

POLICY BRIEF

FINANCING OPTIONS FOR THE TREATMENT OF RARE DISEASES IN CHILE



EVIPNet-Chile

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The Evidence Informed Policy Network (EVIPNet), is an initiative promoted by the World Health Organization. It has a focus on low-and middle-income countries and seeks to promote country-level collaboration between policymakers, researchers and civil society in order to facilitate the development and implementation of health policies through the use of the best available scientific evidence.

EVIPNet-Chile started its activities in the first half of 2011 and brings together decision makers from the Ministry of Health (MINSAL) and the National Health Fund (FONASA), together with scholars from the Research Unit in Health Policy and Systems Research at the Pontificia Universidad Católica de Chile (PUC) and the School of Public Health, at the University of Chile.

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KEY MESSAGES

- **What is the problem?**

Patients with rare diseases in Chile do not have guaranteed access to treatment and authorities at the Ministry of Health face the challenge of ensuring this access:

- Rare diseases affect a small number of patients in relation to the general population of each country, but together they represent millions of people who, according to their evolution and the existence of diagnostic tools, can improve their health status.
- Although its overall prevalence in Chile is unknown, patients with rare diseases are a socially, economically and health-wise disadvantaged group, especially in cases where their drug treatments consist of very high-cost drugs (orphan drugs).
- MINSAL has funded, through public financing, only a few health problems that require very high-cost drugs. However, projected spending growth by MINSAL, a pharmaceutical market with monopolistic characteristics, and the high cost of the drugs has compelled MINSAL to explore other funding sources.

- **What evidence do we have about access to treatment for rare diseases and how can it be implemented in Chile?**

There is little scientific evidence regarding access to rare diseases treatment. The lack of systematic reviews, and the scarcity of specific evidence related to the topic stand out. Due to the aforementioned problems, this Policy Brief has chosen to focus on mechanisms to improve financial access to treatment. The search was narrowed to the following four sources of funding:

- **Option 1 - General Taxes:** The literature is consistent in mentioning its ease of implementation and its potential for decreasing coverage gaps with a relatively stable income, but not without the downside of being subject to public scrutiny for paying for actions with a low cost-effectiveness due to their low frequency and high price. If implemented, this option involves fiscal financing through MINSAL's budget.
- **Option 2 - Mandatory insurance:** Less susceptible to political interference, this tax depends on formal employment and therefore on the size of the formal sector. Hence, this option is not suitable when there are high rates of informal employment or high payroll deduction rates.
- **Option 3 - Voluntary insurance:** This option allows the collection of funds from people who have the ability to pay. This type of insurance must be regulated since it could undermine solidarity and encourage risk selection. If implemented, the fee would go towards supplementary health insurance premiums.
- **Option 4 - Innovative mechanisms:** There are many diverse mechanisms included in this option. For instance, increasing taxation rates for large companies or currency transactions and the emission of diaspora bonds.

REPORT

The problem of financing orphan drugs for rare diseases concerns affected individuals and health systems alike. In fact, international agencies such as WHO / PAHO regard that access to essential medicines must be guaranteed by countries, including high-cost essential drugs, since they cause a significant financial impact on households and makes them to susceptible to falling into or remaining in poverty¹.

Rare diseases have generated interest for a long time although the initiative to meet the needs of people with less common diseases arises, for obvious socioeconomic reasons, in more developed countries, although these conditions are not specific to those countries. The problems in dealing with these diseases are mainly related to their high cost of treatment.

The European Union defines rare diseases, including those of genetic origin, as those life-threatening or chronically debilitating diseases that have a prevalence below 5 cases per 10,000 inhabitants. It also considers as an orphan drug any drug, prosthetic, biological agent or dietary preparation meant for the treatment of a rare disease.

We face a very diverse group of diseases that generate a very complex problem. This fact has led patients and their families, who clearly consider themselves a disadvantaged group, to claim that their socio-sanitary needs be addressed. This is especially true for diseases that require treatment with high-cost orphan drugs.

In its document on rare diseases², the Commission of the European Communities defines the problem in terms of four main points. First, the lack of recognition and visibility that these diseases have within current health information systems, which in turn creates obstacles for obtaining resources. Second, the lack of policies regarding these diseases in the member states noting that a more efficient use of scarce resources could result by channeling them through a specific plan. A third point raised is that of unequal access to specialized health care, the existence of fragmented research and an inadequate legislative framework on the subject. Finally, the Commission mentions the principle of subsidiarity and the need to exploit the economies of scale that would be generated if the small number of patients were treated at a European, and not national, level.

The European Project for Development of National Plans for Rare Diseases (EUROPLAN)³ notes that the funding of National Plans or Strategies in this area should take into consideration the importance of the sustainability of the process of medical care as a whole, and that the costs associated with such strategies should be evaluated "under the global values of universality, access to good quality care, equity and solidarity [...] and should be balanced with the subsequent savings in health care and social costs derived from having the rare disease patients in better health".

The regulatory measures applied in these countries are related with the economic incentives the industry requires to prioritize the development of orphan drugs. The United States started in 1983 and later Japan adopted its own measures. The industry responded to such incentives so that by the year 2007 under the Orphan Drug legislation 282 drugs and biological products had entered the market in the United States of America, while in the 8 to 10 years prior only a dozen of them had done so. These processes, however, are now facing new problems associated with prices that are considered excessive.⁴

Through the *Life Saving Drugs Program*, eligible patients in Australia have free access to high-cost drugs. The drugs covered by the program must have been proven to be clinically necessary and effective to the

Pharmaceutical Benefits Advisory Committee (PBAC) in addition to having been considered as not cost-effective and therefore not included in the Pharmaceutical Benefits Scheme. The government finances this program through funds which are discussed annually in Parliament in order to monitor and control the associated budget, as this spending, due to the nature of these drugs, would be basically driven by demand⁵.

In Latin America, countries in general have not created specific, systematic, formal mechanisms of access to orphan drugs. In spite of this, many countries, including Chile, have experienced partial improvement in access, through price negotiations with international producers and some limited-time public funded special programs. Once the high-cost drugs are prescribed the governments that do finance them do so basically due to the influence of interest groups or when they are forced to do so by way of legal action, without any prioritization or rational choice mechanisms⁶.

During the last decade the Chilean Ministry of Health has made efforts to address this issue and has developed some initiatives in this regard that have focused on funding certain health problems requiring very high-cost orphan drugs through programs provided by FONASA via public funding. Faced with projections that demonstrate that significant financial resources would be required over the coming years and the presentation in the near future of a bill on the subject in Congress, health authorities have decided to investigate alternative forms of funding.

From an ethical point of view, a complex problem of justice presents itself given the existence of different theories and approaches that generate opposing interpretations with regards to the need to give special consideration to rare diseases. From a utilitarian analysis, which proclaims "the greatest good", resources should be used in order to maximize the benefits to society. Therefore, the question necessarily emerges regarding the decision to fund these treatments that due to their high cost will involve restricting funding for the treatment of people with more common diseases. On the other hand, the rights-based approach promotes the obligation to offer all members of society a minimum of health services that meet their needs, even if this means funding treatments for rare diseases. Whatever approach is chosen, if social preferences requiring coverage of these conditions exist, then the discussion of these theories requires that the definition of rare disease, as well as inclusion/exclusion criteria, cost-effectiveness, efficiency, evidence and equity be discussed.

The topics mentioned in the preceding paragraph generate the need to carefully analyze the pros and cons of funding orphan drugs as well as the criteria on which decisions will be based.

To narrow the scope of this summary we have chosen one aspect of the policy options available for improving financial access to expensive drugs for rare diseases: funding sources for this type of disease. This choice is based on the interest of the national health authority. Health authorities in Chile have manifested their intention of presenting a bill defining funding mechanisms for the treatment of people living with very rare diseases.

For the purpose of this policy brief, some key considerations concerning the Chilean health system and pharmaceutical market are listed below:

- The Chilean health system has a public/private mix consisting of both public and private insurance and health care providers. The public sector is composed of the establishments that make up the National Health Service; which are the Ministry of Health and its dependent institutions: the 29 Health Services, the Public Health Institute, the National Public Health Procurement Office, FONASA and the Superintendence of Health.

- MINSAL oversees the development of the nation's health and acts as the national health authority. The main function of the National Health Services System is to provide health benefits through a healthcare network composed of urban and rural hospitals, rural medical stations, and rural health posts while also exercising regulatory functions. The Public Health Institute serves as the National Reference Laboratory, which involves standardization and quality control for laboratories and pharmaceuticals⁷.
- FONASA is the public health insurer. It finances the health services provided through the public health system and establishes contracts with public and private health providers, and sets tariffs. The Superintendence of Health is responsible for overseeing both private (ISAPRE) and public (FONASA) health insurers and healthcare providers.
- Funding for FONASA comes from fiscal contributions to public insurance and payroll tax. Employees must mandatorily contribute 7% of their salaries towards their health insurance (be it in the private or public health sector). This fund receives contributions from employees who choose FONASA as well as transfers from the national budget destined for the care of the nation's homeless and financing of public health programs. Private insurance is provided through the ISAPREs. In 2010, FONASA covered 74.1% of the population whereas the ISAPREs had a 16.5% market share⁸. Of the remaining population, 9.4% belonged to other insurance systems (Armed Forces) or did not belong to any formal insurance scheme.
- In Chile, financial coverage of drugs in general, and that of high-cost drugs in particular, is far from universal. In fact, when taking into consideration the total out-of-pocket expenses associated with health, medication is the component with the highest relative weight (30%), and this proportion increases towards the poorest quintiles (38%)⁹. The 2007 Family Budget Survey shows a similar situation with 32% of out-of-pocket healthcare expenditure going towards pharmaceuticals¹⁰.
- In this context, the implementation of the Explicit Health Guarantees Plan (GES), one of the four pillars of the 2005 Chilean health reform, meant a breakthrough in terms of financial access to medications, including them as part of the healthcare services guaranteed for a group of 69 health conditions. This system, which some have classified as positive discrimination¹¹, facilitates financial access to affordable medicines associated with high prevalence chronic health problems in Chile (diabetes, hypertension) as well as to some drugs associated with low prevalence but high-cost health conditions such as hemophilia and relapsing remitting multiple sclerosis. The majority of rare diseases, however, have been excluded from such guarantees.

THE PROBLEM

Authorities in Chile are faced with the challenge of establishing a funding mechanism that will ensure access to treatment for patients with rare diseases requiring high-cost drugs. This problem can be better understood by keeping in mind the following facts: 1) The burden of rare diseases with high-cost treatments the health system must handle; 2) the drugs that the health system must provide in order to fill patient needs; 3) The health system mechanisms that determine access to and use of very high-cost orphan drugs and 4) the current existence of funding programs for very high-cost orphan drug treatments. In this context, governance, financing and equity issues should also be taken into consideration in order to understand the causes of the problem.

1) Burden of Rare Diseases

Rare diseases are known as those that affect a small number of people compared to the general population. In Europe, a disease is considered rare when it affects 1 person per 2,000 whereas in the United States a disease is considered rare if it affects fewer than 200,000 of its inhabitants¹². Rare disease status may change over time: at the beginning AIDS was an extremely rare disease, then it was rare, and now it is increasingly common in some populations.

Six to seven thousand rare diseases are known to date and each week five new rare diseases are described in the medical literature¹³. The numbers depend, among other things, upon the precision of the definition. A pattern that is currently considered unique depends on the state of our knowledge, the accuracy of the biological and clinical analysis results and the manner in which we choose to classify diseases in general.

Eighty percent of rare diseases have an identifiable genetic origin, they concern 3% to 4% of births¹⁴. Other rare diseases are caused by infections (bacterial or viral), or allergies, or are due to degenerative, proliferative or teratogenic (chemicals, radiations, etc) causes. Some rare diseases are also caused by a combination of genetic and environmental factors. But for most rare diseases the etiological mechanisms are still unknown due to lack of research to find the physiopathology of the disease.

Despite the rarity of each rare disease, according to a well-accepted estimation, about 25 million Americans and 30 million Europeans have a rare disease. This has been called the paradox of rarity and it can be understood in a simple manner with the following statement: "Although the diseases are rare, patients with rare diseases are many."

The complex social health problems these diseases generate as a whole are derived primarily from the fact that they are "few". The problems can be summarized as follows¹⁵:

- Each rare disease has few patients.
- There are few professionals with experience in the proper management of these diseases.
- There are few specific medications for each rare disease or group of rare diseases.
- There are few adequate social benefits and services.
- There are few educational services tailored to the reality of these patients.
- There is little coordination amongst research activities.
- There are few useful health indicators, for proper decision-making.
- There are few resources earmarked specifically for rare diseases.

In Chile, the real magnitude of the problem is unknown since national health surveys fail to identify such low prevalence diseases. In turn, existing prioritization mechanisms, which are basically GES and which constitute pathways towards inclusion in the budget, fail to capture these problems because they are based on disease burden, cost effectiveness and social preferences and rare disease generally do not qualify due to their low prevalence and high cost. Multiple Sclerosis and Cystic Fibrosis are considered rare diseases in the United States and the European Union and exceptionally be included in GES.

2) Orphan Drugs

The so-called 'orphan drugs' are intended to treat diseases so rare that sponsors are reluctant to develop them under usual marketing conditions. In economic terms, orphan drugs may be defined as: "Drugs that are not developed by the pharmaceutical industry for economic reasons but which respond to public health needs"¹⁶.

Patients with rare diseases have historically been underserved by commercial drug development. Over time, a consensus has emerged in many countries to address this disparity by means of specific legislation for drugs to treat rare diseases. In several countries, orphan drug legislation has been enacted, which has successfully encouraged the development of drugs that, in the absence of such interventions, would not be commercially viable¹⁷. This started with the Orphan Drug Act, passed in the United States in 1983, which was followed by Japan in 1993 and Australia in 1997. Europe followed in 1999 with a common EU policy on orphan drugs. Table 1 shows a global comparison of different policies for such drugs.

Table 1: Worldwide comparison of the various policies on orphan drugs¹⁸

	United States	Japan	Australia	European Union
Legal Framework	Orphan Drug Act of 1983	Orphan drug regulation (1993)	Orphan drug policy (1998)	Regulation (EC) No 141/2000 (2000)
Administrative authorities involved	FDA / OOPD (*)	MHLW /OPSR (*) (Orphan Drug Division)	TGA (*)	EMA / COMP (*)
Prevalence of the disease (per 10,000 individuals, justifying the status of orphan drug)	7,5	4	1,1	5
Estimated population affected, prevalence rate (per 10,000 individuals)	20 million, 7.3	Information not available	Information not available	25 - 30 million, 6,6 - 8
Marketing exclusivity	7 years	10 years	5 years (similar to other drugs)	10 years
Tax credit - Tax credit or tax reduction	Yes: 50% for clinical trials	Yes: 6% for any type of study, limited to 10% of corporate tax	No	Managed by the member states
Research grants	NIH and other programs	Government Funds	No	EU-FP6' + national measures
Reconsideration of applications for orphan drug status	No	Yes	Yes (every 12 months)	Yes (every 6 years)

Technical assistance for the preparation of application documents	Yes	Yes	No	Yes
Accelerated marketing procedures	Yes	Yes	Yes	Yes (via centralized procedure)

Sources: 1999 European Parliament - STOA Publications - 167-PE orphan 780/Fin.St. Presentation of Prof. Josep Torrent-Farnell (president of the COMP) at the 'Annual Euro Meeting 2001', Barcelona, 6-9 March 2001.

(*) Abbreviations:

- FDA: Food and Drug Administration
- OOPD: Office of Orphan Products and Development
- OPSR: Orphan Drug division
- MHLW: Ministry of Health, Labour and Welfare
- TGA: Therapeutic Good Administration
- EMEA: European Agency for the Evaluation of Medicinal Products
- COMP: Committee for Orphan Medicinal Products
- NIH: National Health Institute
- EU-PF6: Sixth framework programme of European Community (EU-FP6)

Unlike those drugs that address health problems that are most prevalent, developing drugs to treat rare diseases in normal market conditions is not profitable for the pharmaceutical industry. Research and drug development is long (about 8 years), the cost to industry is high and outcomes are uncertain (of every 10 molecules tested, usually only 1 has a therapeutic effect). Under this scenario, if the industry produces them, the problem is the high final selling price, which occurs mainly for the following reasons¹⁹:

- Because of rarity, the development costs have to be recouped from sales to a limited number of patients worldwide, with consequently high acquisition costs per patient.
- The incentives have focused on motivating interest in research and development of orphan drugs based on patents or marketing exclusivity that permit monopolies to be in place for extended periods of time (10 years for the EU). This enables pharmaceutical companies to sell their products at high prices for a long time.

Under the standard methods of health technology assessment incorporating economic evaluation, orphan drugs do not usually prove to be cost-effective and this, coupled with their high cost, means that funding and patient access may be limited. However, these restrictions may not be in line with societal preferences¹⁷

3) Access to high-cost orphan drugs

One of the problems patients undergo is being able to get treatment. In some occasions, even though the drugs are on the market they are not available in the country, in other circumstances the drugs are in a clinical investigation phase and in other instances they are unobtainable due to lack of funding. Table 2 displays the 2010 average costs per patient for FONASA²⁰ for some rare diseases that fall into the last group:

Table 2: Examples of average costs for rare diseases FONASA 2010

Disease	Average cost per patient per year (M Chilean pesos)
1. Fabry Disease	75.142
2. Gaucher Disease	192.377
3. Pompe Disease	70.339
4. Paroxysmal Nocturnal Hemoglobinuria	192.465
5. Mucopolysaccharidosis I	98.651
6. Mucopolysaccharidosis II	586.637
7. Mucopolysaccharidosis VI	212.351
8. Tyrosinemia type I	101.667

Note: Includes only the cost of drugs

Source: FONASA, Santiago, Chile, March 6, 2011

In Chile an important part of drug financing is paid via private spending, mostly out-of-pocket payments, a significant burden on the family budget. Since the diagnosis of rare diseases has become more common due to the progressive development of health technologies, the issue of orphan drugs funding is of recent date. The high prices of the drugs of some orphan drugs hinders access to treatment and leads affected families to poverty or impoverishes them even more.

4) Programs in Chile

A number of initiatives have sought to facilitate access to high-cost orphan drugs:

Law No. 19.779 of the year 2002: 800 million Chilean pesos were earmarked to reimburse duties and taxes paid in the import of high-cost drugs for rare diseases. The laws were primarily intended to facilitate access to anti-retroviral treatment for HIV / AIDS, but did not preclude its use for other expensive orphan drugs.

In 2005, the Committee for the Implementation of a National Drug Policy, developed the "Proposal for a guide to institutional action and response to rare diseases in Chile."

On October 24, 2006 MINSAL established a Technical Advisory Committee on Rare or Infrequent and Catastrophic Diseases with representatives from MINSAL, FONASA and the Institute of Public Health. The Committee produced a list of diseases feasible to be financed by the public healthcare system²¹.

The inclusion criteria for the list were:

- Diseases with an incidence of less than 1/10.000 LB.
- Existence of treatments available that demonstrate a significant change in the natural history of the disease.
- Diseases with unknown incidence, presumably more than 1/10.000 NV, whose treatments are expensive and meet the aforementioned criteria.
- Currently not included in the list of GES diseases or other programs.

The list drawn up considered a total of 20 diseases, it included the number of patients diagnosed to date, the estimated prevalence, specific treatment available and the individual or family annual cost of treatment in case it could be accurately determined.

Since 2007, MINSAL and FONASA have the "High-Cost Drugs Program". Only orphan drugs that are on a prioritized list are financed, within a limited budget framework, which, on occasion, limits patient coverage. The following conditions are included: dystonia, treatment with botulinum toxin; severe dwarfism, growth hormone treatment; Guillain Barre, immunoglobulin treatment; and Gaucher disease, treatment with imiglucerase.

In March 2011 FONASA prepared a draft of a proposal for a special fund destined to finance access to high-cost orphan drugs. FONASA made projections for eight rare diseases and carried out a 10-year forecast²⁰. As shown in Table 3, according to these projections, just these 8 diseases in the tenth year required 76.913 billion Chilean pesos, equivalent to US\$ 153 million.

Table 3: Total expenditure estimated by FONASA for 8 rare diseases, 10-year projection

Disease	Current Demand CD (MMS)	Gap (ED-CD) (N°)	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8	Year 9	Year 10
Fabry Disease	3.006	15.104	5.561	7.988	10.293	12.484	14.565	16.542	18.420	20.204	21.899	23.509
Gaucher Disease	6.156	3.078	6.425	6.681	6.924	7.155	7.375	7.583	7.781	7.969	8.148	8.317
Pompe Disease	141	1.336	342	531	706	870	1.023	1.166	1.299	1.424	1.540	1.648
Paroxysmal Nocturnal Hemoglobinuria	385	14.242	2.669	4.801	6.790	8.647	10.380	11.998	13.507	14.916	16.232	17.459
Mucopolysaccharidosis I	789	2.762	1.230	1.641	2.025	2.383	2.718	3.030	3.321	3.593	3.847	4.083
Mucopolysaccharidosis II	8.800	4.693	9.973	11.068	12.090	13.044	13.934	14.765	15.541	16.265	16.934	17.597
Mucopolysaccharidosis VI	1.274	1.486	1.614	1.931	2.227	2.503	2.761	3.002	3.226	3.434	3.621	3.789
Tyrosinemia type I	1.017	1.627	1.169	1.314	1.452	1.582	1.707	1.825	1.937	2.043	2.144	2.241
TOTAL EXPENDITURE (MMS)	21.567	44.329	28.983	35.954	42.507	48.669	54.462	59.909	65.032	69.637	73.383	76.913
ANNUAL GROWTH (MMS)			7.416	6.971	6.553	6.161	5.793	5.447	5.123	4.605	3.746	3.529

Source: Estimated expenditure selected Rare Diseases. Subdepartment Benefit Plan. National Health Fund in Chile. Santiago. March 6, 2011

These amounts of money are considered for a population that, as shown in Table 4²⁰, is very large.

Table 4: Current demand, potential demand, reference population and prevalence for 8 rare diseases

Disease	Current demand (CD) (N°)	Cost of treatment (M\$)	Estimated prevalence (/100.000)	Reference population	Source	Median survival (years)	Potential demand (PD) (N°)
Fabry Disease	40	75.142	1,75	General pop.	Orphanet	Not applicable	302
Gaucher Disease	32	192.377	1,16	Newborns	Gene Reviews	20	60
Pompe Disease	2	70.339	0,68	Newborns	Meikle et al	15	27
Paroxysmal Nocturnal Hemoglobinuria	2	192.465	0,55	General pop.	Orphanet	Not applicable	95
Mucopolysaccharidosis I	8	98.651	1,14	Newborns	Meikle et al	15	44
Mucopolysaccharidosis II	15	586.637	0,74	Newborns	Meikle et al	15	29
Mucopolysaccharidosis VI	6	212.351	0,43	Newborns	Meikle et al	15	17
Tyrosinemia type I	10	101.667	1,00	Newborns	Gene Reviews	20	52

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Notes:

The overall population estimate is taken from Chile 2011 INE 17,248,450 .
 The estimate of newborns is coming to 260,000 whereas the 2008 will have 248 366 (INE).
 According to Gene reviews for tyrosinemia, "...is estimated that fewer than 50% of affected individuals are diagnosed while alive".

5) Considerations on the Problem

Some of the underlying causes of the access problem to drugs for people living with rare diseases can be summarized as follows:

- Governance Arrangements
 - A national policy on financial access to drugs does not exist nor does one for expensive drugs for rare diseases. Current legislation allows for some drugs to be covered by laws such as GES or via public funding. Due to the absence of a common approach towards the problem of rare diseases described in the preceding section, there is too much heterogeneity.
 - Decision makers have determined to adopt prioritization criteria to select the health conditions that the system must address (i.e. GES). When faced with the most commonly used prioritization criteria, rare diseases do not qualify in any ranking since they do not represent, as a specific cause of illness, a priority no matter what parameter is being measured; the magnitude of the problem, burden of disease, cost-effectiveness or any combination thereof. These forms of prioritization, however, do not take into consideration whether these treatments rank high amongst a country's social preferences¹⁷.
- Financing Arrangements
 - We can identify three areas of analysis: the source of the funding itself, the resource management mechanism (collection and distribution) and the price paid for the drug.
 - The source of funding for special programs concerning drugs in Chile has traditionally been via general taxation and public spending by way of FONASA. Given the large amounts required to assist such few patients, MINSAL is assessing other ways to finance high cost orphan drugs.
 - Currently, MINSAL is in the process of drafting a bill regarding financing mechanisms for the therapeutic treatment of people living with very rare diseases. Among the requirements that have been outlined for a disease to be considered are²²:
 - Prevalence be 0.18 per 10,000 people, or less,
 - The disease constitute a real and proven threat to life, in the understanding that, if it follows its natural course, a short life expectancy and onerous conditions of survival are to be expected,
 - There is proven effective treatment available, that is, one that has shown a reasonable improvement in patient quality of life or life expectancy,
 - There are clinical guidelines for the management of these patients,
 - The treatment is not currently financed by existing mechanisms or programs,
 - The cost of such treatment would be economically catastrophic, defined as a treatment whose monthly cost or applicable copayment is equivalent to 30 times the monthly minimum wage.
 - Management/ distribution of resources has changed with the inclusion of some pathologies in GES or in FONASA's Special Program for High Cost Drugs. Other orphan drugs are financed via Extraordinary Aid Funds. This diversity creates inequities and a system that is too fragile to face the problem.
 - Price is a determinant factor in defining the need of a policy for funding expensive drugs for rare diseases. The issue is the high cost involved in treating each patient..

- The need to ensure the research and development required for orphan drugs has been addressed in many countries by way of extended licenses or market exclusivity, subsidizing R & D and long-term purchasing alliances between governments and laboratories aimed at reducing prices.
- Delivery Arrangements

Given the nature of the orphan drugs used in rare diseases, they are not usually available in the public sector drug arsenal or in the private sector. For this reason, negotiations or direct purchases by patients, patient associations and government or private agencies are required. Importation is another, although more cumbersome, alternative available for purchasing these products.

- Equity considerations

In Chile, a specific policy addressing the problem of rare diseases does not exist. In spite of the fact that in 2006 the MINSAL established the Technical Advisory Committee on Rare or Infrequent and Catastrophic Diseases²³, it only managed to meet for a few months and stopped working without achieving its goal of establishing an access policy for the therapies required by bearers of rare diseases. Hence, the current scenario does not have the consistency that one would expect, and instead is full of what seem to be dissimilar solutions. An example is that, on the one hand, Cystic Fibrosis (CF) is included in the list of the 56 diseases that were considered GES right from the beginning of Chile's recent health reform;¹ and Multiple Sclerosis (MS) was subsequently included as well². Both health conditions are not rare diseases under international standards. Other diseases, such as Dystonia or Primary Growth Hormone Deficiency, have been addressed by incorporating them into FONASA's Special Program for High-Cost Drugs and other diseases have been supported through the use of Extraordinary Aid Funds. This latter alternative however, because of budgetary constraints, has only been able to be utilized by some of the people suffering from these diseases, which obviously seems unfair for those who in spite of suffering the disease addressed by the Fund are excluded from treatment.

¹ Chile is estimated that CF has an incidence of approximately 40-50 new cases annually, which associated with a median survival of 12 years, is roughly equivalent to a prevalence of 3-4 per 100,000 population.

² MS prevalence in Chile would be between 11.7 and 13.4 per 100,000 inhabitants.

POLICY OPTIONS

Conceptual and Theoretical Framework

In the context of a health system, funding expensive drugs for the treatment of rare diseases is closely related to the financing mechanisms present in the system as a whole. According to World Health Report, 2000²⁴, in addition to the primary goal of any health system associated with improving the health of the individuals under its care; a second goal would be equity in the financial contributions made by these individuals. The second goal is particularly important when considering the possibility that healthcare needs could result in catastrophic spending, indicating that equitable funding implies that the risk each household faces due to healthcare costs is distributed according to the ability to pay and not according to the risk of disease. In this scenario we can review financing mechanisms that permit risk sharing and offer financial protection (a system that meets this goal ensures financial protection for all its beneficiaries).

According to Kutzin (2001)²⁵ the three functions that health system financing must meet are revenue collection, pooling of funds and the purchasing of services. In addition, in financing we must differentiate the initial funding sources (individuals / families / employees, employers / corporations, NGOs, international agencies, donors, etc.), the collecting organizations (central government, local governments, social security agencies, commercial insurers, etc.) as well as the contribution mechanisms (general taxes, excise taxes, earmarked taxes, mandatory contributions, voluntary contributions, grants, loans, etc.).

Recognizing the importance of financial protection in achieving better access to health care, World Health Organization (WHO) member countries in 2005 (Resolution WHA58.33)²⁵ committed themselves to promoting the development of health financing systems focused on achieving the goal of universal coverage. In this context, the 2010 World Health Report²⁵ identified an over-reliance on direct payments for health services (out-of-pocket expenses) as one of the three fundamental problems that countries face in achieving this goal. This reaffirms the importance of increasing funding through pooled funds or prepayments, which would in turn allow progress on the three dimensions of universal coverage: the population covered, the services covered and the proportion in which they are financially covered.

So far, coverage of high-cost drugs to treat rare diseases has been a generally neglected, representing a major challenge in the three dimensions of universal coverage mentioned above, and therefore, in developing the financing mechanisms that will facilitate effective financial protection.

As stated earlier, in Chile the financial coverage of drugs in general, and that of high-cost of drugs in particular, is far from universal. Medications are the component with the largest relative weight with regards to total out-of-pocket expenses associated with healthcare (30%), with this proportion increasing in the poorest quintile¹⁰. GES permitted advances in terms of financial access to medications, including them as part of the interventions under guarantee and therefore extending onto them the financial protection guarantee that determines copayments based on a maximum reference tariff established for beneficiaries of both FONASA and ISAPRES. Financial access is therefore provided for affordable medicines for high prevalence chronic health problems in Chile (diabetes, hypertension) as well as for drugs associated with low prevalence but high-cost health problems (hemophilia, remittent recurrent multiple sclerosis) but not for the high-cost drugs associated with rare diseases which, except for cystic fibrosis, have not been included in the GES.

Methodology

We conducted a systematic literature search in MEDLINE, Health Systems Evidence (McMaster University) and CENTRAL (The Cochrane Central Register of Controlled Trials) in order to identify systematic reviews with which to inform this policy brief. Given the scarcity of evidence regarding the issue, we conducted a broader search using the MeSH term "rare diseases" and "orphan drugs" which yielded no relevant results. With regards to the frame issue *financial access to drugs*, a policy brief on mechanisms of financial access to health services for vulnerable populations was identified. The search was updated without obtaining new results. Pertinent websites were also reviewed as were appropriate references cited in the studies most related to the topic. Experts were contacted to identify unpublished articles and gray literature.

Many options can be selected to address the problems underlying the financial access of orphan diseases. This Policy Brief has stated as its goal the review of further evidence concerning four options associated with different contribution mechanisms (general taxation, mandatory contributions, voluntary contributions and innovative financing mechanisms) in relation to the financing of health services and more specifically, in those cases where the evidence permits, with regards to the financing of high-cost drugs associated with the treatment of rare diseases. The analysis, nonetheless, is based on the sources of contribution and the level at which they have implemented measures for increasing access to medicines. These measures might sometimes occur at the funding level, others at purchasing level and even at the resource allocation level requires specific mechanisms to associate these with general funding sources, since they have a clear effect on the latter.

- **General Taxes:** so far, Chile has favored public financing, which consists of fiscal contributions and individual social security contributions to FONASA. In systems financed by taxes, health services are paid from general government revenues, although there may be some excise duties, that tax products or activities that are harmful to a person's health. Usually when this type of financing exists decisions about funding services are included as part of the general planning regarding public expenditure²⁶. In this manner, regulatory or other measures that are used to promote the use of orphan drugs and that have fiscal effects that eventually collaborate with financing access are incorporated.
- **Mandatory insurance:** usually associated with social health insurance in which health services are paid via contributions to a fund. Payroll is the most common basis for establishing the premium, which is based on the ability to pay, access to services, on the other hand, depends on the individual's need for the services. Usually, the health fund (or funds) is independent of the government, but operates within a strict regulation framework²⁶. In Chile this insurance is carried out through a 7% mandatory contribution that people pay to FONASA or the Isapres. In this analysis, regulatory measures that are used to promote access to orphan drugs under social security financing will be incorporated.
- **Voluntary insurance:** usually associated with private insurance. In health systems, private insurance basically has two ways to provide coverage; either as primary insurance, the main form of insuring healthcare, or through supplemental insurance coverage where they deliver a limited number of benefits not covered by the main insurer. Private insurance is based on risk and the premiums people pay are based on the expected average cost of the services they will utilize. Thus, people belonging to high risk groups pay more and those with a lower risk pay less²⁶. In Chile, there are numerous voluntary insurance providers associated with banks, general insurance companies and also offered by private healthcare providers.

- Innovative financing mechanisms: in line with statements made by the World Health Organization in its 2010 World Health Report, "Financing Health Systems, The Road to Universal Coverage" where innovative funding sources such as the following were discussed:

Special levy on large and profitable companies: a tax/ levy that is imposed on some of the big economic companies in the country

Levy on currency transactions: a tax on foreign exchange transactions in the currency markets
Diaspora bonds: government bonds for sale to citizens living abroad.

Financial transaction tax: a levy on all bank account transactions or on remittance transactions

- Solidarity contribution through mobile phones: solidarity contributions that enable people and businesses to make voluntary donations through their monthly mobile phone bill.
- Alcohol consumption tax: an excise tax on alcoholic beverages.
- Price transparency, albeit not a direct mechanism of funding, has been proven effective in lowering prices and therefore contributing to greater access (Brazil), consequently the implementation of *Price Banks* should not be disdained.

The focus will be on identifying evidence for the following four options which are currently being discussed in the Chilean health sector. For options 1 and 2 findings on financial access to health interventions in general and in particular orphan drugs are summarized. For options 3 and 4, due to the smaller amount of evidence found, analysis is limited to financial access to health interventions in general.

Option 1 - Financing via general taxation

This alternative implies that the funds used to finance health services are raised through general taxes (VAT, income, fees, etc.), which are levied on all economic activities and not on any particular activity which would generate revenues to finance a specific program or project (earmarked taxes). Basically this collection includes all primary sources of financing (individuals, companies, etc.) and is generally associated with Beveridge Models or National Health Service type of Health Systems with universal coverage²⁷.

Countries like the United Kingdom, Spain, Italy, Scandinavia and Canada base funding for their National Health System (NHS) on this type of mechanism²⁸. In Chile, in 2009 56.4% of public sector resources allocated towards financing health expenditures came from fiscal contributions²⁹, or in other words, they were provided by the government through the national budget, which stems from general taxation. Most of the funding for the public health system therefore comes from these taxes.

The increase in coverage either in terms of the services covered or the proportion of the population covered involves either a rate hike (in one or more of the aforementioned taxes), or the diversion of resources from other sectors such as housing or education or from the same health sector (reduction or elimination of other programs). All of these options are generally not well received. Moreover, this mechanism is pro-cyclical (revenue and economy performance of the economy move in the same direction), which makes this mechanism particularly vulnerable in times of economic crisis³⁰.

- **Results of systematic reviews**

No systematic reviews that addressed funding of high cost orphan drugs via general taxes were identified.

- **Existing evidence**

There is extensive literature that addressing the generic issue of health financing via general taxation, especially related to international agencies like the World Health Organization²⁵ and other specialized organizations³¹. The literature lays out main features, costs and benefits of general taxation. Implementation is approached in two steps; first the general aspects of the financing via general taxation and then specifics about orphan drugs and funding attributable to that origin.

A summary of the overall key findings of the evidence found is presented in Table 5.

Table 5: Summary of the evidence found relevant to Option 1 - Funding through general taxation

Category finds	Summary of findings
Benefits	<ul style="list-style-type: none"> • It can provide a stable source of revenue for funding services.²⁵ • Its tax base is broader and covers all citizens or residents therefore decreasing coverage gaps found in other funding sources^{31,32}. • The increased coverage is associated with increased risk pooling³²⁶ and greater purchasing power³¹.

³ Many diseases and accidents are not predictable and are a financial risk to the insurance agency. The risk pooling is a method that distributes risk between members of a community ("pool") to spread the risk once it occurs, so that everyone pays a small and acceptable price.

	<ul style="list-style-type: none"> In terms of equity, it is associated (depending on how they are defined), with positive redistributive effects and with the provision of merit goods⁴³¹ Works in line with government health policies²⁵.
Potential harms	<ul style="list-style-type: none"> By not being an exclusive funding source for the particular problem, it competes with other issues and sectors of the economy²⁵. Taxes are a highly political mechanism³¹. The collection is generally pro-cyclical, putting the continuity of programs at risk in times of economic crisis³¹. Taxes have the potential to generate unwanted distortions in the normal functioning of the economy³¹. Depending on whether the tax is direct or indirect, undesirable distributional effects can be generated. Direct taxes (e.g. those on income, income, etc.) are generally considered progressive and redistributive whereas indirect taxes (e.g. VAT) are generally considered regressive³¹.
Cost and cost-effectiveness with regards to the status quo	No specific evidence available.
Uncertainty regarding possible damage	No specific evidence available.
Main elements of the policy choice if it has been implemented elsewhere	Finances orphan drugs in several European countries. The way the health system is financed determines its use (e.g.: Spain) ³³ .
Comments regarding the cost and cost-effective with regards to the status-quo	Easy to implement and costs are related to justifying why actions are financed if they are not very cost-effective.
Comments regarding possible damage	Aligned with politics, it is important to know whether there is a public willingness to fund services with low cost-effectiveness if other cost-effective alternative uses for these resources exist.

Source: authors

Along with the above, series of specific findings related to regulatory measures used to promote rational access to orphan drugs at levels other than the funding source were found. Among them are tax exemption (total or partial) for the R & D and production of orphan drugs have been used since the early eighties. This occurs in European countries and the U.S. where most of the pharmaceutical industry is located. There is also funding of orphan drugs via the public budget without explicitly stating it. Something similar happens with special risk pooling in the Uruguayan National Resource Fund³⁴, where the risk pool is accompanied by a health technology assessment system, that tries to emulate NICE (in UK), so that in addition to funding, costs are also contained through rational consumption. There is also evidence regarding price control for

⁴ Refers to positive social goods, such as health and education.

innovative products, regional and national price negotiations (international pricing negotiations in some cases allowed access to financing of certain disease that at the time, were rare or infrequent events, such as HIV-AIDS). Another type of policy that qualifies are the flexibility of international trade regulations and intellectual property that can be performed in accordance with the TRIPS, as well as risk sharing agreements contracts between governments and industry.

This information is summarized in the table below.

Table 6: Specific mechanisms of financing with tax implications

Category finds	Summary of findings				
	TAX incentives for R & D and explicit coverage, subject to rational use	Price negotiations and TRIPS flexibilizations	National risk pooling	Risk-sharing agreements	Price regulation: reimbursement and copayments
Benefits	Has increased orphan drugs in developed countries	Significant decrease in spending due to discounts and tax savings achieved	Financing based on population cases can admit additional non-fiscal contributions	May allow more access.	The price pay the user decreases, increasing access
Potential harms	If not in line with R & D, social distortions occur It is argued that although there are new drugs they are too expensive	It does not describe damage evidenced in practice. But there may be subsequent retaliation in case of non-compliance in the negotiations	Technical selection mechanisms are important for cost control	No specific evidence available.	There are critical assessments of the price regulation system in the world
Cost and cost-effective in relation to the status quo	No specific evidence available.				
Uncertainty regarding possible harms	No specific evidence available.				
Main elements of the policy choice if it has been used elsewhere	Fiscal incentives (taxes) to for country's pharmaceutical industry so they can investigate, develop and manufacture orphan drugs	Mercosur countries and the Andean region, including Chile, participated in price negotiations for bulk purchases of drugs for HIV, supported by international organizations. Countries have considered TRIPS	A central fund is created that finances access to high-cost treatments for beneficiaries of the social security system after passing an initial health technology and	Government and industry agree to certain conditions for access to orphan and high-cost drugs. They are	A reference price which provides the basis for the refunds to be made by the government and / or insurance

		flexibilization in order to provide lower-priced drugs.	economic evaluation.	promoted by the industry.	which in turn, eventually determines a co-payment.
Comments regarding the cost and cost-effective in relation to the status-quo	Policy is not implementable in Chile. We would be limited to supporting countries that do have a pharmaceutical industry so that they to maintain and improve policy	These policies have a low economic cost and high benefits.	Using a single pooling for the whole country must generate profits and efficiency.	TBenefit or harm depends on the results of the negotiation between government and industry	In a fully deregulated system, such as Chile, it could be a breakthrough, but it is difficult to implement
Comments regarding possible harms	If Europe and the U.S. could generate policies to mitigate they could influence prices in Latin America	The elements of TRIPS flexibility, although legal, could result in punishment in other areas of foreign trade	In spite of what was previously stated, the addition of more treatments should be restricted in order to balance the mechanism's tendency towards deficits.	If the negotiation is not good, it could result in an even worse scenario	No specific evidence available.

Source: authors

We should be aware that although we did not find any evidence of the existence of affirmative action programs such as GES that incorporate orphan drugs (GES actually does not include any orphan drug, except for Cystic Fibrosis y Multiple Sclerosis, even though it does include other types of drugs), this formal prioritization mechanism with explicit guarantees is a mechanism to be considered in Chile, since it is the most important prioritization system existent in the country. We must also mention that other information was found, not specific to orphan drugs and therefore not been considered in the specific analysis, such as centralized purchasing which reduces costs therefore increasing available resources which also can indirectly lead to greater efficiency and availability of fiscal resources.

Option 2 - Funding via mandatory insurance

This alternative implies that the funds used to finance health services are collected through a mandatory contribution that is generally based on insuree salaries or on a broader income base (as is the case in France, Germany, Netherlands, Switzerland, etc.). This type of mechanism is usually associated with social security or a private insurer which administers the social contribution and generally differs with regards to the type of taxes levied. These can be contributions or premiums based on salary (the same percentage for all taxpayers), or through risk-adjusted individual premiums³⁵.

Since these instruments are associated with wages, the main primary sources of funding are the employees and employers, and, in principle, are associated with coverage for the contributors and their families. The success of this mechanism (mandatory) is therefore correlated with the extent of formal employment, and the possibility of including self-employed workers and the informal sector³⁶. In this case, since the contributions are solely for financing health services, the resources required for increasing services or increasing the proportion in which they are covered require either a shift of resources from other sectorial programs or projects or increased premiums.

Countries like Germany and France are characterized by financing their health systems mainly through social security mechanisms (with the option to opt for private insurance in Germany) whereas countries like Switzerland are characterized by the high presence of private insurance and the obligation of citizens to enroll²⁸. Meanwhile, in Chile, both mechanisms coexist (FONASA and ISAPREs respectively). In the case of the public insurance system, contributions correspond to premiums based on salary, equivalent to 7%, that in the case of dependent workers is mandatory. In 2009, insuree social premium contributions to the public system corresponded to 35.8% of the resources had to finance health expenditures²⁹.

- **Results of systematic reviews**

No systematic reviews that addressed financing of high- cost orphan drugs via mandatory insurance were found.

- **Existing evidence**

Although there are systematic reviews regarding social insurance and rare diseases, ample literature exists, especially from international agencies like the World Health Organization²⁵ and the International Labour Organization, on social insurance. Table 7 summarizes the main characteristics as well as the costs and benefits and ways of implementation of this option. In turn, there is evidence of specific mechanisms, which usually financed implicitly these drugs (and other drugs and treatments), in a context of institutional arrangements for social security. These are presented in Table 8.

Table 7: Summary of the evidence found relevant to Option 2 - Financing through mandatory insurance

Category findings	Summary of findings
Benefits	<ul style="list-style-type: none">• It can provide a stable source of revenue for funding services²⁶.• Cash flow is visible²⁶.• As a source 'marked' for health, it is less exposed to political interference³¹.• In general, systems financed through social

	<p>security are more intent on offering their by beneficiaries “choices” than those funded through general taxation³¹.</p> <ul style="list-style-type: none"> • It can contribute to establishing patient rights with health care providers²⁶. • Depending on the number of funds (and their characteristics) they may be associated with a high risk pooling and purchasing power³¹. • Combines risk sharing with mutual support, since services are allocated according to needs and the financial burden is distributed according to the ability to pay³⁷. • It can operate in accordance with governmental health policy goals, while maintaining a certain degree of independence from the government²⁶.
Potential harms	<ul style="list-style-type: none"> • The problems derived from ensuring coverage for informal workers (beneficiaries are generally only the contributors and their families)²⁶. • Existing coverage gaps threaten public finances, as populations not covered by insurance eventually require publicly funded programs³¹. • Depending on the number of funds (and their characteristics) there may be problems of adverse selection. For example, in the context of multiple competing funds in the absence of a risk compensation fund, and with the possibility of charging risk-adjusted premiums³¹. • There is concern about whether mandatory contributions increase labor costs (the charge is imposed on the employer or the employee)²⁶³¹
Cost and cost-effective with regards to the status quo	<p>Premiums are financed via a percentage reduction from insuree income (or earnings) and depends on the amount of identifiable revenue, therefore working better in scenarios with an important formal sector, with known income²⁶.</p>
Uncertainty regarding possible damage	<p>An important question is whether it is best that the funds for rare diseases derive from payroll contributions. It could be considered that the payroll is already a major source of taxation: income tax, pension contributions, etc.. If the discount rate is already high (i.e., the proportion of total mandatory deductions is high) it is not advisable to use this source for other deductions²⁶.</p>
Main elements of the policy choice if it has been implemented elsewhere	<p>There was no literature on its use to fund specific rare diseases.</p>

Comments regarding cost and cost-effectiveness with regards to the status-quo	Given the history of health financing in Chile, this option would probably be easier to implement here than in other countries. It could be carried out by defining that in addition to the 7% currently deducted towards health, and additional percentage be added for financing for rare diseases.
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Source: authors

In addition to the aforementioned information, more specific evidence was found regarding methods of financing high-cost orphan drugs, such as implicitly including them in the benefits catalogs that social security will mandatorily cover. This would involve defining involving / exclusion criteria. They would also be implicitly includes, when implementing risk-adjusted funds to high costs or high risks, called shared risk funds, also known as catastrophic illness funds ... We can also consider patient co-payments/refunds that exist in countries where there is price regulation.

Table 8: Specific funding mechanisms for mandatory insurance

Category findings	Summary of findings		
	Coverage implied in plans is subject to rational use	Shared risk pooling for catastrophic spending	Price Reimbursement and Regulation and co-payments
Benefits	Allows access to orphan drugs if they are in the benefit plan or if judicially demanded	Increased system efficiency and fairness (not specific to orphan drugs)	Facilitates access (not unique to orphan drugs)
Potential harms	Without health technology associated mechanisms efficiency and safety are not ensured. In developed countries they generally are whereas in other countries this only occurs exceptionally.	There is evidence that “pushing” of cases to incorporate treatments and services	There is some controversy regarding the distortions and problems that price regulation systems may have
Cost and cost-effective with regards to the status quo	No specific evidence was available.		
Uncertainty regarding possible harms	No specific evidence was available.		
Main elements of the policy choice if it has been implemented elsewhere	In general, high-cost drugs are authorized under the existing institutional mechanism for all drugs and their mere approval makes them admissible as	Insurers share risk based on a common pool and profit according the high-cost/risk events their affiliates have	The simplest: Do not allow prices to exceed those current internationally (not unique to orphan drugs) Price ceiling or reference

	expense. (developed countries) They are forcible admitted through judiciary procedures (less developed countries)		prices
Comments regarding cost and cost-effectiveness with regards to the status-quo	No specific evidence was available.		
Comments regarding possible harms	Implicit inclusion systems make efforts to include health technology assessment to limit the inclusion of drugs.	The problem tends to be resolved via health technology assessment HTA and institutional consolidation	No specific evidence was available.

Source: authors

Option 3 - Funding via voluntary insurance

This alternative implies that the funds used to finance health services are raised through contributions by individuals who voluntarily insure themselves. While usually associated with private insurance, it could either be primary insurance (on which the health system financing is based) or supplemental insurance (those that provide additional coverage to primary insurance, such as copayments or medication)³⁸. As in the case of mandatory insurance, contributions can likewise be adjusted for individual or community risk.

The voluntary nature of this mechanism makes it vulnerable to the problem of adverse selection (those with increased risk of adverse events have more incentives to enroll), which, especially in the context of a system which is financed predominantly by such contributions, can lead to population segmentation of the into different risk groups, making it difficult to finance premiums for those at greatest risk (which could end up uninsured).

The U.S. is the most typical example of countries that finance their system predominantly through voluntary private insurance, while in general in other developed countries voluntary insurance plays a complementary role³².

In Chile, voluntary private insurance also plays a complementary role, according to a study carried out by the Superintendence of Health³⁹. These policies are generally focused on collective agreements requested by an employer or other entity (eg, unions), in order to take advantage of the risk pooling and lower premiums obtained with regards to individual health insurance. Another form of voluntary insurance is catastrophic health insurance that address high-cost accidents, and illnesses. Indemnity health insurance plans, which pay the amount insured upon diagnosis of the diseases included in the policy, are also available, without deductibles. The market for supplementary insurance, both in individual and grupo format, is highly concentrated in Chile, with 58% of the market share of the individual plans and 48.6% of the market share of the group plans being held by the three largest insurance companies³⁹.

- **Results of systematic reviews**

We identified no systematic reviews that addressed financing of high cost of orphan drugs via voluntary insurance.

- **Existing evidence**

Although the available evidence is limited on this option, a summary of the findings are presented in Table 6.

Table 6. Summary of the evidence found relevant to Option 3 - Funding through voluntary insurance

Category finds	Summary of findings
Benefits	<ul style="list-style-type: none"> • Many developed countries use additional private insurance ⁵ to fill gaps in its public financing system and pay for the existing increased demand for health services⁴⁰. • Private insurance provides an opportunity for the employee, who is able to afford it, to contribute directly to their healthcare costs and captures private funds to finance the growing demand for health services⁴⁰. • When public funding is low, private insurance can serve as a transition, building capacity ⁶ in the healthcare sector, providing coverage for certain segments of the population, therefore allowing limited tax returns to be targeted towards vulnerable groups⁴⁰. • Finally, experiences in Germany, Holland and Sweden show how in countries that move towards universal coverage, the role of private insurance can change⁴¹.
Potential harms	<ul style="list-style-type: none"> • The voluntary nature of this type of insurance is the greatest source of problems in terms of market segmentation and competition through risk selection and not necessarily via efficiency which therefore generates inequalities in access to this type of insurance (and the care they provide)³¹. • The coverage gaps that are generated also threaten public finances, as populations not covered eventually require publicly funded programs³¹. • Private insurance tends to be individualistic and devoid of solidarity⁷. Health authorities must use policies, incentives and regulations to encourage the goal of ensuring equitable access⁴⁰. • Institutions recognized to be guarantors of fairness are often weak in developing countries. Establishing a monitoring role of private insurers should lie within the health authority⁴⁰. • Private funding for orphan drugs faces the dilemma that the insured pays their premium during the period they are at risk²⁵ Since most

⁵ Called this way because they supplement public funding coverage.

⁶ It refers to the generation of infrastructure to meet the financing gap and pave the way to universal coverage.

⁷ Insurance in which the population is segmented by individual risk and a tendency towards risk sharing does not exist.

	<p>of these diseases are congenital, the insuree loses the incentive to contribute when they have born all their children because the risk disappears. This possible lack of continuity associated with this type of insurance is the main threat to the viability of this option for financing orphan drugs.</p>
<p>Cost and cost-effectiveness with regards to the status quo</p>	<p>Developed countries that rely on private insurance to cover large segments of the population or those countries in which private insurance plays a prominent role must intervene significantly in order to ensure consumers protection and equity⁴¹</p>
<p>Uncertainty regarding possible harms</p>	<p>No high-income country uses private insurance as the primary method for ensuring poor or high risk populations. Even in the U.S., which has the largest private insurance market in the world, the poor and elderly are covered by way of large publicly-funded programs (Medicare, Medicaid)⁴⁰. Comment: this limits the possibility of evaluating the consequences of funding based solely on private insurance.</p>
<p>Main elements of the policy choice if it has been implemented elsewhere</p>	<p>No literature on its use to fund specific rare diseases was found.</p>

Source: authors

Option 4 - Financing via innovative mechanisms

This option aggregates all the options not mentioned in the above alternatives. The 2010 World Health Report²⁵ emphasizes the importance of finding unconventional financing mechanisms especially while looking to achieve universal coverage. The report mentions, among those options with a high fundraising capacity: a) levying a special tax for large profitable companies (taxes already implemented: mining companies in Australia, mobile phone companies in Gabon, pharmaceutical companies in Pakistan), and b) a tax on currency transactions. The Report also mentions other options with an average fundraising capacity such as diaspora bonds, taxes on financial transactions, donations through mobile phones bills and specific taxes on harmful products (such as tobacco, alcohol and unhealthy food).

Hughes et al. (2005)⁴² mention risk-sharing agreements and '*no cure, no pay*' approaches in the specific case of funding high-cost drugs. The first would involve a negotiation between health authorities and the pharmaceutical company based on the projected health gains to be achieved with treatment, and a drug price reduction (up to a pre-set cost-effectiveness threshold) if such gains are not met. The second format is similar, except that in the absence of the expected results, the pharmaceutical company would refund the amount paid by the health authorities.

In Chile, an example of marked taxes used to finance health programs is Law No. 19,888 which established the temporary increase (which later became permanent) of the VAT in order to finance the 2005 health reform. Another example of an innovative financing mechanism in the health sector in Chile is the Telethon Foundation, a private, nonprofit organization created in 1986 to channel and distribute the proceeds from their campaigns (usually annual) towards the rehabilitation of disabled people. Likewise, outside the field of health, the Ministry of Finance's Law No. 20,026 approved in 2005, established a specific tax on mining activities (known as a mining royalty) that, although not specifically mentioned in the Law itself, would be used to finance research and development (R & D).

- **Results of systematic reviews**

No systematic reviews that addressed financing of high cost of orphan drugs through the use of innovative financing mechanisms were identified.

- **Existing evidence**

Existing evidence on innovative financing mechanisms comes from its application in other areas, some of which are unrelated to health. The effects observed in other areas can however be used to predict the effects they would have if applied towards funding orphan drugs. In this sense, the 2010 World Health Report²⁵ serves as a guide. Table 8 and 9 summarize the most relevant evidence findings according to the innovative mechanism analyzed.

Table 8: Summary of the evidence found relevant to Option 4 - Financing through innovative mechanisms. In particular, we analyze the special tax on large profitable companies, the tax on foreign currency transactions and diaspora bonds

Category Findings	Summary of findings for each innovative financing mechanism		
	Special levy on large and profitable companies	Levy on currency transactions	Diaspora Bonds ⁸⁴³⁴⁴
Benefits	<ul style="list-style-type: none"> • Has the potential to raise large sums of money²⁵. • Flows may be predicted according to the company's financial statements. • The large sums of money collected²⁵ provide buyers with bargaining power vis-a-vis the suppliers. • Since it is a dedicated tax (exclusive for the specific program cited in the tax), it does not compete with other health programs nor with other sectors³¹ 	<ul style="list-style-type: none"> • Has demonstrated the greatest capacity to raise funds^{45 46}. • The large sums of money collected provide buyers with bargaining power vis-a-vis the suppliers²⁵ • It has the potential to reduce speculation and help stabilize the exchange rate⁴⁷. • Since it is a dedicated tax (exclusive of the specific program cited in the tax), it does not compete with other health programs nor with other sectors³¹. • Since Chile is a country with a highly globalized economy, it has good fundraising potential²⁵. 	<ul style="list-style-type: none"> • They have an intermediate fundraising capacity²⁵. • It allows money to be delivered quickly and not deferred in time²⁵. • It appears as a fundraising option in countries where, for lack of confidence, obtain private financing through traditional instruments is difficult⁴⁴. • Since these bonds are dedicated (exclusive for a specific program), they do not compete with other health programs nor with other sectors³¹.
Potential harms	<p>No harms has been described to date. However, it is expected that this policy will not be well received by companies, which might jeopardize the feasibility of its implementation. If implemented, the possibility that it might create distortions in investment⁴⁸ exists.</p>	<p>No harms has been described to date. However, from the standpoint of economic efficiency, can increase costs and decrease the volume of transactions, generating a distortion in intertemporal preferences investment and location (if different countries have different policies on this)⁴⁷.</p>	<p>No harms has been described to date. This option however does pose a risk to investors since debt service is done in local currency and not US\$ or Euros⁴⁴.</p>
Main elements of the policy choice if it has been implemented	<p>Some examples of companies on which this tax has been used: mining (Australia), mobile phones (Gabon), pharmaceutical</p>	<p>It has not been formally implemented, but it is described that coordination with other financial markets would be required if implementation on a larger scale is wanted²⁵.</p>	<p>The governments of 8 countries have pledged funds to pay these bonds to the "International Financing Facility for Vaccines",</p>

⁸ Diaspora bonds are bonds that raise resources from the Diaspora (dispersed community) living in a foreign country.

elsewhere	(Pakistan), and airline tickets (Unitaid) ⁴⁹⁵⁰ . The latter, since 2006 has collected nearly U.S. \$ 1.3 billion that have financed the purchase of drugs for HIV / AIDS, tuberculosis and malaria in 93 countries ⁵¹ .		associated with the GAVI Alliance. They have also been used in India, Israel and Sri Lanka, not only restricted to health ²⁵ .
Comments in relation to cost and cost-effectiveness with regards to the status quo	Since a tax with these characteristics used to finance orphan drugs currently does not exist, the most profitable industries in Chile (such as private banking) would have to be identified and the impact that the tax might have on them and their customers, evaluated.	If this measure impacts strongly on the value of the dollar in the country, it could have important undesirable socio-economic effects, which could detract from the benefits accrued through this form of fundraising.	No empirical data exists, but it is anticipated that costs may exist according to capital market variations, and this may, in turn, have a positive or negative effects according to market fluctuations.
Uncertainty regarding possible harms	This option could discourage private enterprise if it is a very high tax or if it levied on an unstable industry, this should be taken into consideration when choosing the market to intervene and the magnitude of the rate.	<ul style="list-style-type: none"> • This option could be detrimental to importers and could increase the price of imported goods, given the eventual rise of the dollar. • Should be evaluated according to the free trade agreements that Chile has subscribed in order to comply with clauses relating to the financial market. 	<ul style="list-style-type: none"> • If bond payments do not purport additional funds, they may not mean a real increase in funding. • If the Government can not pay off the bonds this could harm buyers. • There is a risk that bond prices may vary over time, resulting in that a transaction made at a particular time that was not the most appropriate ends up costing the government more at payment time.

Source: authors

Table 9: Summary of the evidence found relevant to Option 4 - Financing through innovative mechanisms. In particular, we analyze the financial transactions tax, donations through mobile phones, and the excise tax alcohol / tobacco/ unhealth foods

Category finds	Summary of findings for each innovative financing mechanism		
	Financial transaction tax	Mobile phone voluntary solidarity contribution	Alcohol / Tobacco/Unhealthy Foods excise tax
Benefits	<ul style="list-style-type: none"> • It has an intermediate potential fundraising²⁵. • In countries with high banking activity, such as Chile, has a high probability of raising a stable and sustained²⁵. • They have the potential to reduce speculation⁴⁷. • Being a strong funding source (unique for a specific program), it competes with other health programs, and other sectors³¹. 	<ul style="list-style-type: none"> • Has proven ability to raise funds²⁵. • Have low relative costs and sustainability management. • It can be deployed quickly²⁵. • Being a strong funding source (unique for a specific program), it competes with other health programs, and other sectors³¹. 	<ul style="list-style-type: none"> • Pigovian Taxes⁹ have the potential to eliminate distortions associated with externalities⁵². • There is ample margin to levy them without greatly affecting income²⁵. • These taxes at the same time reduce the consumption of these harmful factors harmful factors, having a positive impact on the population, the economy and health system expenditures²⁵. • Since it is a dedicated tax (exclusive for the specific program cited in the tax), it does not compete with other health programs nor with other sectors³¹.
Potential harms	No harms has been described to date. It can however create investment distortions ⁴⁷ .	No harms has been described to date.	No harms has been described to date. However, this type of dedicated, marked duties are usually met with detractors (amongst industry and consumers) that threaten the feasibility of its implementation ⁴⁴ .
Cost and cost-effectiveness with regards to the status quo	May discourage financial exchanges, due to either the increased costs for the banks or by	The cost of this measure is low and it is possible to raise	The implementation cost is low and the benefits; economic, social and

⁹ These are that taxes that are levied on market activities that have negative externalities.

	having them transferred to customers with the resulting price increase. Proceeds may therefore not be as large as expected ⁴⁷ .	considerable ²⁵ ..	sanitation-wise are very high ²⁵ .
Uncertainty regarding possible harms	This option could be detrimental to small and medium enterprises for which these taxes imply a greater burden in comparison to larger companies. In addition, if it affects transactions carried out by people, they may also be affected by increased prices.	Depends critically on the "mindset" people have towards donations, so this option could be unstable and difficult to project.	No harms has been described to date.
Main elements of the policy choice if it has been implemented elsewhere	This option was implemented in Brazil in the nineties but was replaced by a tax on capital flows. In Gabon, a transaction tax on currency transactions was applied.	The global market for telephone services is U.S. \$ 750 billion, so that taking only 1% would imply collecting a sizeable amount of money, especially important in low-and middle-income countries. Implementation and operation costs may run between 1 to 3% of the amount collected ⁵³ .	During 1985-86 alcohol prices were raised by 40% in Moscow. This was followed by a sharp reduction in consumption, hospitalizations and alcohol related deaths. However, a few years later several of the findings were reversed ⁵⁴ . If a tax of at least 40% was levied on the price of alcohol, this could generate a significant increase in revenue as well as reduce the adverse effects of consumption ⁵⁵ .
Stakeholder Vision and experience	There seems to be more opposition to this tax by interest groups ⁵⁶ .	Since it is a voluntary contribution, it is generally well perceived by interest groups.	The tobacco tax increase is driven by the "WHO Framework Convention on Tobacco Control" ⁵⁷ . On the other hand, groups that advocate individual liberty and the tobacco companies would be the main opponents.

Source: authors

Finally, it should be noted that there is a significant amount of collateral evidence that shows that worldwide there is a set of regulatory systems for the pharmaceutical industry, which for orphan drugs constitutes the general context under which they are produced, distributed and consumed. We refer specifically to the regulatory schemes present in European countries, the countries in the what is know as the Australasian region³⁵ and in the United States, although the latter has a relatively low regulatory intensity.

These regulatory systems, in general, are based on the objectives of cost control, quality assurance and rational access to medicines posed by governments and health ministries. They rely on measures aimed, on

the one hand, at demand, such as fees and co-payments and secondly, at supply, with measures such as the obligation to provide relevant information and base treatment on clinical guidelines, as well as the creation of generic drugs lists and budgetary controls (present in primary care in the UK). The industry is also subject to economic regulation; ranging from price control systems to the application of reference pricing systems, the profit control in the price (as in United Kingdom) as well as through the imposition of cost-effectiveness assessments by public agencies such as England's NICE.

CONSIDERATIONS OF THE IMPLEMENTATION

A first consideration to keep in mind is that there is an executive bill being introduced to Congress that must therefore be debated. This bill must comply with all the steps and procedures a legislative initiative goes through from the moment it is introduced in Congress until it is approved and sent to the President.⁵⁸

The legislative branch in Chile aims to contribute to the passing of laws, either by approving or rejecting bills proposed by the Presidency or Congress. The exercise of this function is necessarily carried out through both houses of Congress, the Senate and the House of Representatives, which are the only institutions invested with the right to promote legislative initiatives. Both chambers, in turn, have standing committees that inform the bills so that decisions can be made in the House of Representatives and Senate. During this period, both the executive and legislative branches can make amendments to the bills that can modify either the form or the subject of the project under study. There is also an instance called the Mixed Commission, composed of senators and representatives, that provides solutions to disputes that may arise between the chambers over a certain text. Their proposals are later debated by both chambers.

This brief outline of the legislative process permits a glimpse of the large number of stages a bill must pass through before becoming a law, as well as the numerous modifications that can occur along the way. The high number of legislative initiatives pending in Congress must also be noted.

A second consideration is the translation of the options presented in this brief into the form or presentation they would most likely adopt within the Chilean health system. The interpretation in this regard is shown in Table 10¹⁰.

Table 10: Chilean adaptation of policy options

Financing Options	Translation to the reality of Chile
Option 1: Financing via general taxation	Fiscal funding by way of the MINSAL's budget. Subject to: <ul style="list-style-type: none"> - Mandatory coverage of FONASA beneficiaries subject to rational use - Creation of a national risk pool - Price negotiations and TRIPS flexibilizations - Venture agreements with industry - Price regulation
Option 2: Financing via mandatory insurance	Financing under mandatory pension contribution. Subject to: <ul style="list-style-type: none"> - Mandatory coverage in health plans subject to rational use - Creating a shared risk pool for medicines or for catastrophic events - Price regulation
Option 3: Funding via voluntary insurance	Financing through premiums paid for supplemental health insurance
Option 4: Funding via innovative mechanisms	Financing through a specific tax flagged for high-cost orphan drugs.

Source: authors

¹⁰ The adaptation to the Chilean context was made based on the expert opinion of the EVIPNet Chile team.

Finally, Table 11 presents some implementation considerations that should be contemplated on different levels; system, patient / individual, provider and organization, based on the expert opinions of the members of EVIPNet Chile.

Table 11: Deployment considerations for the system, patient / individual, provider and organization

Levels	Option 1 Financing through general taxation	Option 2 Financing through mandatory insurance	Option 3 Financing through voluntary insurance	Option 4 Financing through innovative mechanisms
System	It implies that this health problem is, recognized as a public good and is therefore funded via general taxes regardless of the individual being on private or public health insurance.(ISAPRE or FONASA) ¹¹	It implies that high cost orphan drugs are included in the mandatory health services delivered by both FONASA and Isapres.	In Chile there are many insurance ⁴⁰ companies that deliver supplementary health insurance.	It implies generating a specific tax earmarked for high cost orphan drugs. It would be similar to the Reserved Copper Law (No. 13 196) which grants 10% of all sales made abroad by Codelco (National Copper Corporation) to the armed forces to finance weapons purchases. ⁵⁹
Organization	In general, high-cost orphan drugs have no substitutes, they cannot be replaced by another product and therefore constitute the only alternative for the patient. In this context, new forms of purchasing must be developed to obtain products at a lower price.			
Provider	One problem that needs to be addressed is that lack of specific health policies for rare diseases and lack of experience result in delayed diagnoses and poor access to medical care, with all the adverse consequences that this entails.			
Patient / Individual	It will certainly be necessary to rationalize the use of resources and therefore only give high cost orphan drugs to those who would achieve significant benefits in quality of life and survival.		This option is different from previous ones in the aspect mentioned at this point. In this alternative, access to treatment depends largely on whether the individual is insured against the event.	It will certainly be necessary to rationalize the use of resources and therefore only give high cost orphan drugs to those who would achieve significant benefits in quality of life and survival.

Source: authors

Chile does not start from zero with respect to ways of funding its health system, In fact, Chile has gone through different phases. After running a state- funded national health service for 30 years, it opted in 2000 for a mixed public/ private approach to health insurance, guaranteeing universal access to quality treatment for a set of explicitly defined conditions.. The decision of which funding mechanism is appropriate for high-

¹¹ Similar to the model implemented for the National Immunization Program.

cost orphan drugs is influenced not only by the evidence that emerges from the review of the best available data described in this document, but also from that experience.

After an exhaustive search no systematic reviews were found and very few studies on the topic were uncovered, so the logic of the best available evidence was used. This is probably one of the main challenges that we detected: there is a need for more research in this area.

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