RBFHSS
Revista Brasileira de Farmácia Hospitalar e Serviços de Saúde

Editorial

Medicines pricing and reimbursement: innovation, competitiveness, and access

Precificação e incorporação de medicamentos: inovação, competitividade e acesso

Adriana Mitsue IVAMA-BRUMMELL, Daniella PINGRET-KIPMAN, Claudia Serpa OSORIO-DE-CASTRO, Jaime ESPÍN, Vania Cristina CANUTO-SANTOS, Romilson de Almeida VOLOTÃO, Augusto Afonso GUERRA-JUNIOR, Gabriela Bittencourt MOSEGUI
DOI: 10.30968/rbfhss.2022.131.0679

Access to medicines is a key component for ensuring the universal right to health and for "Promoting health throughout the life cycle and universal health coverage (UHC)", one of the Sustainable Development Goals (SDG). It accounts for one of the main health expenditures. Most new medicines, which are increasingly expensive, do not always offer added therapeutic benefits in relation to existing options, nor are the benefits proportional to their high prices.[1] At the same time, incentives to maintain old, safe and effective medicines on the market may not be present.

Figure 1. Pricing and reimbursement and the correspondence between reimbursement and "incorporação".

The Drug Market Regulation Chamber (CMED) authorises the maximum prices of medicines, a mandatory requirement for commercialisation in Brazil. New medicines with added therapeutic value cannot be more expensive than the same medicine in the reference countries (external reference pricing, ERP). For drugs without added therapeutic benefit, the maximum price should be the lowest between the ERP and the drugs authorised for the treatment of the same condition (internal reference pricing, IRP).[2]

The National Committee for Health Technology Incorporation in the SUS (Conitec) considers scientific evidence, economic evaluation (verifying if the analysed technology is more clinically advantageous than the existing alternatives) and, generally, its budget impact. Once these issues are assessed, a technology can be or not incorporated into the SUS.

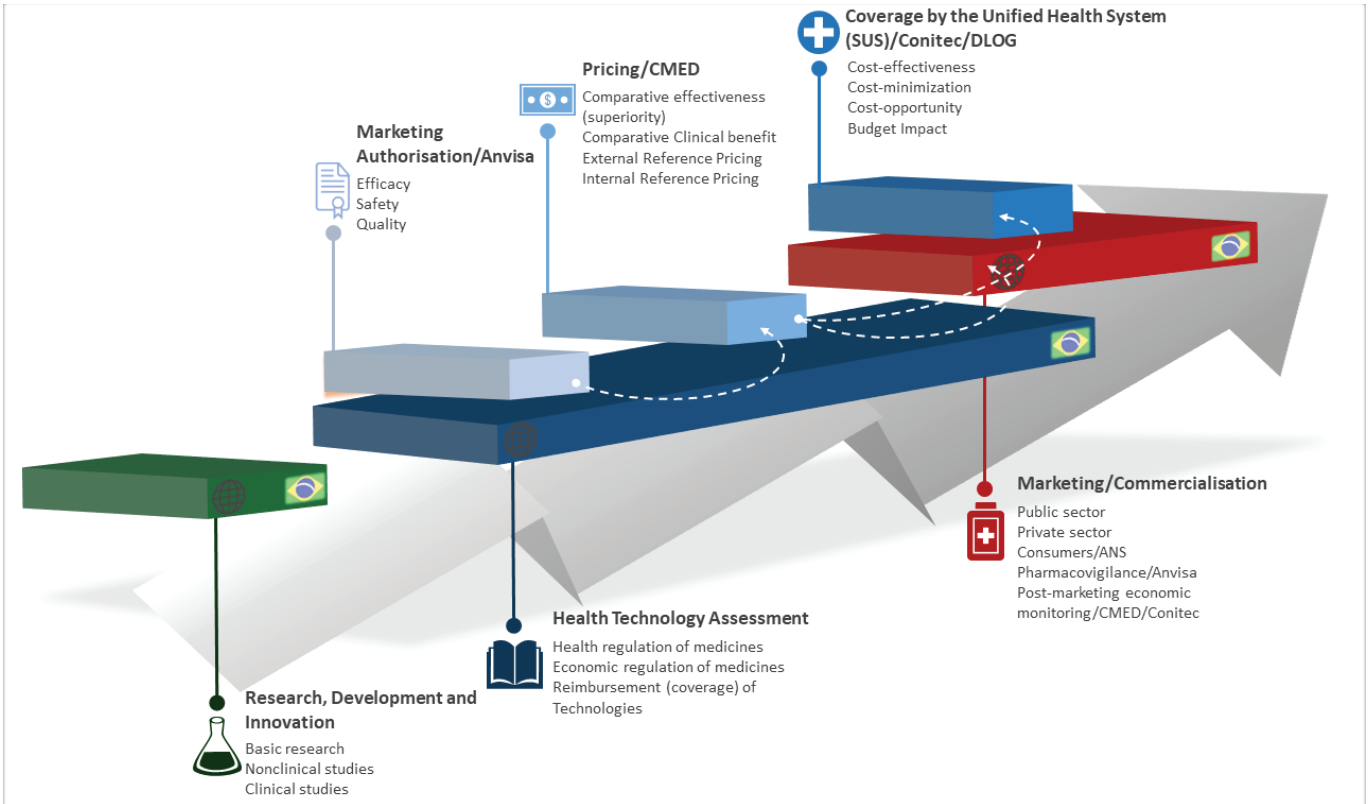
The Pharmaceutical Pricing and Reimbursement Information (PPRI) network Glossary, defines reimbursement as: Coverage of the cost of reimbursable medicines by a public payer [social health insurance/national health system (NHS)].[3] In the Brazilian context, the term reimbursement corresponds to *incorporação* (incorporation), indicating the uptaking or coverage of medicines by the Brazilian Unified Health System (*Sistema Único de Saúde*, SUS).

Health systems are facing challenges to achieve their goals, such as ensuring access to these technologies in a timely and sustainable manner, given the inelasticity of demand. These challenges include limited resources, inequity and ethical dilemmas, regarding individual and collective rights, among others.[1] Thereby, pricing and reimbursement (Figure 1) are important steps in the medicine life cycle (Figure 2).[2-4]

The pharmaceutical sector is highly profitable. Since 2009, global pharmaceutical revenue has been growing steadily, reaching $1.3 trillion in 2020, and is expected to exceed $1.6 trillion in 2025, with annual growth forecast of 3% to 6% over the next five years.[5] In 2019, pharmaceutical revenue in Brazil was $37.7 billion dollars in purchasing power parity (PPP), with 5.3 billion packages of 5,897 products, 1,935 active ingredients or fixed dose combinations in 13,888 packagings.[6,7] The Brazilian Unified Health System (*Sistema Único de Saúde,* SUS) witnessed a variation in medicines expenditure, from around $6.3 billion in 2010 to $8.2 billion in 2016.[8] Public pharmaceutical expenditure represented 0.1% of Gross Domestic Product (GDP), while private pharmaceutical expenditure corresponded to 1.5% of GDP (30% of the family health expenditure).[9] In this context, public policies and pricing and reimbursement mechanisms must encourage innovation and competitiveness and, at the same time, ensure access to medicines and technologies that really matters for those who need them.[10,11]

Rua Vergueiro, 1855 - 12° andar
Vila Mariana - São Paulo - SP, Brazil
CEP 04101-000 - Tel./Fax: (11) 5083-4297
atendimento@sbrafh.org.br/www.sbrafh.org.br

Figure 2. Medicines' life cycle in Brazil.



ANS: Private Health Insurance and Plans; Anvisa: Brazilian Health Regulatory Agency; CMED: Drug Market Regulation Chamber; Conitec: National Committee for Health Technology Incorporation to the Unified Health System; DLOG: Logistics Department/Ministry of Health; SCMED: Executive secretariat of the Drug Market Regulation Chamber; SUS: Unified Health System.

Adapted from: Ivama-Brummell AM, Ronchini MAK, Pingret-Kipman D, *et al*. with the authors' permission.[4]

In this editorial, we present a special series, organised by invitation of the Brazilian Journal of Hospital Pharmacy and Health Services (RBFHSS), whose objective is "to characterise the panorama of medicines pricing and reimbursement in Brazil and other countries, to present and discuss its implementation, effects, gaps and opportunities for improvement, from the perspective of experts and different stakeholders". Along the next issues, case studies carried out by experts from different countries will be published, outlining pricing and reimbursement policies in the context of their respective health systems, considering the life cycle of medicines. We also intend to explore the intersection with themes such as health litigation, the importance of international cooperation and networking, education of health professionals and different perspectives, such as managers, health professionals, academia, among others.

Defining pricing and reimbursement

As social goods, medicines have peculiar features. There are some market failures, as it is known in economic language. It can include a possible gap between who chooses the medicine (prescriber), the user (patient) and who finances it, the SUS, generating an agency-related problem. There are also information asymmetries, such as, differences in information (and knowledge) among stakeholders (researcher, manufacturer, prescriber, pharmacist and user), among others.[12] Addressing these market failures, as well as improving the sustainability and access to this market, justify regulation.[12] There are also different approaches from the value point of view. For the industry, there is generally no connection or proportionality between cost, added therapeutic benefit and price, exploring the "value" of these therapies according to "willingness to pay". Policy makers, managers and users normally consider value from the perspective of "value for money".[13]

To enter the Brazilian market, medicines must have marketing authorisation by the Brazilian Health Regulatory Agency (Anvisa) and maximum price authorised by the Drug Market Regulation Chamber (CMED), referred here as pricing (Figure 1). The economic regulation of medicines in Brazil aims to guarantee the population's access to these goods and, at the same time, the competitiveness of the pharmaceutical sector.[14] In its 20 years of existence, this regulatory framework has had important achievements, but gaps and opportunities for improvement also exist. For example, pricing regulation is carried out at market entry, not always considering market dynamics and the medicine's life cycle neither new evidence.

The reimbursement or uptake (Figure 1), exclusion or changes of health technologies, as well as the development and amendments of Clinical Guidelines- PCDT in the SUS, are carried out by the Ministry of Health (MS) with the assistance of the National Committee for Health Technology Incorporation in the SUS (Conitec), which celebrated its tenth anniversary in 2021.[15] Anvisa, CMED and Conitec have different roles, but these are complementary and contribute to guaranteeing access and achieving the objectives and principles of the SUS.

In 2019, 59.7 million (28.5%) of the Brazilian population was covered by private health or dental insurance.[16] Some medicines and other health technologies are covered by private health insurance, including treatments like those used in oncology or rheumatology. This market is regulated by Private Health Insurance and Plans (ANS) as well as the list of medicines and technologies covered. Medicines prices covered cannot be charged over the CMED ceiling.

How do pricing and reimbursement impact the daily practice of Pharmacy?

Access to medicines is a complex phenomenon (Figure 2). In 1999, one of the biggest problems in Brazil were the high prices, prices were not regulated, and generics were not available. A treatment with branded ciprofloxacin 500mg corresponded to 25 days of minimum wage. After the generic policy was established and prices regulated by CMED, prices fell.[2,17] The same treatment with generics could be purchased with 1.9 days of minimum wage in 2012 and today, costs the equivalent to 0.5 days of a minimum wage (Figure 3).[18–20]

Figure 3. Affordability and availability: example of the treatment with ciprofloxacin

In 1998, according to the Medicines Parliamentary Inquiry Committee (CPI) prices of medicines were high and with huge variations. According to the price in this report, 14 tablets of 500mg brand ciprofloxacin were equivalent to 25 days of minimum wage. In 1999, a generic policy was established by law.[17] The prices of generic drugs are regulated by CMED (Resolution 02/2004), corresponding to a maximum of 65% of the price of the reference medicine.[2] In 2012, the same treatment was equivalent of 13.7 days of a minimum wage for a branded medicine, 2.2 days for a branded generic (*similar*) and 1.9 for a generic in a private pharmacy in the South of Brazil.[18] In 2021, according the maximum authorised price, the same treatment could be purchased with the equivalent to 0.5 day of a minimum wage. According to the price list of CMED from July 2021, there were 44 presentations of ciprofloxacin 500mg, 2 branded, 27 generics and 15 branded generics (*similares*).[20]

In the Covid-19 pandemic, we see issues related to both access to drugs and medical devices, such as price increases, shortages, and stock outs. There are huge research and development efforts with international cooperation and solidarity never seen in history, such as the ACT Accelerator (Access to Covid-19 Tools Accelerator), C-TAP (Covid-19 Technology Access Pool) and Covax Facility, an alliance to accelerate the development, production and distribution of vaccines, in order to ensure access to participating countries, facilitated by the World Health Organization (WHO) and other international organizations, in addition to technology transfer partnerships. Despite this, unfortunately, there are limitations and inequality of access, mainly concentrated in richer countries with greater technological domain.[21] At the time of writing this editorial, of the 147 vaccines for Covid-19 in clinical development, prices of 26 had been identified in the international market, between US$1.92 and US$40.0, of which five are authorised for use in Brazil, four with marketing authorisation (Pfizer, Astrazeneca/Fiocruz, Sinovac/Butantan and Janssen-Cilag/Johnson) and one with import authorisation, under controlled conditions (Gamaleya/União Química).[22,23] However, the existence of vaccines is not enough, as they must be accessible, economically viable, safe and used effectively in the greatest number of users as possible.[21]

In 2020, the gene therapy onasemnogen abeparvovec was approved in Brazil. The most expensive therapy in the world, with prices on the international market of approximately US$2.1 million per patient, being indicated for the treatment of spinal muscular atrophy (SMA).In December 2020, in the absence of evidence of added therapeutic benefit over existing therapeutic alternatives, CMED approved a maximum provisional price that was 77% lower than the manufacturer's intended price (US$ 531,173.2). Nevertheless, the company appealed the decision and decided not to commercialise the medicine by the approved price. In Brazil, this therapy has been object of numerous lawsuits and the Ministry of Health spent US$ 79 million to fund the treatment of 46 patients by October 2021, generating a huge opportunity cost to the Brazilian Unified Health System (SUS). This resources would be more than enough to treat all patients with SMA per year at the maximum price approved by CMED for government procurement (PMVG) or to treat nearly 6 thousand patients with specialty drugs.[24]

In 2022, the Ministerial Council of CMED partially granted the company's appeal and authorised a maximum price of onasemnogene abeparvovec in Brazil to USD 1.3 million, more than twice the price previously approved.[25] On March 8, 2022, Novartis launched onasemnogene abeparvovec in Brazil.[26] There has been little questioning as to why the product is so expensive, whether the price is fair or even proportional to the therapeutic benefits and uncertainties about its safety and effectiveness in the long term. These are just a few examples of the complexity and enormous challenges faced by health systems and the importance of pricing and drug reimbursement in promoting access.

We believe that this series of articles will contribute to producing and disseminating knowledge, identifying best practices, and stimulating debate, not only from health, but also from economics, law and other related areas, on the role, importance and need of pricing and reimbursement in a context of an immense therapeutic arsenal and limited resources, both in Brazil and in other countries. Therefore, this series can contribute to inform policy and decision making, encourage the formation of opinions of professionals and students, and strengthen social participation.

Funding sources

No funding was received for the writing for this manuscript.

Conflict of interest statement

The authors declare that there are no conflicts of interest regarding this article.

Acknowledgement

The authors thank Priscila Gebrim Louly from the Department of Management and Incorporation of Health Technology and Health Innovation (DGITS), Secretariat of Science, Technology, Innovation and Health Strategic Supplies (SCTIE); Executive Secretariat of the National Committee for Health Technology Incorporation at SUS (CONITEC), Ministry of Health of Brazil; Huseyin Naci from the Department of Health Policy, London School of Economics and Political Science (LSE), United Kingdom and Elisângela da Costa Lima, from the Observatory of Medicines Surveillance and Use, Pharmacy School, Federal University of Rio de Janeiro, for their valuable contribution in reviewing an earlier version of the manuscript.

References

1. World Health Organisation (WHO). Towards Access 2030. 2017 Accessed on: 1 Sep 2021. Available in: https://www.who.int/medicines/publications/Towards_Access_2030_Final.pdf?ua=1.
2. Brasil. Drug Market Regulation Chamber (CMED). Resolution CMED no. 2, 5 March 2004 (consolidated version). 2004.
3. Pharmaceutical Pricing and Reimbursement Information (PPRI). Reimbursement (Funding). 2021 Accessed on: 14 Aug 2021. Available in: https://ppri.goeg.at/node/945.
4. Ivama-Brummell AM, Ronchini MAK, Pingret-Kipman D, *et al.* Brazil: Pharmaceutical pricing and reimbursement policies. 4th PPRI Conf Med Access Challenge Vienna, Austria 23-24 October, 2019 Country poster book. Vienna: PPRI/GOEG; 2019. p. 6.
5. IQVIA Institute. Global Medicine Spending and Usage Trends: Outlook to 2025. 2021.
6. Brasil. Câmara de Regulação do Mercado de Medicamentos. Secretaria Executiva. Anuário Estatístico do Mercado Farmacêutico 2019/2020. Brasília, DF; 2021.
7. The World Bank. PPP conversion factor, GDP (LCU per international $). The World Bank. 2021 Accessed on: 6 May 2021. Available in: https://data.worldbank.org/indicator/PA.NUS.PPP?locations=BR.
8. Vieira FS. Evolução do gasto com medicamentos do sistema único de saúde no período de 2010 a 2016. Rio de Janeiro, Brasil: IPEA; 2018.
9. Brasil. Ministério da Economia. Instituto Brasileiro de Geografia e Estatística (IBGE). Conta-Satélite de Saúde: Brasil 2010-2017 CSS. 2019.
10. OECD. New Health Technologies: managing access, value and sustainability. OECD Publications. Paris: OECD; 2017. DOI: 10.1787/9789264266438-en.
11. World Health Organisation (WHO). WHO Guideline on Country Pharmaceutical Pricing Policies. Geneva; 2020.
12. Magalhães LCG de. Estrutura de mercado, estratégias de crescimento e de inovação e desempenho recente da indústria farmacêutica no Brasil. Universidade de Campinas; 2006.
13. Mazzucato M. The Value of Everything: making and taking in the global economy. Milton Keynes: Penguin; 2019.
14. Ivama-Brummell AM, Ortiz JA, Pingret D, *et al*. 18 years of economic regulation of medicines in Brazil: outcomes, challenges and lessons learnt. J Pharm Policy Pract. 2019;12(S1):14–15.
15. Brasil. Lei nº 12.401, de 28 de abril de 2011. Altera a Lei no 8.080, de 19 de setembro de 1990, para dispor sobre a assistência terapêutica e a incorporação de tecnologia em saúde no âmbito do Sistema Único de Saúde- SUS. DOU 29 Abr 2011. Available in: http://www.planalto.gov.br/ccivil_03/_Ato2011-2014/2011/Lei/L12401.htm.
16. Brasil. Instituto Brasileiro de Geografia e Estatística (IBGE). Pesquisa Nacional de Saúde 2019: informações sobre domicílios, acesso e utilização dos serviços de saúde. Rio de Janeiro; 2020.
17. Brasil. Lei nº 9.787, de 10 de fevereiro de 1999. Altera a Lei no 6.360, de 23 de setembro de 1976, que dispõe sobre a vigilância sanitária, estabelece o medicamento genérico, dispõe sobre a utilização de nomes genéricos em produtos farmacêuticos e dá outras prov. DOU. 1999;
18. Bertoldi AD, Helfer AP, Camargo AL, *et al*. Is the Brazilian pharmaceutical policy ensuring population access to essential medicines? Global Health. BioMed Central; 2012;8(1):6. DOI: 10.1186/1744-8603-8-6.
19. World Health Organization (WHO)/Health Action International (HAI). Measuring medicine prices, availability, affordability and price components. 2nd edition. Geneva; 2008.
20. Brasil. Câmara de Regulação do Mercado de Medicamentos (CMED). Listas de preços de medicamentos — Português (Brasil). Anvisa. 2021 Accessed on: 25 Jul 2021. Available in: https://www.gov.br/anvisa/pt-br/assuntos/medicamentos/cmed/precos.
21. Wouters OJ, Shadlen KC, Salcher-Konrad M, *et al.* Challenges in ensuring global access to COVID-19 vaccines: production, affordability, allocation, and deployment. Lancet. 2021; DOI: 10.1016/s0140-6736(21)00306-8.

22. World Health Organization (WHO). COVID-19 vaccine tracker and landscape. 2021. Accessed on: 11 Mar 2022. Available in: https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines.

23. Brasil. Agência Nacional de Vigilância Sanitária (Anvisa). Vacinas- Covid-19. 2021 Accessed on: 11 Mar 2022. Available in: https://www.gov.br/anvisa/pt-br/assuntos/paf/coronavirus/vacinas.

24. Ivama-Brummell AM, Wagner AK, Pepe VLE, *et al.* Ultraexpensive gene therapies, industry interests and the right to health: the case of onasemnogene abeparvovec in Brazil. Br Med J Glob Heal. 2022;(7:e008637):1–5. DOI: 10.1136/bmjgh-2022-008637.

25. Brasil. Câmara de Regulação do Mercado de Medicamentos (CMED). Conselho de Ministros. Ata da 1a reunião do Conselho de Ministros da Câmara de Regulação do Mercado de Medicamentos - CM/CMED/2022. 2022 Available in: https://www.gov.br/anvisa/pt-br/assuntos/medicamentos/cmed/reunioes-CMED/conselho-de-ministros/1AtadoConselhosdeMinistros.pdf. Accessed on: 9 Mar 2022.

26. Novartis Brasil. É com orgulho que a Novartis anuncia o lançamento de ZOLGENSMA® (onasemnogeno abeparvoveque) no Brasil. Available in: https://www.novartis.com.br/news/e-com-orgulho-que-novartis-anuncia-o-lancamento-de-zolgensma-onasemnogeno-abeparvoveque-no. Accessed on: 10 Mar 2022.

Adriana Mitsue IVAMA-BRUMMELL is a pharmacist, health regulatory expert at the Executive Secretariat of the Drug Market Regulation Chamber (CMED), Brazilian Health Regulatory Agency (Anvisa), Brazil, visiting fellow at the Department of Health Policy, London School of Economics and Political Science (LSE), United Kingdom, and guest editor for the Series "Pharmaceutical pricing and reimbursement policies" of the RBFHSS.

Daniella PINGRET-KIPMAN is a pharmacist, health specialist consultant at the Executive Secretariat of the Drug Market Regulation Chamber (CMED), Brazil, and guest editorial board member of the Series "Pharmaceutical pricing and reimbursement policies" of the RBFHSS.

Claudia Serpa OSORIO-DE-CASTRO is a pharmacist, senior researcher and professor at the Department of Medicines Policy and Pharmaceutical Services (NAF), PAHO/WHO Collaborating Centre in Pharmaceutical Policies, at the National School of Public Health, Oswaldo Cruz Foundation (NAF/ENSP/Fiocruz) (Brazil). and guest editorial board member of the Series "Pharmaceutical pricing and reimbursement policies" of the RBFHSS.

Jaime ESPÍN is a health economist, professor at the Andalusian School of Public Health (EASP), Spain, and guest editorial board member of the Series "Pharmaceutical pricing and reimbursement policies" of the RBFHSS.

Vania Cristina CANUTO-SANTOS is an economist, public policies and governmental management expert (EPPGG) of the Ministry of Economy, director of the Department of Management and Incorporation of Health Technologies and Health Innovation (DGITS), Science, Technology, Innovation and Strategic Supplies Secretariat (SCTIE); Executive Secretariat of the National Committee for Health Technology Incorporation at SUS – CONITEC), Ministry of Health in Brazil, and guest editorial board member of the Series "Pharmaceutical pricing and reimbursement policies" of the RBFHSS.

Romilson de Almeida VOLOTÃO is a lawyer, Executive Secretary of the Drug Market Regulation Chamber (CMED), Brazil, and guest editorial board member of the Series "Pharmaceutical pricing and reimbursement policies" of the RBFHSS.

Augusto Afonso GUERRA-JUNIOR is a pharmacist, Coordinator of the Collaborating Centre for Health Technology Assessment (CCATES-SUS), Associate professor at the Department of Social Pharmacy, Faculty of Pharmacy, Federal University of Minas Gerais (UFMG), Brazil, and guest editorial board member of the Series "Pharmaceutical pricing and reimbursement policies" of the RBFHSS.

Gabriela Bittencourt MOSEGUI is a pharmacist, professor at the Department of Health and Society, vice-dean of the Community Health Institute, Fluminense Federal University (UFF), Brazil, and guest editorial board member of the Series "Pharmaceutical pricing and reimbursement policies" of the RBFHSS.