the submission of applications for this type of product, particularly by pharmaceutical laboratories, is in practice not actively encouraged⁴⁰.

The fact that prior registration by Anvisa is a requirement may be one of the main obstacles to the submission of applications by pharmaceutical laboratories since, as mentioned above, in addition to the regulatory barriers to medicines in this country, from a strategic viewpoint, companies are unlikely to make an application for registration without being certain that the product will be absorbed by national health programs that tackle diseases such as tuberculosis, malaria, Hansen's disease, and leishmaniasis and are characterized by historically centralized funding and exclusive access to treatment under the SUS.

Certain products for diseases of poverty that have been launched over recent years by the pharmaceutical industry are already included on some country lists but have yet to be submitted for evaluation by the SUS, such as miltefosine for leishmaniasis, bedaquiline for tuberculosis, artemolane + piperazine for malaria, and even new soluble formulations of benznidazole for Chagas disease, all of which are not registered in Brazil.

The alternative route to prior registration seems to be review via the internal demand of the Ministry of Health, since five of the products requested for these diseases are not registered and would need to go through the import process via

an international body to ensure their availability on the SUS.

There are three underlying reasons behind this "technological negligence": (i) the small number of studies considering diseases of poverty, which consequently leads to fewer innovations; (ii) limited mobilization of the pharmaceutical industry and society to request the incorporation or review of treatments for these types of disease; and (iii) the health technology evaluation process is not adapted to cater for low-cost technologies and diseases of poverty.

A proactive stance in fostering the review of such products would be likely to result in increased access to essential medicines and ensure more effective treatment of diseases that affect unempowered people, who are less able to put pressure on the health system. One proposal to promote a more equitable review of technologies centers on the promotion by the SUS of "technology horizon scanning" of emerging innovations and technologies for poverty-related diseases.

Vital et al.⁴¹ suggest that the adoption of effective methods for technology horizon scanning by the Ministry of Health would help prioritize new and emerging health technologies for the SUS and inform investment in the research and development of medicines that address the country's needs.

Final considerations

The creation of Anvisa in 1999, and CONITEC in 2011, reflect the evolution of public policies that have driven improvements in the provision of health care services by the SUS. However, the present study reveals the need to further advance the regulation of medicines that do not attract commercial interest. The current regulatory process poses a number of barriers to access to technologies for vulnerable groups. Furthermore, to ensure access to full and effective treatment, there is an overriding need to improve mechanisms for evaluating health technologies and encourage entities linked to the SUS to submit applications to CONITEC for the review of products and innovations for diseases of poverty.

A limitation of this study is the classification adopted for diseases of poverty, which, depending on the theoretical framework and the definition employed, can alter the scope of diseases and, therefore, the information being analyzed.

Finally, It is important to stress that the health agenda encompassing diseases of poverty

deserves particular attention and special status for state funding, be it in the area of research and development, medicine production, improving access to technologies already adopted by the SUS, or the creation of an effective legal and health framework.

Collaborations

RS Santana was responsible for study conception, data collection and analysis, and discussing and drafting the article. EO Lupatini collaborated in the critical analysis, drafting and revision of the text. SN Leite supervised the study and contributed to the critical analysis, drafting and revision of the text.

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